

# California Department of Public Health Newborn Screening Program

## Descriptions of Disorders Detectable via MS/MS

### Using Newborn Screening Dried Blood Spots

- Notes:*
- *Diagnosis and management of these disorders should be coordinated with a designated Metabolic Special Care Center.*
  - *These treatment guidelines are general and not comprehensive.*
  - *Special medical diets require prescription, adjustments and ongoing follow-up with a Metabolic Center*
  - *Fact sheets for primary care providers and parents guides are available for each condition through the California Newborn Screening Program.*

### AMINO ACID DISORDERS

<b>Disorder: Argininemia</b>	
AKA: Arginase Deficiency	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased arginine.
<b>Enzyme Defect</b>	Deficiency of arginase
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>• Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Hyperammonemia, protein intolerance, episodic vomiting, neurologic damage if undiagnosed and possible death.
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Low protein diet, restricted in arginine</li> <li>• Special Medical diet: Low protein flour, pastas and rice developed specifically to reduce levels of arginine in patients. For babies, special formulas can be made to give the correct balance of nutrients. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>• Sodium phenylbutyrate</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Argininosuccinic acid lyase (ASAL) deficiency</b>	
AKA: ASA Deficiency, Argininosuccinic Aciduria ,Argininosuccinase deficiency	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased citrulline. [Increased glutamine, argininosuccinate, and ammonia not detected on screen]
<b>Enzyme Defect</b>	Deficiency of the enzyme argininosuccinate lyase (ASAL).
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>• Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Hyperammonemia, lethargy, vomiting, hypothermia, hyperventilation, hepatomegaly, trichorexis nodosa (brittle hair; pili torti), coma and death.
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Low protein diet</li> <li>• Special medical diet: Low protein foods such as flour and pasta which will help enhance urea cycle activity and waste nitrogen incorporation. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>• Arginine supplementation</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Citrullinemia</b>	
<b>AKA:</b> Arginosuccinic acid synthetase (ASAS) deficiency	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased citrulline [Increased glutamine and ammonia not detected on screen]
<b>Enzyme Defect</b>	Deficiency of the enzyme arginosuccinic acid synthetase.
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Clinical picture varies: hyperammonemia, vomiting, diarrhea and numerous neurological complications including mental retardation, hypotonia, lethargy, coma, seizures and death can occur.
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Sodium benzoate and/or sodium phenylacetate</li> <li>Supplementation with arginine</li> <li>Protein restriction</li> <li>Special medical diet: Utilize foods which are specifically made to be low in protein and geared toward patients with such disorders by minimizing the amount of citrulline in the products. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Homocystinuria</b>	
<b>AKA:</b> Cystathionine beta synthase (CBS) deficiency	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased methionine [Homocyst(e)ine not detected on screen]
<b>Enzyme Defect</b>	Enzymatic defect in the methionine transulphuration pathway. [Note- other defects in methionine remethylation (MTHFR, methionine synthetase, etc.) will not be detected by elevated methionine.]
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Clinical manifestations include skeletal and ocular problems, mild to moderate mental retardation in some instances; thromboembolism and osteoporosis may also occur
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Methionine restriction with cystine supplementation</li> <li>Special medical diet: Specially made low protein foods, such as low protein pasta and flour, help keep the amount of methionine low and cystine supplemented to help combat the symptoms of this disease. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Betaine supplementation</li> <li>Vitamin B<sub>6</sub> may benefit milder forms</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Maple Syrup Urine Disease (MSUD)</b>	
<b>AKA:</b> Branched chain ketoaciduria, Branched chain ketoacid decarboxylase deficiency	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased leucine (+isoleucine), and increased ratio of leucine (+isoleucine)/alanine [Alloisoleucine not detected on screen]
<b>Enzyme Defect</b>	Deficient activity of the enzyme complex involved in the oxidative decarboxylation of the alpha-keto acid derivatives of leucine, isoleucine, and valine.
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	The infant begins to feed poorly which is followed by vomiting, lethargy, muscular hypertonicity, seizures, coma and death; “maple syrup” odor. May have a later age of onset.
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Leucine, isoleucine, and valine restriction.</li> <li>Special medical diet: Many foods are made especially for those with this disease, low protein varieties of many common foods exist such as flour and pasta. This allow patients to get the carbohydrates and sugars they need while maintaining a low protein diet. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Evaluate for possible thiamin responsiveness (rare).</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Phenylketonuria (PKU)</b>	
<b>AKA:</b> Phenylalanine hydroxylase (PAH) deficiency, Hyperphenylalaninemia	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased phenylalanine, decreased tyrosine, increased ratio Phe/Tyr
<b>Enzyme Defect</b>	Phenylalanine hydroxylase (PAH) Bioprotein synthesis disorders (GTPCH, DHPR, etc.)
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Recall filter paper specimen, testing of amino acid panel at State Genetic Disease Laboratory.</li> <li>If recall positive referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Microcephaly, mental retardation, seizures, autistic-like behavior, and fair-light complexion, hair color and eye color; “mousy/musty” odor
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Phenylalanine restriction, tyrosine supplementation</li> <li>Special medical diet: This disease requires patients to rely on foods that are not only low in protein but also low in phenylalanine and phe exchanges to help keep their phe levels low. There are medical foods made specifically for individuals afflicted with PKU. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Tetrahydrobiopterin supplementation in some</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

**Disorder: Tyrosinemia Type 1, Hepatorenal**

AKA: Hereditary tyrosinemia, Congenital tyrosinosis, Tyrosinemia Type 1, Fumarylacetoacetate hydrolase (FAH) deficiency

<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased succinylacetone
<b>Enzyme Defect</b>	Deficiency of enzyme fumarylacetoacetate hydrolase (FAH)
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Liver failure with cirrhosis, ascites, jaundice, coagulopathy; hepatomas, renal enlargement, renal tubular dysfunction (Fanconi syndrome), rickets, neurologic porphyria-like crises; “boiled cabbage” odor
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Phenylalanine and tyrosine restriction</li> <li>Special medical diet: A Diet low in protein and tyrosine is necessary to help keep this disease effects at a minimum. Special medical food that is low in protein as well as methionine and tyrosine exists specifically for those who are afflicted with Tyrosinemia. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>NTBC (inhibitor of 4-hydroxyphenylpyruvate dioxygenase) to decrease formation of fumaryl-acetoacetate.</li> <li>Liver transplant if NTBC is ineffective.</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

**ORGANIC ACID DISORDERS****Disorder: 2-Methylbutryl-CoA Dehydrogenase Deficiency (2-MBCD)**

<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C5 acylcarnitine
<b>Enzyme Defect</b>	Deficiency in 2-methylbutryl-CoA dehydrogenase (2-MBCD)
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	One patient on record
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Carnitine supplementation</li> <li>Dietary isoleucine restriction</li> <li>Special medical diet: Products which are low in protein as well as isoleucine can aid in reducing the affects of this disease. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: 3-hydroxy-3-methylglutaryl CoA lyase deficiency (HMGCoA lyase deficiency)</b> <b>AKA: Hydroxymethylglutaric Acidemia</b>	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C5OH acylcarnitine
<b>Enzyme Defect</b>	Deficiency of 3-hydroxy-3-methyl-glutaryl CoA lyase
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory when available.</li> </ul>
<b>Symptoms if untreated</b>	Severe metabolic acidosis without ketosis; hypoglycemia with fasting; “cat’s urine” odor
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Avoidance of fasting; aggressive intervention when hypoglycemia impending</li> <li>Restriction of dietary protein (leucine), supplementation with carbohydrate</li> <li>Special medical diet: The need for the patient to have a high carbohydrate low protein and fat diet is aided through the use of medical foods specifically geared toward this dietary balance as well as a limit to the intake of C5OH acylcarnitine. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Carnitine supplementation</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: 3-Methylcrotonyl CoA carboxylase (3-MCC deficiency)</b> <b>AKA: 3-Methylcrotonylglycinuria</b>	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C5OH acylcarnitine
<b>Enzyme Defect</b>	Deficiency of the enzyme 3-methylcrotonyl CoA carboxylase May be seen as part of a multiple carboxylase deficiency syndrome
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Metabolic acidosis and hypoglycemia. Some may be asymptomatic.
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Low protein diet, restricted in leucine restricted diet</li> <li>Special medical diet: A plan that is low in leucine as well as protein and high in carbohydrates in general can be aided through the use of special medical foods, such as low protein pasta or rice, that are made specifically for this disease.</li> <li>Carnitine supplementation</li> <li>Glycine supplementation</li> </ul>

<b>Disorder: Beta-ketothiolase Deficiency (BKT)</b>	
AKA: 3-Oxothiolase deficiency; SKAT	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increase in C5-OH, C5:1 acylcarnitines
<b>Enzyme Defect</b>	Deficiency of 3-oxothiolase
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Recurrent severe ketoacidosis, vomiting, Reyes-like episodes
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Low protein diet</li> <li>Carnitine supplementation</li> <li>Glycine supplementation</li> <li>Avoidance of fasting</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Glutaric Acidemia, Type I (GA-1)</b>	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C5DC acylcarnitine
<b>Enzyme Defect</b>	Deficiency of glutaryl CoA dehydrogenase
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Macrocephaly at birth; progressive neurological problems (movement disorder), episodes of acidosis/ketosis, vomiting, hepatomegaly.
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Low protein diet, restricted in lysine and tryptophan</li> <li>Special medical diet: A low protein diet, especially restricting the amino acids lysine and tryptophan, is greatly aided through the use of medical foods which are geared toward help individuals with this disorder. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Carnitine supplementation.</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Isovaleric Acidemia (IVA)</b>	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C5 acylcarnitine
<b>Enzyme Defect</b>	Deficiency of isovaleryl CoA dehydrogenase
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there..</li> </ul>
<b>Symptoms if untreated</b>	The clinical course includes poor feeding, acidosis, and seizures with coma and death following quite soon if treatment is not begun; "sweaty feet" odor
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Low protein diet, restricted in leucine</li> <li>Special medical diet: A diet supplemented with special medical foods which are geared toward a low protein and low leucine diet can greatly help individuals with this disorder keep within their dietary guidelines. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Carnitine supplementation</li> <li>Glycine supplementation</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Methylmalonic Acidemia (MMA)</b>	
<b>AKA:</b> Methylmalonyl CoA mutase deficiency	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C3 acylcarnitine. ±C4DC
<b>Enzyme Defect</b>	Defect in methylmalonyl CoA mutase or synthesis of cobalamin (B <sub>12</sub> ) cofactor (adenosylcobalamin); at least five distinct biochemical causes of this disorder have been identified
<b>Recommended follow-up</b>	<ul style="list-style-type: none"> <li>Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.</li> </ul>
<b>Symptoms if untreated</b>	Life threatening/fatal ketoacidosis and hyper-ammonemia often appears during first week of life; later symptoms include failure to thrive, mental retardation, and episodes of coma with a risk of death
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Low protein diet, restricted in isoleucine, valine, methionine, threonine</li> <li>Special medical diet: As there are many amino acids which are restricted as a result of this disorder, medical foods which are low in protein and fat, as well as all of these amino acids is very important for those afflicted with the disorder to keep with their dietary guidelines. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Carnitine supplementation</li> <li>Cobalamin (vitamin B<sub>12</sub>) useful in some cases.</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Propionic Acidemia (PA)</b>	
<b>AKA:</b> Propionyl CoA carboxylase (PCC) deficiency	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C3 acylcarnitine
<b>Enzyme Defect</b>	Defect in propionyl CoA carboxylase $\alpha$ or $\beta$ subunit, or biotin cofactor May be seen as part of a multiple carboxylase deficiency syndrome
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Disorder usually presents acutely with feeding difficulties, lethargy, vomiting and life-threatening acidosis. Seizures and retardation are common.
<b>Treatment</b>	<ul style="list-style-type: none"> <li>Low protein diet, restriction of isoleucine, valine, methionine, threonine</li> <li>Special medical diet: As there are many amino acids which are restricted as a result of this disorder, medical foods which are low in protein and fat (such as low protein pasta and rice), as well as all of these amino acids is very important for those afflicted with the disorder to keep with their dietary guidelines. Patient is unable to eat most meat, dairy and nut products because of protein content.</li> <li>Carnitine supplementation.</li> <li>Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

## FATTY ACID OXIDATION DISORDERS

<b>Disorder: Carnitine-Acylcarnitine Translocase Deficiency (CAT deficiency)</b>	
<b>AKA:</b> CACT	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C16, C18:1 acylcarnitines
<b>Enzyme Defect</b>	Deficiency of carnitine translocase
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Hypoketotic hypoglycemia, hepatomegaly, cardiomyopathy, weakness, cardiorespiratory collapse, death.
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Effectiveness of treatment is variable and not well known, even with treatment there is a risk of death, especially with newborn with symptoms</li> <li>• Avoidance of fasting</li> <li>• Sometimes recommend: low –fat, high-carbohydrate diet, carnitine supplementation, and/or medium chain triglyceride oil.</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Carnitine Palmitoyl Transferase Deficiency Type 1 (CPT-1)</b>	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased Ratio: C0/(C16+C18:1)
<b>Enzyme Defect</b>	Deficiency of carnitine-palmitoyltransferase- I
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Hypoketotic hypoglycemia, hepatomegaly, coma, seizures
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Avoidance of fasting, aggressive intervention when hypoglycemia impending</li> <li>• Low fat diet</li> <li>• Medium chain triglyceride supplementation</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Carnitine Palmitoyl Transferase Deficiency- Type 2 (CPT-2 deficiency)</b>	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C16, C18:1 acylcarnitines
<b>Enzyme Defect</b>	Deficiency of carnitine palmitoyl transferase II
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Severe hypoglycemia hypoketosis, cardiomyopathy, polycystic/dysplastic kidneys in neonatal cases, hepatomegaly, hypotonia, seizures, hyperammonemia
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• High carbohydrate, limited fat diet</li> <li>• Avoidance of fasting</li> <li>• May include supplementation with MCT and L-carnitine</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Carnitine Transporter Deficiency (CTD) Carnitine Uptake Deficiency (CUD), (systemic carnitine deficiency)</b>	
<b>AKA:</b> Primary Carnitine Deficiency,	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Decreased free carnitine (“C0 acylcarnitine”)
<b>Enzyme Defect</b>	Defect of carnitine transporter
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Hypoketotic hypoglycemia, cardiomyopathy, skeletal myopathy, sometime liver dysfunction and hyperammonemia
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Carnitine supplementation</li> <li>• Avoidance of fasting</li> <li>• Sometimes a low fat, high carbohydrate diet is recommended</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Glutaric Acidemia Type 2 (GA-2)</b>	
<b>AKA:</b> Multiple acyl CoA dehydrogenase deficiency (MADD)	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C4, C5 [variable increase of other acylcarnitines]
<b>Enzyme Defect</b>	Deficiency of electron transfer flavoprotein (ETF) or electron transfer flavoprotein dehydrogenase (ETF-DH)
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Severe neonatal form: hypoglycemia, hyperammonemia, hepatomegaly, cardiomyopathy, “sweaty feet” odor, often with polycystic kidneys Later onset form generally milder, may have hypoglycemia, Reye-like symptoms
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Avoidance of fasting; aggressive intervention when hypoglycemia and/or acidosis impending.</li> <li>• Regulation of dietary fat intake</li> <li>• Sometimes in addition to low fat also recommend low protein and high carbohydrate diet</li> <li>• Carnitine supplementation</li> <li>• Riboflavin supplementation</li> <li>• Sometimes glycine supplements</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

**Disorder: Long chain hydroxyacyl-CoA dehydrogenase deficiency (LCHAD deficiency or LCHADD)**

**AKA:** 3-OH Long Chain Acyl CoA Dehydrogenase Deficiency

<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C16OH, C18:1OH, C18OH acylcarnitines
<b>Enzyme Defect</b>	Deficiency of long chain hydroxyacyl CoA dehydrogenase, or the mitochondrial trifunctional protein
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Clinical variability: hypoglycemia, vomiting, lethargy, coma, seizures, hepatic disease, cardiomyopathy, rhabdomyolysis, progressive neuropathy; in some older patients, pigmentary retinopathy
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Avoidance of fasting; aggressive intervention when hypoglycemia impending</li> <li>• Medium chain triglyceride supplementation</li> <li>• Sometimes other supplements including L-carnitine and/or DHA (docosahexanoic acid)</li> <li>• Sometimes low fat, high carbohydrate diet recommended</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

**Disorder: Medium Chain Acyl CoA Dehydrogenase Deficiency (MCADD)**

<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C8, and usually also C6-C10 acylcarnitines
<b>Enzyme Defect</b>	Deficiency of medium chain acyl CoA dehydrogenase
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Fasting intolerance, hypoglycemia, hyperammonemia, acute encephalopathy, cardiomyopathy, liver failure
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Avoidance of fasting; aggressive intervention when hypoglycemia impending.</li> <li>• Carnitine supplementation</li> <li>• Regulation of dietary fat intake</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

**Disorder: Short Chain Acyl CoA Dehydrogenase Deficiency (SCADD)**

**AKA:** None

<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C4 acylcarnitine
<b>Enzyme Defect</b>	Deficiency of short chain acyl CoA dehydrogenase
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Lethargy, vomiting, delayed development, muscle weakness, hypotonia. May be asymptomatic.
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Avoidance of fasting; aggressive intervention when hypoglycemia impending.</li> <li>• Carnitine supplementation</li> <li>• Regulation of dietary fat intake</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

<b>Disorder: Very Long Chain Acyl CoA Dehydrogenase Deficiency (VLCADD)</b>	
AKA: None	
<b>Diagnostic Metabolites on MS/MS Screen</b>	Increased C14, 14:1, 14:2 acylcarnitines
<b>Enzyme Defect</b>	Deficiency very long chain acyl CoA dehydrogenase
<b>Recommended follow-up</b>	Referral to CCS-approved Metabolic Center for diagnostic work-up and development of treatment plan. Diagnostic testing should be done at state NBS Metabolic Disorders Confirmatory Laboratory for tests available there.
<b>Symptoms if untreated</b>	Hypoketotic hypoglycemia with cardiomyopathy and/or liver failure; rhabdomyolysis
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Avoidance of fasting; aggressive intervention when hypoglycemia impending</li> <li>• Medium chain triglyceride supplementation</li> <li>• Carnitine supplementation (controversy regarding high doses)</li> <li>• Sometimes a low fat, high carbohydrate diet is recommended</li> <li>• Parent/patient education on diet, other preventive health measures, and early identification of warning signs that require immediate medical attention.</li> </ul>

### Submitted

Guidelines Committee, California Department of Health Services, Newborn Screening Program MS/MS Project: S. Cederbaum, B. A. Barshop, M. Lipson, S. Levine, W. Wilcox, S. Winter.

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