Isovaleric acidemia
(IVA; Isovaleryl-CoA dehydrogenase deficiency; IVD deficiency;
Isovaleryl-CoA carboxylase deficiency)

Technical advisory committee report

Treatment
Responds well to treatment which prevents otherwise high mortality or developmental delay and mental retardation.

Available Technology – Screen
Screening is quite effective at identifying affected infants (good sensitivity).

However, screening also identifies some infants with a mild form of IVA who may not require treatment. And, screening may also identify 2 MBDH (2-methylbutryryl-CoA dehydrogenase) deficiency, a mild condition that is relatively frequent among Hmong populations and has no specific treatment and GA-2 (glutaric academia type II, also known as multiple acyl-CoA dehydrogenase deficiency). Infants on some common antibiotics may have false positive results.

Concordance with Treatment and Screening Technology criteria:
Most concordance

Estimated frequency
1 in 102,000 births

Disorder family: organic acidemia

Primary screening analyte: C5 (Schulze, Lindner et al. 2003)

Secondary screening analytes: C5/C2 (Schulze, Lindner et al. 2003)

Variability in clinical presentation:

Three clinically different forms have been described:

With the acute form, “the infants are well at birth, but within a few days (usually 3 to 6, but it may be as early as the first day of life or as late as 14 days of age) begin to refuse feeding and to vomit, becoming dehydrated, listless, and lethargic. They are often hypothermic and may have tremors or twitching and convulsions.” “The typical progression is that patients become cyanotic and lapse into a coma followed by death.” (Sweetman and Williams 2001)

“an acute neonatal form characterized by overwhelming illness with coma, resulting in death in over 60% of infants” (Berry, Yudkoff et al. 1988)

With the chronic form, “The first episode of illness usually occurs during the first year of life. Episodes often follow upper respiratory infections or increased intake of protein-rich foods. The recurrent episodes typically involve vomiting, lethargy progressing to coma, acidosis with ketonuria, and the characteristic “odor of sweaty feet’ due to elevated Isovaleric acid levels.” (Sweetman and Williams 2001)

New mild phenotype, “One unexpected finding to arise from newborn screening studies is the identification of individuals with only mild elevations of isovaleryl-CoA related metabolites in plasma and urine, orders of magnitude lower than in the classic forms of IVA, and apparently only partial reduction in IVD activity.” (Vockley and Ensenauer 2006)
Burden if untreated:

“Without appropriate treatment, Isovaleric acidemia is a highly lethal disease” (Tanaka 1990)

“Most patients with chronic intermittent Isovaleric acidemia have normal psychomotor development, but some have developmental delay and mild or even severe mental retardation.” (Sweetman and Williams 2001)

Efficacy of treatment/benefits of early intervention:

“If detected early and treated properly, patients with Isovaleric acidemia can achieve normal development.” (Tanaka 1990)

“Early diagnosis and treatment with a protein restricted diet and supplementation with carnitine and glycine are effective in promoting normal development in severely affected individuals.” (Vockley and Ensenauer 2006)

Unintended consequences of screening:

“It is clear that the newborn screening patients who carry the common mutation either in a homozygous or compound heterozygous state and their sibs skew the spectrum of IVA with more than half of individuals representing a new mild phenotype and potentially remaining asymptomatic” (Vockley and Ensenauer 2006)

“the incidence of Isovaleric aciduria was significantly higher in the screening population than in clinically detected cases” (Dionisi-Vici, Deodato et al. 2006)

Miscellaneous:

Using data from a MS/MS screened population of 164,000 newborns. A secondary screen for C5/C2 was not used: “Although there were 35 infants flagged for C5 (28 of the infants were NICU/VLBW infants), we were not aware of any cases of IVA or 2MBCD deficiency in the population screened” (Zytkovicz, Fitzgerald et al. 2001)

Bibliography


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Isovaleric Acidemia
(IVA)

What is IVA?
Enzymes help start chemical reactions in the body. IVA happens when an enzyme called “isovaleryl-CoA dehydrogenase” is missing or not working well. This enzyme helps break down harmful “isovaleric acid.” This acid builds up in the blood and causes problems when a child with IVA eats food with leucine. Leucine is in all foods that have protein (such as meat, beans, peanut butter, milk).

What Causes IVA?
People with IVA have a pair of genes that don’t work as they should. These genes cause the “isovaleryl-CoA dehydrogenase” enzyme to not work well or not be made at all.

What Symptoms or Problems Occur with IVA?
[Symptoms are something out of the ordinary that a parent notices.]
Babies with IVA seem healthy at birth. Symptoms often start between one day and two weeks of age. IVA causes periods of illness called Metabolic Crises. Some of the first signs are:
- poor appetite
- too much sleepiness, low energy
- vomiting
- feeling cold
- “sweaty feet” odor

If a Metabolic Crisis is not treated, a child with IVA may develop:
- breathing problems
- seizures
- strokes
- mental retardation
- coma, sometimes leading to death

The less severe kind of IVA shows up later in childhood. Some problems may include:
- poor growth
- learning difficulties

What is the Treatment for IVA?
Early treatment prevents Metabolic Crises and related problems. Treatment should start as soon as you know your child has IVA. Treatment usually lasts all life long. Treatment often includes:

1. Low-leucine diet, medical foods and formula – Most children need to eat foods low in leucine (such as vegetables and fruit). Special medical foods and formulas are usually part of the diet. You will get a food plan that has the right amount of protein and nutrients to keep your child healthy. Your child should continue a special food plan for life. High-protein foods your child should limit or not eat include:
   - milk and milk products
   - meat and poultry
   - fish
   - eggs
   - dried beans and peas
   - nuts and peanut butter

2. Medications – The doctor may prescribe the amino acid Glycine to help the body get rid of isovaleric acid. This can help prevent Metabolic Crises in children with IVA. L-carnitine may also help some children. This is safe and natural and helps the body make energy. Only use the kind your doctor tells you to use. Do not use any medication or supplement without checking with your doctor.

Things to Remember
Even minor illnesses such as a cold or the 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

Children with IVA need to eat more starchy foods (bread, cereal, rice, noodles) and drink more fluids when they are ill - even if they’re not hungry - or they could have a Metabolic Crisis. They also need to not eat protein foods when they are sick. If they can’t eat, or if they show signs of a Metabolic Crisis, they may need to be treated in the hospital.
Very long-chain acyl-CoA dehydrogenase deficiency
(VLCAD deficiency, VLCADD)

Technical advisory committee report

Treatment
Treatment before onset of symptoms (can be quite early) is highly effective in preventing mortality and morbidity.

Available Technology – Screen
Screening is quite effective at identifying affected infants (good sensitivity).

However, screening also identifies some infants who are only carriers (will not develop disease) and some who have a less severe, later onset form of VLCAD. Differentiating between these can be difficult. Children’s can use DNA testing to help establish the diagnosis and the genotype/phenotype correlation is reported to be good. It is important to keep treating the child until the disease has been confirmed or ruled out.

Other
Minnesota found about 1 baby in 50,000 with this condition – it was more common than expected.

Concordance with Treatment and Screening Technology criteria:
Most concordance

Estimated frequency
1 in 86,000 births

Disorder family: fatty-acid oxidation

Primary screening analyte: C14:1 (Zytkovicz, Fitzgerald et al. 2001)

Secondary screening analytes: C14, C16 (Chace, Kalas et al. 2003)

Variability in clinical presentation:
Three forms with good genotype/phenotype correlation: severe childhood form – hypoglycemia and cardiomyopathy (usually die before age 1), milder childhood form – hypoglycemia (some will die without treatment) and adult form – skeletal muscle degeneration leading to renal failure. (Andresen, Olpin et al. 1999)

Burden if untreated:
“Approximately 50% of patients have died within 2 months of presentation.” (Cox, Souri et al. 1998)

Babies with the severe childhood form and some with the milder childhood form will die without treatment. (Andresen, Olpin et al. 1999)
Efficacy of treatment/benefits of early intervention:

“Although VLCAD is relatively rare, timely and correct diagnosis leads to dramatic recovery, so that detection by newborn screening could prevent the onset of arrhythmias, heart failure, metabolic insufficiency, and death.” (Wood, Magera et al. 2001)

In 8 patients identified by NBS, “during follow-up, mild, common infectious illness did not result in metabolic decompensation in any patient.” (Spiekerkoetter, Sun et al. 2003)

Unintended consequences of screening:

A recent publication reported two babies with positive first screens that had normal subsequent screens. One was diagnosed with VLCAD deficiency and the other is a carrier. (Schymik, Liebig et al. 2006)

Miscellaneous:

From ~1.6 million screened infants: “To date, in both Germany and Massachusetts, no individual with clinically diagnosed VLCADD has been reported who had a normal acylcarnitine profile on newborn screening. This strongly suggests that MS/MS-based screening is highly sensitive.” (Spiekerkoetter, Sun et al. 2003)

“Most likely, a presymptomatic diagnosis would have avoided at least part of a lengthy and intensive prediagnosis hospitalization that had an estimated cost of $400,000.” (Wood, Magera et al. 2001)

Bibliography


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Newborn Screening FACT Sheet

Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)

What is VLCAD?
VLCAD is a type of fatty acid oxidation disorder. People with VLCAD can’t break down certain types of fat into energy for the body.

What Causes VLCAD?
Enzymes help start chemical reactions in the body. VLCAD happens when an enzyme called “very long chain acyl-CoA dehydrogenase” is missing or not working. This enzyme breaks down certain fats from the food we eat into energy. It also breaks down fat already stored in the body.

What Symptoms or Problems Occur with VLCAD?
[Symptoms are something out of the ordinary that a parent notices.]

There are three forms of VLCAD — infant, childhood, and adult. Symptoms can be mild or serious. Infant and childhood types of VLCAD may cause periods of illness called Metabolic Crises, or low blood sugar. Some of the first signs of a Metabolic Crisis are:

- Too much sleepiness
- Behavior changes (such as crying for no reason)
- Irritable mood
- Poor appetite

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

- Breathing problems and seizures
- Coma, sometimes leading to death

Other problems include enlarged liver, enlarged heart, and muscle problems.

What is the Treatment for VLCAD?
The following treatments are often used for children with VLCAD:

1. Do not go a long time without food – Babies and young children with VLCAD should eat often to avoid low blood sugar or a Metabolic Crisis. They shouldn’t go without food for more than 4 to 6 hours. Some babies may need to eat even more often. Children with VLCAD should have a starchy snack (such as bread, cereal, rice) before bed and another during the night. They need another snack first thing in the morning. Raw cornstarch mixed with water, milk, or other drink is a good source of long-lasting energy. Your dietitian can give you ideas for good night-time snacks.

2. Diet – Sometimes your child will need to eat a diet low in fat (lean meat and low-fat dairy foods) and high in carbohydrates (such as bread, noodles, fruits, vegetables). Your dietitian will make any needed diet changes. Dietitians know what are the correct foods to eat.

3. MCT oil and L-carnitine and other supplements – Your doctor may prescribe MCT oil. This special oil has medium chain fatty acids that can be used in small amounts for energy. Sometimes the doctor will prescribe L-carnitine. This is safe and natural and helps the body make energy.

Things to Remember
Always call your doctor when your child has any of the following:

- Poor appetite
- Too much sleepiness
- Vomiting
- Diarrhea
- An infection
- A fever
- Continued muscle pain or weakness
- Reddish-brown color to the urine

Children with VLCAD need to eat extra starchy food (such as bread, cereal, rice) and drink more fluids during any illness. When they become sick, they often need to be treated in the hospital to prevent serious health problems.
Long-chain L-3-OH acyl-CoA dehydrogenase deficiency
(Isolated long-chain L-3-hydroxy-acyl-CoA dehydrogenase deficiency; LCHAD)

Technical advisory committee report

Treatment
Early identification and treatment is effective in preventing mortality, which is otherwise high. However some will still have episodes of metabolic decompensation but not developmental delay or mental retardation.

Available Technology – Screen
Overlap between test results in the normal population and the affected group makes setting cutoff levels challenging. If the cutoff is too high, affected infants will be missed; if it’s too low there will be many false positives (many will be carriers). Also, the screening test does not differentiate between LCHAD deficiency and a similar, but less treatable condition: trifunctional protein deficiency. DNA testing can aid diagnostic differentiation between the two conditions. Differential diagnosis is established by skin biopsy and fibroblast studies. This can be time consuming but not clinically threatening since treatment is the same for both conditions.

Other
Some mothers carrying fetuses with LCHAD deficiency develop severe liver disease (acute fatty liver of pregnancy) or HELLP syndrome (hemolysis, elevated liver function tests, and low platelets)

Concordance with Treatment and Screening Technology criteria:
Most concordance

Estimated frequency
1 in 120,000 births

Disorder family: fatty-acid oxidation

Primary screening analyte: C16OH (Zytkovicz, Fitzgerald et al. 2001; Chace, Kalas et al. 2003)

Secondary screening analytes: C18:1OH, C18OH, C16, C14, C14:1 (Chace, Kalas et al. 2003)

Variability in clinical presentation:
~1/4 of patients present with a chronic form (liver disease, failure to thrive, feeding difficulties and/or hypotonia)
~3/4 of patients present with acute metabolic crisis (hypoketotic hypoglycemia) – 82% of these exhibited some of the chronic form’s symptoms prior to crisis so there may not be a difference between the groups other than the event that triggered the metabolic crisis. (den Boer, Wanders et al. 2002)

Burden if untreated:
38% of fifty patients died before or within 3 months after diagnosis. Ninety-four percent of survivors “were reported to be generally ‘in good condition’. However, morbidity in this group is still high, with recurrent metabolic crises and other clinical problems.” (den Boer, Wanders et al. 2002)
“About half the patients died, either from the first episode or with progressive disease ending in cardiorespiratory failure.” (Roe and Ding 2001)

**Efficacy of treatment/benefits of early intervention:**

No patient in den Boer study died during follow-up (den Boer, Wanders et al. 2002)

“Few patients treated prospectively with long-term outcome assessment have been reported. 30% continue to have episodes of metabolic decompensation.” (2005)

**Unintended consequences of screening:**

The same metabolites are elevated in babies with trifunctional protein deficiency. Differential diagnosis can be made by skin biopsy and fibroblast studies. (Matern, Strauss et al. 1999; Rinaldo, Matern et al. 2002)

**Miscellaneous:**

DNA studies can help determine LCHAD deficiency because about 60 percent of alleles in patients are the E474Q mutation. (Rinaldo, Matern et al. 2002)

Mothers carrying fetuses with LCHAD deficiency can be at risk for severe liver disease due to acute fatty liver of pregnancy (AFPL) and HELLP syndrome (hemolysis, elevated liver function tests, low platelets). This complication probably results from the metabolic defect of the affected fetus in combination with the mother being heterozygous for a fatty acid oxidation disorder. (Rinaldo, Matern et al. 2002)

**Bibliography**

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Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)

What is LCHAD?
LCHAD is a type of fatty acid oxidation disorder. People with LCHAD have problems breaking down fat into energy for the body.

What Causes LCHAD?
Enzymes help start chemical reactions in the body. LCHAD happens when an enzyme called “long chain 3-hydroxyacyl-CoA dehydrogenase” is either missing or not working. This enzyme breaks down certain fats from the food we eat into energy. It also breaks down fat already stored in the body.

What Symptoms or Problems Occur with LCHAD?
[Symptoms are something out of the ordinary that a parent notices.]
LCHAD can cause mild problems in some people and more serious problems in others. Babies and children with LCHAD usually begin to show symptoms sometime from birth through age two. LCHAD causes periods of low blood sugar.

The first symptoms of low blood sugar are:
- extreme sleepiness or tiredness
- weakness
- nausea
- vomiting
- feeling irritable or jittery
- behavior changes (such as crying for no reason)

If low blood sugar is not treated, a child with LCHAD can develop:
- breathing problems
- swelling of the brain
- seizures
- coma, sometimes leading to death

Symptoms often show up after having nothing to eat for more than a few hours. They also show up when a child with LCHAD gets sick or has an infection. Nerve problems and vision problems can happen later.

What is the Treatment for LCHAD?
The following treatments are often used for children with LCHAD:

1. Do not go a long time without food – Babies and young children with LCHAD need to eat often to avoid low blood sugar. They should not go without food for more than 4 to 6 hours. Some babies need to eat even more often. It is important that babies be fed during the night.

   Young children with LCHAD should have a starchy snack (such as bread, cereal, rice) before bed and another during the night. They need another snack first thing in the morning. Raw cornstarch mixed with water, milk, or other drink is a good source of long-lasting energy. Your dietitian can give you ideas for good night-time snacks. Dietitians know what are the correct foods to eat.

2. Diet – Sometimes a low-fat, high-carbohydrate (such as vegetables, bread, fruits) diet is advised. People with LCHAD cannot use certain building blocks of fat called “long chain fatty acids.” A dietitian can help create a food plan low in these fats.

3. MCT oil, L-carnitine and other supplements – People with LCHAD often use MCT oil. This special oil has medium chain fatty acids. It can be used in small amounts for energy. Doctors prescribe L-carnitine for some children. This is safe and natural and helps body cells make energy. It also helps the body get rid of harmful wastes. Some doctors suggest taking DHA. This may help prevent loss of eyesight.

Things to Remember
Always call your doctor when your child has any of the following:
- poor appetite
- low energy or too much sleepiness
- vomiting
- diarrhea
- an infection
- a fever
- continuing muscle pain or weakness
- reddish-brown color to the urine

Children with LCHAD need to eat extra starchy food and drink more fluids during any illness.
Trifunctional protein deficiency  
(Mitochondrial trifunctional protein deficiency; MTP deficiency; TFP)

Technical advisory committee report

Treatment
Long term outcome information is limited. Treatment appears to be of benefit but not highly effective. Even with early detection and treatment, as many as half of affected infants may die within the first several months after birth. Surviving children may still suffer significant morbidity.

Available Technology - Screen
Screening test does not differentiate between TFP and LCHAD deficiencies (see LCHAD).

Concordance with Treatment and Screening Technology criteria:
Most concordance

Estimated frequency
1 in 140,000 births

Disorder family: fatty-acid oxidation

Primary screening analyte: C16OH – same profile as LCHAD (Matern, Strauss et al. 1999)

Secondary screening analytes: C18:1OH, C18OH, C16, C14, C14:1 – same profile as LCHAD (Matern, Strauss et al. 1999)

Variability in clinical presentation:
Three forms: neonatal lethal (first days after birth), neonatal hepatic and late-onset, mild neuromyopathic. (Spiekerkoetter, Sun et al. 2003)

More severe than LCHAD with earlier presentation and severe cardiac involvement. (den Boer, Dionisi-Vici et al. 2003)

Burden if untreated:
Of 21 patients in den Boer survey, 16 died. Other symptoms common were hypotonia, feeding difficulties, failure to thrive, peripheral neuropathy and liver disease. (den Boer, Dionisi-Vici et al. 2003)

Efficacy of treatment/benefits of early intervention:
Benefit of treatment for mild form – can prevent myoglobinuria, which can be life-threatening. (Spiekerkoetter, Bennett et al. 2004)
Treatment uncertain – “Several patients in our series deteriorated with progressive cardiomyopathy despite dietary treatment.” (den Boer, Dionisi-Vici et al. 2003)

“Two patients in whom the diagnosis was made before birth died in spite of early treatment.” (den Boer, Dionisi-Vici et al. 2003)

**Unintended consequences of screening:**

The same metabolites are elevated in babies with LCHAD. Differential diagnosis can be made by skin biopsy and fibroblast studies. (Matern, Strauss et al. 1999; Rinaldo, Matern et al. 2002)

**Bibliography**


*last modified: 8/25/2006*
Trifunctional Protein Deficiency
(TFP)

What is TFP?
TFP is a type of fatty acid oxidation disorder. People with TFP deficiency can’t break down fat into energy for the body.

What Causes TFP?
Enzymes help start chemical reactions in the body. TFP happens when a group of enzymes called “trifunctional protein” is missing or not working. TFP breaks down certain fats from the food we eat into energy. It also breaks down fat already stored in the body.

What Symptoms or Problems Occur with TFP?
[Symptoms are something out of the ordinary that a parent notices.]

Babies and children with early and childhood TFP have periods of illness called Metabolic Crises. Some of the first symptoms of a Metabolic Crisis are:
- too much sleepiness
- behavior changes (such as crying for no reason)
- irritable mood
- muscle weakness
- poor appetite

If a Metabolic Crisis is not treated, a child with TFP can develop:
- breathing problems
- seizures
- coma, sometimes leading to death

What is the Treatment for TFP?
The following treatments are often used for children with TFP deficiency:

1. Do not go a long time without food – Babies and young children with TFP need to eat often to avoid low blood sugar and Metabolic Crises. They should not go without food for more than 4 to 6 hours. Some babies need to eat even more often. It is important that babies be fed during the night. Your dietitian can give you ideas for good night-time snacks. Dietitians know what are the right foods to eat.

2. Diet – Sometimes your child needs a diet low in fat (such as lean meat and low-fat dairy foods) and high in carbohydrates (such as bread, noodles, fruits, vegetables). People with TFP cannot use certain building blocks of fat called “long chain fatty acids.” A dietitian can make a food plan low in these fats.

3. MCT oil and L-carnitine – MCT oil is often used for people with TFP. This special oil can be used in small amounts for energy. Sometimes the doctor will prescribe L-carnitine. This is safe and natural and helps body cells make energy. It also helps the body get rid of harmful wastes.

Do not use any medication without checking with your doctor.

Things to Remember
Always call your doctor when your child has any of the following:
- poor appetite
- low energy or too much sleepiness
- vomiting
- diarrhea
- an infection
- a fever
- continued muscle pain or weakness
- reddish-brown color to the urine
Glutaric acidemia type 1
(Glutaric aciduria type I, Glutaryl-CoA dehydrogenase deficiency, Dicarboxylic aminoaciduria, Glutarate-aspartate transport defect; GAI)

Technical advisory committee report

**Treatment**
Most, but not all, infants do well if detected and treated early. Some (about 25%) will develop some neurological degeneration despite early treatment.

**Available Technology - Screen**
Screening test is very good at detecting affected infants (good sensitivity). The test may also be positive for some infants with glutaric academia type II (also known as multiple acyl-CoA dehydrogenase deficiency) a rare condition with variable presentation and treatability or MCAD (medium chain acyl-CoA dehydrogenase) deficiency, a condition on the current screening panel that is detected by testing for a different compound.

**Other**
GA-1 may cause brain damage that can be mistaken for “shaken baby syndrome”.

**Concordance with Treatment and Screening Technology criteria:**
Most concordance

**Estimated frequency**
1 in 60,000 births

**Disorder family:** organic acidemia

**Primary screening analyte:** C5DC (Zytkovicz, Fitzgerald et al. 2001)

**Secondary screening analytes:** none

**Variability in clinical presentation:**
Four different clinical presentations
1. Infant appears normal has an acute metabolic crisis (90% of the time during the first 24 months of life) with subsequent neurological findings that improve slightly then remain static.
2. Infants have a period of normal development, acute crisis and subsequent neurological findings as above, but then progresses slowly with recurrent episodes of illness when the child develops infection.
3. Approximately 25% of infants gradually develop motor delay. Hypotonia, dystonia, and dyskinesia during the first years of life without any apparent acute crisis.
4. Individuals can be completely asymptomatic without any crisis and normal development. (2006)

**Burden if untreated:**

“Without treatment, almost all patients with GA1 develop an incapacitating dystonic-dyskinetic disorder…” (Goodman and Frereman 2001)
“Clinically abrupt stroke like putaminal necrosis is the most distinctive and crippling manifestation of GA1, and the major determinant of both morbidity and mortality. Most patients (78%) are diagnosed after they develop striatal necrosis, and their outcomes are poor.” (Strauss, Puffenberger et al. 2003)

Most symptomatic patients, if untreated, die within the first ten years of life. (2006)

**Efficacy of treatment/benefits of early intervention:**

“Recognition of this biochemical disorder before the brain has been injured is essential to outcome.” (Baric, Zschocke et al. 1998)

“There is increasing evidence that striatal degeneration can be prevented in many patients by treatment with L-carnitine (100 mg/kg per day) and by prompt and vigorous treatment of intercurrent illnesses with fluids, insulin, and glucose… more than 80 % of patients treated in this way have developed normally.” (Goodman and Frerman 2001)

“…onset of injury is between 2 and 18 months, with a peak window of susceptibility from 6 to 14 months. No child in our cohort developed basal ganglia injury after the second birthday” (Strauss, Puffenberger et al. 2003)

“Early diagnosis of GA1 in asymptomatic infants is of great importance since encephalopathic crises appear to be preventable, and in patients who are already neurologically impaired early recognition and intervention may minimize brain damage.” (Baric, Zschocke et al. 1998)

**Unintended consequences of screening:**

C5DC is a secondary analyte for GA II (also known as multiple acyl-CoA dehydrogenase deficiency), and is sometimes elevated in babies with MCAD deficiency. (Zytkovicz, Fitzgerald et al. 2001)

**Bibliography**


**last modified:** 9/1/2006
What is GA1?
GA1 is a type of organic acid disorder. People with GA1 can't break down the amino acids lysine and tryptophan from the foods they eat.

What Causes GA1?
Enzymes help start chemical reactions in the body. GA1 happens when an enzyme called “glutaryl-CoA dehydrogenase” is missing or not working. This enzyme breaks down glutaric acid. Glutaric acid is made when the body breaks down lysine, hydroxylysine and tryptophan. When a child with GA1 eats food with these amino acids, glutaric acid builds up in the blood. All foods with protein contain these amino acids.

What Symptoms or Problems Occur with GA1?
[Symptoms are something out of the ordinary that a parent notices.]

Newborns with GA1 are usually healthy, but many are born with a large head. Other symptoms usually start between 2 months and 4 years of age.

GA1 causes periods of severe illness called Metabolic Crises. Some early signs of a Metabolic Crisis are:
- poor appetite
- too much sleepiness or lack of energy
- irritable mood
- feeling jittery
- nausea
- vomiting
- low muscle tone (floppy muscles and joints)
- weak muscles

If untreated, more symptoms can follow:
- tics or muscle spasms
- rigid muscles
- jerking movements of the arms and legs
- poor coordination and balance
- high levels of acids in the blood
- seizures
- brain swelling, or blood in the brain
- coma, sometimes leading to death

What is the Treatment for GA1?
Treatments for babies and children with GA1 are:

1. Medication – The doctor may prescribe riboflavin for your child. This is a vitamin that helps the body use protein. It helps remove glutaric acid from the blood. The doctor might also prescribe L-carnitine. This is safe and natural and helps the body make energy. Don’t use any medicine without checking with your doctor.

2. Food plan, including medical foods and formula– Most children need to eat foods low in lysine and tryptophan. The diet often includes special medical foods and formulas. The following foods should not be eaten at all or limited:
   - milk, cheese and other milk products
   - meat and poultry
   - fish
   - eggs
   - dried beans and peas
   - nuts and peanut butter

3. Blood tests – Regular blood tests will measure your child’s amino acid levels.

Things to Remember
Minor illness such as a cold or the flu can cause a Metabolic Crisis in babies and children with GA1. Call your doctor right away when your child has any of the following:
- loss of appetite
- low energy or too much sleepiness
- vomiting
- fever
- infection or illness
- behavior or personality changes (such as crying for no reason)

Sick children often don’t feel hungry. If they can’t eat or show signs of a Metabolic Crisis, they may need to be treated in the hospital.
Methylmalonic acidemia – mut
(Methylmalonic acidemia, Vitamin B-12 non-responsive; Methylmalonic aciduria due to methylmalonic coA mutase deficiency; Methylmalonic aciduria due to MCM deficiency; MMA due to MCM deficiency; MCM deficiency; Complementation Group mut; Methylmalonyl coA mutase, included; Mut, included)

Methylmalonic acidemia – Cbl A, B
(Methylmalonic acidemia, Vitamin B12- responsive; Methylmalonicaciduria, vitamin B12-responsive, due to defect in synthesis of adenosylcobalamin, cblA complementation type; Mehtylmalonicaciduria, cblA type; MMAA; Methylmalonicaciduria, vitamin B12-responsive, due to defect in synthesis of adenosylcobalamin, cblB complementation type)

Technical advisory committee report

Estimated frequency
Combined: 1 in 39,000 births (MUT: 1 in 79,000; CblA,B: 1 in 77,000)

Treatment
Early detection and treatment provides some benefit in reduced mortality and improved developmental outcomes but effectiveness is variable (B12 responsive forms tend to have a milder disease). Even with early treatment many affected children will have neurological impairment, kidney failure, and other complications. Those who receive kidney transplants tend to do well with them.

Available Technology - Screen
The screening test is fairly effective at detecting infants with these disorders although false negatives have been reported (imperfect sensitivity). Also the test cannot distinguish between the two forms of methylmalonic acidemia nor between them and propionic academia, another condition on the recommended panel. Differential diagnosis is difficult and typically entails extensive testing including cell culture, however treatment for these conditions is similar. False positive screening results are a problem. The impact of false positive results may be mitigated for some by awaiting results of a second screening test before initiating a diagnostic workup.

Other
Maternal vitamin B-12 deficiency can cause false positives

Concordance with Treatment and Screening Technology criteria:
Most concordance

Disorder family: organic acidemia

Primary screening analyte: C3 (Zytkovicz, Fitzgerald et al. 2001)


Variability in clinical presentation:
Complete deficiency (mut0) – 80% present with clinical symptoms in first week of life. Partial deficiency (mut –) – less than half present in first week of life. Some patients are asymptomatic. (Matsui, Mahoney et al. 1983)
About 40% of Cbl A patients present with symptoms in the first week of life; another 50% present within the next three weeks. About 1/3 of Cbl B patients present with symptoms in the first week of life; another 20% present within the next three weeks. (Matsui, Mahoney et al. 1983)

Burden if untreated:

<table>
<thead>
<tr>
<th>Symptoms at onset</th>
<th>Cbl A (N=14)</th>
<th>Cbl B (N=11)</th>
<th>mut⁻ (N=5)</th>
<th>mut⁰ (N=15)</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>lethargy</td>
<td>78</td>
<td>83</td>
<td>100</td>
<td>85</td>
<td>84</td>
</tr>
<tr>
<td>failure to thrive</td>
<td>75</td>
<td>86</td>
<td>40</td>
<td>77</td>
<td>73</td>
</tr>
<tr>
<td>recurrent vomiting</td>
<td>58</td>
<td>86</td>
<td>80</td>
<td>77</td>
<td>73</td>
</tr>
<tr>
<td>dehydration</td>
<td>64</td>
<td>86</td>
<td>100</td>
<td>62</td>
<td>71</td>
</tr>
<tr>
<td>respiratory distress</td>
<td>89</td>
<td>67</td>
<td>50</td>
<td>55</td>
<td>67</td>
</tr>
<tr>
<td>muscular hypotonia</td>
<td>44</td>
<td>57</td>
<td>33</td>
<td>91</td>
<td>63</td>
</tr>
<tr>
<td>developmental retardation</td>
<td>36</td>
<td>33</td>
<td>25</td>
<td>65</td>
<td>47</td>
</tr>
<tr>
<td>hepatomegaly</td>
<td>11</td>
<td>67</td>
<td>0</td>
<td>57</td>
<td>41</td>
</tr>
<tr>
<td>coma</td>
<td>50</td>
<td>29</td>
<td>40</td>
<td>38</td>
<td>40</td>
</tr>
</tbody>
</table>

Table – numbers represent percentages of patients in each group (Matsui, Mahoney et al. 1983)

Efficacy of treatment/benefits of early intervention:

“In our series of cases, expanded newborn screening decreased early mortality and symptoms at diagnosis were less severe. Moreover, the short-term neurodevelopmental outcome seems to be more favourable in patients detected by newborn screening.” (Dionisi-Vici, Deodato et al. 2006)

From same study as the above table, mut groups are not responsive to Vitamin B₁₂. Of mut⁰ patients, 60% died and 40% were alive, but impaired developmentally. Of mut⁻ patients, 40% died, 20% were impaired developmentally and 40% were unaffected. 90% of Cbl A patients and ~40% of Cbl B patients are responsive to Vitamin B₁₂. Of CblA patients, 8% died, 23% were alive, but impaired developmentally and 69% were unaffected. Of Cbl B patients, 30% died, 40% were impaired developmentally and 30% were unaffected. (Matsui, Mahoney et al. 1983)

From study of patients with methylmalonic and propionic acidemias: “Most surviving patients showed poor nutritional status with growth retardation and about 40% present some kind of visceral or neurological impairment.” and “In summary, it appears that there is some improvement in survival and in developmental outcome. The price to be paid is a higher morbidity with, for some patients, a very poor quality of life.” (de Baulny, Benoist et al. 2005)

“Patients with vitamin B₁₂ responsive MMA have a better survival and long-term prognosis with a milder phenotype, but they are still at risk of neurological impairment.” (Deodato, Boenzi et al. 2006)

Unintended consequences of screening:

“It is quite difficult to distinguish a severe case of MMA from PA using MS/MS.” (Chace and Kalas 2005)

Need confirmation of methymalonic acidemia and designation (i.e. mut or Cbl) via studies with cultured cells. (Fenton, Gravel et al. 2001)
Bibliography


last modified: 9/6/2007
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.
Propionic acidemia
(Propionyl-CoA carboxylase deficiency, PCC deficiency, Ketotic glycinemia, Ketotic hyperglycinemia, PA)

Technical advisory committee report

Treatment
Although there is some benefit of reduced mortality and some improvement in outcome, treatment is even less effective than for MMA (above). Even with early detection and treatment most children will have acute episodes of illness. Screening may identify some infants with milder forms of the disease.

Available Technology - Screen
The screening test has the shortcomings discussed under methylmalonic acidemias (above) although some infants with propionic academia have higher levels on the screening test than those with methylmalonic acidemias.

Concordance with Treatment and Screening Technology criteria:
Most concordance

Estimated frequency
1 in 72,000 births

Disorder family: organic acidemia

Primary screening analyte: C3 (Zytkovicz, Fitzgerald et al. 2001)

Secondary screening analytes: C2 (Chace, Kalas et al. 2003); C3/C2 and C3/C16 ratios (Chace and Kalas 2005)

Variability in clinical presentation:
Most present in the newborn period with severe acidosis. Others present later with acute encephalopathy, episodic ketoacidosis or developmental retardation. Others still are asymptomatic (Fenton, Gravel et al. 2001)

Burden if untreated:
Developmental delay, seizures, cerebral atrophy and EEG abnormalities. (Fenton, Gravel et al. 2001)

“Metabolic acidosis and hyperammonemia leading to severe neurological damage, coma and death. Cases with milder phenotypes are being identified in newborn screening.” (2005)

Efficacy of treatment/benefits of early intervention:
“In our series of cases, expanded newborn screening decreased early mortality and symptoms at diagnosis were less severe. Moreover, the short-term neurodevelopmental outcome seems to be more favourable in patients detected by newborn screening.” (Dionisi-Vici, Deodato et al. 2006)

Diet will “minimize the number of attacks of ketoacidosis but will not necessarily prevent them or allow normal development in all patients.” (Fenton, Gravel et al. 2001)

From study of patients with methylmalonic and propionic acidemias: “Most surviving patients showed poor nutritional status with growth retardation and about 40% present some kind of visceral or neurological impairment.” and “In summary, it appears that there is some improvement in survival and in developmental outcome. The price to be paid is a higher morbidity with, for some patients, a very poor quality of life.” (de Baulny, Benoist et al. 2005)

**Unintended consequences of screening:**

“It is quite difficult to distinguish a severe case of MMA from PA using MS/MS.” (Chace and Kalas 2005)

Need propionyl CoA carboxylase activity test because C3 is also elevated for the methylmalonic acidemias. (Fenton, Gravel et al. 2001)

**Bibliography**

(2005). Newborn Screening: Toward a Uniform Screening Panel and System. ACMG.


*last modified: 8/31/2006*
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.
Citrullinemia type 1
(ASAS; Argininosuccinic acid synthetase deficiency)

Technical advisory committee report

**Treatment**
Clinical presentation is variable from severe and potentially lethal to asymptomatic. Early identification and treatment coupled with aggressive treatment of any subsequent episodes prevents mortality and avoids some, but not all negative consequences.

**Available Technology - Screen**
Screening test is effective at detecting affected infants (good sensitivity) and does not have excessive false positives (good specificity). The screening test is also positive for infants with arginosuccinic academia (ASA), although the test levels are typically higher with citrullinemia. Diagnostic differentiation is not difficult.

**Concordance with Treatment and Screening Technology criteria:**
Most concordance

**Estimated frequency**
1 in 96,000 births

**Disorder family:** amino acid/urea cycle disorder

**Primary screening analyte:** Citrulline (Chace, Kalas et al. 2003)

**Secondary screening analytes:** cit/arg ratio (Zytkovicz, Fitzgerald et al. 2001)

**Variability in clinical presentation:**
In the acute, neonatal “classic” form 56% are symptomatic within four days of age and 67% by one week of age. (Thoene 2004)

Milder variants, asymptomatic individuals, and intra-family variability have been reported. (2006)

**Burden if untreated:**
Toxic build-up of ammonia is accompanied by lethargy, poor feeding, and vomiting. Left untreated brain damage and seizures can occur leading to coma and death. (Engel and Buist 1985)

The longest survival of an untreated infant with the classic form is 17 days. (Thoene 2004)

**Efficacy of treatment/benefits of early intervention:**
“The clinical outcome of citrullinemia has improved and now depends on the degree of hyperammonemia on initiation of effective treatment.” (Sander, Janzen et al. 2003)
“Normal IQ and development are possible if there is no damage from initial or subsequent hyperammonemia episodes.” (2005)

“Improvements in treatment (liver transplantation or the use of combined sodium benzoate/sodium phenylbutyrate) has nowadays improved the outcome.” (Bachmann 2003)

“Low-protein diets have been used successfully and are a mainstay of therapy.” (Ampola 1982)

“Early diagnosis and aggressive management are the keys to nervous system protection. Long-term outcome of all urea cycle disorders remains very guarded.” (Saudubray, Touati et al. 1999)

**Unintended consequences of screening:**

Elevated citrilline is also a primary marker for ASA, although the levels of citrulline are usually significantly more elevated in this disorder than in ASA, which shows mild to moderate elevation. A diagnostic work-up consisting of full plasma amino acids and urine organic acids can distinguish between the two disorders. (Chace, Kalas et al. 2003)

“The false-positive and –negative rates for acute neonatal citrullinemia and argininocuccinic aciduria appear to be low.” (Chace, Kalas et al. 2003)

**Bibliography**


last modified: 8/31/2006
Citrullinemia
(CIT)

What is CIT?
CIT is a type of amino acid disorder. People with CIT can’t rid the body of ammonia. It is made when the body breaks down protein and amino acids.

What Causes CIT?
Enzymes help start chemical reactions in the body. CIT is a condition called “urea cycle disorder.” It happens when an enzyme called “argininosuccinic acid synthetase” (ASAS) is either missing or doesn’t work right. ASAS helps break down amino acids. It also removes ammonia from the body. The amino acid citrulline builds up in the blood when ASAS doesn’t work. Ammonia also builds up. Too much ammonia can cause brain damage. It can cause death if untreated.

What Symptoms or Problems Occur with CIT?

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

Some of the first symptoms of high ammonia are:
- poor appetite
- too much sleepiness or lack of energy
- irritable mood
- vomiting

If untreated, high ammonia can cause:
- muscle weakness
- breathing problems
- problems staying warm
- seizures
- swelling of the brain
- coma, sometimes leading to death

What is the Treatment for CIT?

1. Low-protein diet and/or special medical foods and formula – The best treatment for CIT is a very low-protein diet (avoid meat, fish, eggs, milk products, nuts and beans). There are medical foods such as special low-protein flours, noodles, and rice available. A dietitian will make a food plan for your child. Dietitians know what are the right foods to eat. The doctor or dietitian may give your baby a special formula with the right nutrients and amino acids. People with CIT should follow their food plan for life.

2. Medication – Medications can also rid the body of ammonia. Children with CIT take these by mouth or feeding tube.

3. Blood tests – Regular blood tests will check your child's amino acid and ammonia levels.

Things to Remember
Call your doctor right away if your child has any of the following:
- loss of appetite
- low energy or too much sleepiness
- vomiting
- fever
- infection or illness
- behavior or personality changes (such as crying for no reason)
- problems walking or balancing
- bad headache

Children with high ammonia often need to be treated in the hospital.
**Argininosuccinic acidemia**

(ASA; Argininosuccinicase (ASD) deficiency; Argininosuccinate lyase (ASL) deficiency; Argininosuccinyl-coA-lyase (ASAL) deficiency)

**Technical advisory committee report**

**Treatment**
Similar to citrullinemia, however, outcomes may be somewhat better for those with ASA. A small percentage of babies with ASA do not do well despite treatment.

**Available Technology – Screen**
Again, like citrullinemia the screening test is effective at detecting infants with severe forms of the disorder (good sensitivity) but may miss mild forms (although these will probably be picked up from the second screening specimen). The test does not have excessive false positives (good specificity). The screening test is also positive for infants with citrullinemia, although the test levels are typically lower with arginosuccinic academia (ASA). Diagnostic differentiation is not difficult.

**Concordance with Treatment and Screening Technology criteria:**
Most concordance

**Estimated frequency**
1 in 82,000 births

**Disorder family:** amino acid/urea cycle disorder

**Primary screening analyte:** Citrulline (Chace, Kalas et al. 2003)

**Secondary screening analytes:**
cit/arg ratio (Zytkovicz, Fitzgerald et al. 2001)
cit/phe ratio and cit/tyr ratio (Rashed, Bucknall et al. 1997)
Argininosuccinic acid (Blau 2002)

**Variability in clinical presentation:**

Three subtypes have been reported: the fulminant neonatal form involves an acute onset, with lethargy, hypotonia, irritability, seizures and tachypnea, and is probably due to complete enzyme deficiency. (Ampola 1982)

A second infantile form, with onset in the few first few of life, presents with vomiting, hepatomegaly, and failure to thrive. A third form, which usually presents between one and two years of age, is marked by seizures, ataxia, and mental retardation together with a brittle hair anomaly called trichorrhexis nodosa. (Rattazzi 1979)

**Burden if untreated:**
Rapid-onset hyperammonemia and chronic hepatic enlargement can lead to coma and death. (Summar 2003)
Efficacy of treatment/benefits of early intervention:

“Normal mental and physical development is possible if treatment is initiated before hyperammonemia crisis” (2005)

“Improvements in treatment (liver transplantation or the use of combined sodium benzoate/sodium phenylbutyrate) has nowadays improved the outcome.” (Bachmann 2003)

“Early diagnosis and aggressive management are the keys to nervous system protection. Long-term outcome of all urea cycle disorders remains very guarded.” (Saudubray, Touati et al. 1999)

Unintended consequences of screening:

Elevated citrilline is also a primary marker for citrullinemia, although the levels of citrulline are usually not quite as elevated in this disorder as in citrullinemia, which shows significant elevations. A diagnostic work-up consisting of full plasma amino acids and urine organic acids can distinguish between the two disorders. (Chace, Kalas et al. 2003)

“The false-positive and –negative rates for acute neonatal citrullinemia and argininoacetic aciduria appear to be low.” (Chace, Kalas et al. 2003)

Bibliography


last modified: 8/31/2006
What is ASA?
ASA is a type of amino acid disorder. People with this condition can’t remove ammonia from the body. Ammonia is a harmful substance. It is made when the body breaks down protein and amino acids for use by the body.

What Causes ASA?
ASA is a “urea cycle disorder” (UCD). ASA happens when an enzyme called “argininosuccinic acid lyase” (ASAL) is missing or not working. Enzymes help start chemical reactions in the body. Ammonia builds up in the blood when there is a problem with the ASAL enzyme. Too much ammonia in the blood can cause brain damage. It can also cause death if not treated.

What Symptoms or Problems Occur with ASA?
Symptoms are something out of the ordinary that a parent notices.

There are two kinds of ASA. The severe form starts in babies. They are healthy when born, but soon show symptoms of high ammonia levels. The milder form of ASA starts in childhood.

Some of the first symptoms of high ammonia are:
- poor appetite
- too much sleepiness or no energy
- irritable mood
- vomiting

If not treated, high ammonia can cause:
- muscle weakness
- breathing problems
- problems staying warm
- seizures
- swelling of the brain
- coma, sometimes leading to death

The milder form can also cause mental retardation, seizures, a large liver, and skin and hair problems.

What is the Treatment for ASA?
The following treatments are often used for babies and children with ASA:

1. Low-protein diet and/or special medical foods and formula – The best treatment is a very low-protein diet. There are medical foods such as special low-protein flours, noodles, and rice available. A dietitian will make a food plan for your child. Dietitians know what are the right foods to eat. Your child will need to eat a low-protein diet for life. The doctor or dietitian may give your baby a special formula that has the right nutrients and amino acids.

2. Medication – The doctor might prescribe arginine supplements for your child. Other medicines may be used to prevent high ammonia.

3. Blood tests – Regular blood tests will check your child’s amino acid and ammonia levels.

Things to Remember
Children with high ammonia often need to be treated in the hospital. Call your doctor right away if your child has any of the following:
- loss of appetite
- low energy or too much sleepiness
- vomiting
- fever
- bad headache
- infection or illness
- behavior or personality changes (such as crying for no reason)
- problems walking or balancing