

## BC Newborn Screening Program

## Information Sheet

### Isovaleric Acidemia (IVA) – Organic Acid Disorder

#### What are organic acid disorders?

Organic acid disorders (also sometimes called organic acidemias) are a class of inherited metabolic disorders that occur when the body cannot break certain components of proteins (for example, branched-chain amino acids) and other substances. This leads to an accumulation of harmful substances in the blood and urine, which can cause serious health problems.

#### What is isovaleric acidemia?

In the body, the breakdown of protein produces leucine and other amino acids. Leucine is further processed into a substance called isovaleric acid. An enzyme called isovaleryl-CoA dehydrogenase is then responsible for breaking down isovaleric acid. Isovaleric Acidemia (IVA) occurs when the isovaleryl-CoA dehydrogenase enzyme is not working well or is missing. This leads to elevated levels of isovaleric acid and other harmful substances in the blood.

#### What is its incidence?

Isovaleric acidemia is a rare disease that affects about 1 in every 100,000 to 200,000 babies born in BC.

#### What causes the disease?

Mutations in the gene for isovaleryl-CoA dehydrogenase results in enzyme that is not working well or is deficient.

#### What are the clinical features of the disease?

Although babies with isovaleric acidemia are normal at birth, without treatment they may have an episode of metabolic crisis with encephalopathy, which can progress to coma and death. The first episode usually occurs within the first few days of life and can be triggered by events such as an illness or a fever. Other symptoms include lethargy, failure to thrive, vomiting, difficulty staying warm, seizures, and an odour described as smelling like sweaty feet. Increased amounts of ammonia and acidic substances may be found in the blood (hyperammonemia and acidemia). In the long term, the child may have mental retardation even if they are treated. As the child grows older, the risk of crises and symptoms decrease.

There is also a chronic/intermittent form of IVA with a later presentation, at about one year of age or later. IVA is variable and there may be individuals with the disorder who are mildly affected or are asymptomatic.

#### How is the diagnosis confirmed?

The diagnosis of IVA is confirmed by finding specific urine organic acid and plasma acylcarnitine profiles. Diagnostic testing is arranged by specialists at BC Children's Hospital.

### **What is the treatment of the disease?**

The mainstay of treatment is to prevent fasting, especially when the child is ill. In an acute symptomatic episode, IV glucose and fluids can be given, along with other medications that can help the body to get rid of harmful substances and to decrease the level of acid in the blood.

A low protein diet is often recommended in children with IVA. A special medical formula may also be suggested. Supplementation with carnitine, glycine, and antibiotics may also be considered.

Treatment can prevent metabolic crises and their sequelae. Treatment is coordinated by specialists at BC Children's Hospital.

### **What is the outcome of treatment?**

If treatment is able to prevent episodes of metabolic crisis, children with isovaleric acidemia have a good prognosis. However, response to treatment and therefore the outcome is variable.

### **Can a family have more than one child with IVA?**

Isovaleric acidemia is inherited as an autosomal recessive disorder. The parents of a child who has isovaleric acidemia are assumed to be carriers for the disorder and have a 1 in 4 (25%) chance, in each pregnancy, of having another child with the disorder. Prenatal testing for isovaleric acidemia can be done as early as 10-12 weeks of pregnancy.

Genetic counselling to discuss the benefits of prenatal testing options in more detail is recommended.

Unaffected siblings of a child with isovaleric acidemia have a 2/3 chance of being carriers. Carriers are healthy and do not have symptoms of isovaleric acidemia.

### **Resources**

<http://www.newbornscreening.info/Parents/organicacididorders/IVA.html>  
<http://www.oanews.org/>  
<http://www.geneclinics.org>

Revised November 2009