



## Newborn Screening ACT Sheet

### Elevated C3 Acylcarnitine Propionic Acidemia and Methylmalonic Acidemia

**Differential Diagnosis:** Propionic acidemia (PROP or PA); Methylmalonic acidemias (MMA), including defects in B12 synthesis and transport; maternal severe B12 deficiency.

**Condition Description:** PROP is caused by a defect in propionyl-CoA carboxylase, which converts propionyl-CoA to methylmalonyl-CoA; MMA results from a defect in methylmalonyl-CoA mutase, which converts methylmalonyl-CoA to succinyl-CoA, or from lack of the required B12 cofactor for methylmalonyl-CoA mutase (cobalamin A, B, C, D, and F).

#### Medical Emergency: Take the Following IMMEDIATE Actions

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Consult with pediatric metabolic specialist. (See attached list.)
- Evaluate the newborn; check urine for ketones.
- If elevated or infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport immediately to tertiary center with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Initial testing: plasma amino acids, plasma acylcarnitine profile, and urine organic acids.
- Repeat newborn screen if second screen has not been done.
- Educate family about signs, symptoms and need for urgent treatment of hyperammonemia and metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea).
- Report findings to newborn screening program.

**Diagnostic Evaluation:** Plasma acylcarnitine confirms the increased C3. Blood amino acid analysis may show increased glycine. Urine organic acid analysis will demonstrate increased metabolites characteristic of propionic acidemia or increased methylmalonic acid characteristic of methylmalonic acidemia. Plasma total homocysteine will be elevated in the cobalamin C, D, and F deficiencies. Serum vitamin B12 may be elevated in the cobalamin disorders.

**Clinical Considerations:** Patients with PROP and severe cases of MMA typically present in the neonate with metabolic ketoacidosis, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Long-term complications are common; early treatment may be lifesaving, and continued treatment may be beneficial.

#### Additional Information:

##### Emergency Treatment Protocol

**PROP** <http://www.childrenshospital.org/newenglandconsortium/NBS/PAA.html>

**MMA** <http://www.childrenshospital.org/newenglandconsortium/NBS/MA.html>

##### Gene Tests

**PROP** <http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=NexQvDbtfnPSK&gry=&fnc=y&fw=SoH9&filename=/profiles/oa-overview/index.html>

**MMA** <http://www.genetests.org/servlet/access?db=geneclinics>

<http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=NexQvDbtfnPSK&gry=&fnc=y&fw=Qtlb&filename=/profiles/mma/index.html>

##### Genetics Home Reference

**PROP** <http://ghr.nlm.nih.gov/condition=propionicacidemia>

**MMA** <http://ghr.nlm.nih.gov/condition=methylmalonicacidemia>

##### STAR G FELSI

<http://www.newbornscreening.info/Pro/facts.html>

<http://www.newbornscreening.info/Parents/facts.html>



## Newborn Screening FACT Sheet

### Propionic Acidemia (PROP or PA)

#### What is PROP?

PROP is a type of organic acid disorder. People with PROP can't break down certain amino acids from food.

#### What Causes PROP?

Enzymes help start chemical reactions in the body. PROP happens when an enzyme called "propionyl CoA carboxylase" (PCC) is missing or not working. This enzyme changes certain amino acids so the body can use them. Glycine and propionic acid build up in the blood and cause problems when PCC doesn't work.

#### What Symptoms or Problems Occur with PROP?

*[Symptoms are something out of the ordinary that a parent notices.]*

PROP causes periods of illness called Metabolic Crises. Early symptoms of a Metabolic Crisis are:

- poor appetite
- low muscle tone (floppy muscles and joints)
- too much sleepiness or lack of energy
- vomiting

If a Metabolic Crisis isn't treated, a child with PROP can develop:

- breathing problems
- seizures
- swelling of the brain
- stroke
- coma, sometimes leading to death

Later problems can include:

- mental retardation
- low ability to fight illnesses
- osteoporosis (weak bones)
- inflamed pancreas gland
- skin rashes
- poor growth

#### What is the Treatment for PROP?

The following treatments are often used for children with PROP:

#### 1. Low-protein diet, medical foods and medical

**formula** – The best treatment for PROP is a diet low in protein. Most of the low-protein food will be carbohydrates (such as bread, cereal, noodles, fruits, vegetables). High-protein foods that should be limited or not eaten at all include:

- milk and milk products
- meat and poultry
- fish
- eggs
- dried beans and peas
- nuts and peanut butter

The doctor may prescribe a special medical formula with the right amount of protein. There are also medical foods available for people with PROP.

**2. Do not go a long time without food** – Some babies and young children can have a Metabolic Crisis if they don't eat often enough. They shouldn't go without food for more than 4 to 6 hours. Some children may need to eat even more often. Your dietitian can give you ideas for suitable snacks. Dietitians know what are the right foods to eat.

**3. Medication** – The doctor may prescribe L-carnitine for your child. This is safe and natural and helps the body make energy.

#### Things to Remember

Even minor illness such as a cold or flu can cause a Metabolic Crisis. Call your doctor right away when your child has any of the following:

- loss of appetite
- vomiting
- diarrhea
- infection or illness
- fever

Many children with PROP must be treated in the hospital during illness to avoid serious health problems.



## Newborn Screening FACT Sheet

### Methylmalonic Acidemia (MMA)

#### What is MMA?

MMA is an organic acid disorder. People with MMA can't break down and use certain amino acids and fatty acids from the food they eat.

#### What Causes MMA?

Enzymes help start chemical reactions in the body. Special enzymes break down certain amino acids and fatty acids from the protein in food so that the body can use them. MMA happens when one of these special enzymes is missing or not working. There are a number of different kinds of MMA. Some improve with Vitamin B12 injections (Vitamin B12-responsive), and some do not (Vitamin B12 non-responsive).

#### What Symptoms or Problems Occur with MMA?

*[Symptoms are something out of the ordinary that a parent notices.]*

MMA causes periods of illness called Metabolic Crises. Some of the first symptoms of a Metabolic Crisis are:

- poor appetite
- low muscle tone (floppy arms and legs)
- vomiting
- too much sleepiness or lack of energy

If a Metabolic Crisis is not treated, a child with MMA can develop:

- breathing problems
- seizures
- stroke
- coma, sometimes leading to death

Later problems can include:

- mental retardation
- low ability to fight illnesses
- poor growth
- muscle spasms
- kidney problems
- skin rashes
- tight muscles
- brittle bones

#### What is the Treatment for MMA?

**1. Medication** – Vitamin B12 shots are the main treatment for Vitamin B12-responsive MMA, caused by not enough cobalamin A & B. Vitamin B12 helps most children with the first form (A). It helps about close to half of children with second form (B). Your child's doctor may prescribe L-carnitine. This is safe and natural and helps body cells make energy. Antibiotics may help.

**2. Low-protein diet, medical foods and medical formula** – Foods high in protein should be limited or not eaten at all. They include:

- milk and milk products
- meat and poultry
- fish
- eggs
- dried beans and peas
- nuts and peanut butter

The doctor may give your child a special medical formula. A dietitian will tell you what kind of formula is best and how much to use. Dietitians know what are the right formulas and foods to eat.

#### Things to Remember

Even minor illness can lead to a Metabolic Crisis in children with MMA. Call your doctor right away when your child has any of the following:

- loss of appetite
- vomiting
- diarrhea
- infection or illness
- fever

Children need extra fluids and starchy food (such as bread, rice, cereal, noodles) when they're sick in order to prevent a Metabolic Crisis. During illness, you should limit protein and give your child starchy foods and fluids. Sick children with MMA may need to be treated in the hospital to avoid serious health problems.