Summary of Disorders Included on Louisiana's Required Newborn Heel Stick Screening Panel

State Mandates: R.S. 40:1299 et seq and LAC 48: V. 6303

Disorder	Incidence	Defect	Clinical Symptoms	Goal
Metabolic Disorders				
Disorders of Amino Acid Metabolism				
Citrullinemia (CIT)	1:70,000	Deficiency of arginigosuccinic acid synthase, a urea cycle enzyme, leads to accumulation of citrulline and hyperammonemia	Poor appetite, irritability, heavy or rapid breathing, lethargy, vomiting, disorientation, somnolence, combativeness, coma, cerebral edema	Severe form: immediately on recognition of hyerammonia Milder forms: day 7
Homocystinuria (HCY)	1:344,000	Deficiency of cystathionine synthase leads to accumulation of homocysteine in the serum and increased excretion in the urine	Most newborns have none. Development delay, mental retardation, psychiatric disturbances, seizures, marfanoid stature and ectopia lentis may develop	Identification and treatment/special diet by day 14
Maple Syrup Urine Disease (MSUD)		Decreased activity of the branched-chain alpha ketoacid dehydrogenase complex (BCKAD) which is involved in degradation of branched-chain amino acids (leucine, isoleucine, and valine)	Maple syrup odor in cerumen and urine, irritability, poor feeding, lethargy, intermittent apnea, opisthotonus, stereotyped movements, coma and respiratory failure	Severe form: Immediatley upon recognition of metabolic acidosis; Milder forms: Day 7.

Phenylketonuria (PKU)	LA 1:16,000	Enzyme defect in phenylalanine hydroxylase results in increased phenylalanine in blood and increased phenylketones in urine	Mental retardation, seizures	Identification and treatment, special diet by 10-14 days
Tyrosinemia I and II(TYR)	1:100,000	Hepatic fumarylacetoacetate hydrolase (I) Hepatic cystosolic tyrosine aminotranferase	Type I Usually asymptomatic in the neonate. If untreated it will cause liver disease and cirrhosis early in infancy Type II asymptomatic in the neonate but will cause hyperkeratosis of the skin, corneal ulcers, and in some cases, mental retardation	Upon confirmation of disorder. Treatment <u>≤</u> 1 month
Disorders of Fatty Acid Metabolism				
Carnitine Acylcarnitine translocase deficiency (CACT)/Carnitine Palmitorytransferase Deficiency I and II (CPT I and II)	1:350,000	Acylcarnitines cannot be transported into the mitochondria for fatty acid oxidation thereby limiting Energy production. Heart and skeletal muscle primarily affected.	Marked hypoglycemia, metabolic acidosis, cardiac arrythmias, and facial dysmorphism	Upon recognition of disorder. Avoid fasting. Age appropriate diet.

Carnitine Uptake Deficiency (CUD)	Unknown	Reduced carnitine limits acylcarnitine formation preventing transport of fatty acids into mitochondria thereby limiting energy production. Heart and skeletal muscle particularly affected	Lethargy, hypotonia, hepatomegaly, and cardiac decompensation due to cardiomyopathy. Hypoglycemia is typical in acute episodes	Upon recognition of disorder. Avoid fasting. Age appropriate diet.
Long-Chain Fatty Acid Deficiency (LCHAD	Unknown	Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency results in inability to metabolize long-chain fatty acids with resulting hypoglycemic episodes in times of stress	Occurs during prolonged fasting and/or periods of increased energy demands (fever, stress). Hypoglycemia, elevated liver transaminases, bilirubin, lactate, ammonia, and creatine phosphokinase (CPK)	Upon recognition of disorder. Avoid fasting. Age appropriate diet.
Medium Chain Acyl CoA Dehydrogenase (MCAD)	1:20,000	Deficiency of medium Ccain acyl-CoA dehydrogenase results in inability to metabolize medium- chain fatty acids with resulting hypoglycemic episodes in times of stress	None at birth, but preprandial irritability, lethargy, jitteriness, sweating, and seizures may occur as intervals between feedings increase	Upon recognition of disorder. Avoid fasting. Age appropriate diet.

Trifunctional protein Deficiency	Unknown	Deficiency of enzyme comples known as mitochondrial trifunctional protein. Long chain fatty acids from food and body fat cannot be metabolized, processed, and converted to energy resulting in lethargy and hypoglycemia	Onset of mitochondrial trifunctional protein deficiency may begin during infancy or later in life. In infancy signs and symptoms include feeding difficulties, lethargy, hypoglycemia, hypotonia and liver problems and may be at risk for heart and breathing problems, coma and sudden unexpected death. After infancy syptoms include hypotonia, muscle pain, breakdown of muscle tissue and peripheral neuropathy.	Upon recognition of disorder, avoid fasting. Age appropriate diet
Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)	1:240,000	Deficiency of very long-chain acyl-CoA dehydrogenase results in inability to metabolize long-chain fatty acids with resulting hypoglycemic episodes in times of stress	Presents acutel in the neonate and is associated with high mortality unless treated promptly; milder variants exist. Hepatomegaly, cardiomyopthy and arrthymias, lethargy, hypoketotic hypoglycemia, and failure to thrive	Upon recognition of disorder, Avoid fasting. Age appropriate diet.

Disorders of Ogranic Acid Metabolism				
Beta-Ketothiolase Deficiency (BKD)	1:460,000	Defect in enzyme Mitochondrial acetoacetyl-CoA thiolase	Hypoglycemia, ketonuria, metabolic acidosos	Upon recognition of disorder. Avoid fasting. Age appropriate diet.
Glutaric Acidemia I (GA 1)	1:92,000	Defect of Glutaryl-CoA dehydrogenase , a mitochondrial flavin-dependent enzyme required for catabolism of essential lysine and tryptophan.	Macrocephalic but otherwise asymptomatic. Later signs include metabolic ketoacidosis, failure to thrive, and sudden onset of dystonia and athetosis	Identification on NBS and into treatment by day 7.
Isovaleric Acidemia (IVA)	1/92,000	Disorder of essential leucine breakdown caused by a defect of Isovaleryl-CoA dehydrogenase	Presents with metabolic ketoacidosis, a "sweaty feet" odor, dehydration , hyperammonia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Milder variants without neonatal illness exist.	Recognition of Hyperammonemia, metabolic acidosis. In treatment by 7-10.

Malonic Aciduria	Rare 20 cases	Deficiency of malonyl-CoA decarboxylase. Disease of ketone metabolism and fatty acid oxidation	May present acutely in neonate. Can include hypoglycemia, lactic acidosis, and marked lethargy. More commonly, presents during infancy or later childhood with developmental delay, seizures, vomiting, failure to thrive, hypotonia, hypoglycemia, metabolic acidosis, and cardiomyopathy.	Upon recognition of disorder. Avoid fasting. Age appropriate diet.
Methylmalonic Acidemia (MMA), Proprionic Acidemia (PA), Multiple CoA Carboxylase Deficiency (MCD)	1:46,000	MMA results from a defet in methylmalonyl-CoA mutase which converts methylmalonyl-CoA to succinyl-CoA or from lack of the required B_{12} cofactor for methylmalonyl-CoA mutase (cobalamin A, B, C, D, and F). PA is caused by a defect in propionyl-CoA carboxylase which converts propionyl-CoA to methylmalonyl-CoA;	Present in the meonate with metabolic ketoacidosis, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failture to thrive	Recognition of Hyperammonemia, metabolic acidosis. In treatment by 7-10 days

Proprionic Acidemia (See Above)				
3-Methylcrotonyl-CoA Carboxylase Deficiency	1:50,000	Enzyme defect in 3-methylcrotonyl-CoA carboxylase in infant or mother.	Neonate is usually asymptomatic. Episodic hypoglycemia, lethargy, hypotonia, and mild developmental delay can occur at any time from the neonatal period through childhood	Upon recognition of hyperammonia, metabolic acidosis. In treatment by 7-10 days.
Enzyme Deficiencies				
Biotinidase	1:70,000	Defect in Biotin utilization. (Biotin is a water soluble vitamin.)	Hypotonia, lethargy, seizures, hearing loss, developmental delays, optic nerve atrophy	Identification and treatment/supplementation with Biotin by 10-14 days
Galactosemia	1:60,000	Enzyme defect with resulting elevation of galactose and galactose metabolites.	Classical: Sudden death (E.coli sepsis), jaundice/ hepatomegaly, academia, cataracts, mental retardation Variants: milder symptoms	Identification and treatment/special diet by day 5
Endocrine Disorders				

Congenital Hypothyroidism	LA 1:6,250 US 1:3,600-1:5,000	Insufficient production of thyroxine due to absent, dysfunctional, or ectopic thyroid gland (primary CH) or to defective Thyroid Stimulating Hormone by the pituitary (secondary CH)	Most newborns have none. Jaundice, constipation, coarse facies/tongue, delayed skeletal maturity, posterior fontanelle, bradycardia, hypothermia, mental retardation	Identification and treatment by day 28
Congenital Adrenal Hyperplasia	1:10,000 – 18,000	Deficiency of 21-hydroxylase production by the adrenal gland	Ambiguous genitalia in females; salt-wasting, shock & possibly death	Identification within 30 days and hormone replacement
Hemoglobinopathies				
Hemoglobinopathies	1:385 African American births	Presence of hemoglobin S in combination with another abnormal hemoglobin or beta thalassemia	Sickle Cell Disease associated with sepsis, pain crises, pneumonia, anemia, gallstone, splenic enlargement	Identification and treatment by 1½ to 2 months
Pulmonary/Digestive Disorders				
Cystic Fibrosis	1:31,000	Caused by a mutation in the cystic fibrosis transmembrane conductance regulator	Chronic respiratory problems; pancreatic insufficiency; male reproductive issues	Identification and treatment within 2 months