Newborn Screening ACT Sheet

Elevated C5 Acylcarnitine
Isovaleric Acidemia

Differential Diagnosis: Isovaleric acidemia (IVA,) 2-Methylbutyrylglycinuria (2MBG) (also referred to as short/branched chain acyl-CoA dehydrogenase deficiency or SBCAD deficiency); antibiotic-related (pivalic acid derived) artifact.

Condition Description: IVA and 2MBG result from different defects in the metabolism of the branched chain amino acids, leucine (isovaleryl-CoA dehydrogenase in IVA) and isoleucine (short/branched chain acyl-CoA dehydrogenase in 2MBG). In both conditions specific metabolites accumulate and are potentially toxic.

Take the Following IMMEDIATE Actions

- **Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).**
- **Consult with pediatric metabolic specialist. (See attached list.)**
- **Evaluate the newborn.**
- **If 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 acylcarnitine profile, urine organic acids, urine acylglycines.**
- **Repeat newborn screen if second screen not yet done.**
- **Educate family about signs/symptoms and need for urgent treatment of metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).**
- **Report findings to newborn screening program.**

Diagnostic Evaluation: Plasma acylcarnitine analysis confirms the increased C5. Urine organic acid analysis will show isovalerylglycine in IVA and 2-methylbutyrylglycine in most cases of 2MBG. Urine acylglycine and acylcarnitine analysis may also be informative.

Clinical Considerations: Isovaleric acidemia presents in the neonate with metabolic ketoacidosis, a "sweaty feet" odor, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Milder variants without neonatal illness exist. Long-term prognosis of IVA with appropriate therapy is good. The clinical spectrum of 2MBG is variable. To date, most patients identified by newborn screening with 2MBG are of Hmong descent and remain asymptomatic.

Additional Information:

New England Consortium of Metabolic Programs
http://www.childrenshospital.org/newenglandconsortium/NBS/IVA/IVA_protocol.htm

IVA Emergency Protocol
http://www.childrenshospital.org/newenglandconsortium/NBS/ISOVAL.html

Gene Tests
http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=TQVVBlc6UfmSh&gry=&fcn=y&fw=Qvcz&filename=/profiles/oa-overview/index.html

Genetics Home Reference
http://ghr.nlm.nih.gov/condition=isovalericacidemia

STAR G FELSI
http://www.newbornscreening.info/Parents/organicaciddisorders/IVA.html

Newborn Screening FACT Sheet

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.