



Newborn Screening Program

Physician Pocket Reference

Newborn Screening Laboratory

Potchefstroom Metabolic Diagnostic Laboratory

The newborn Screening Program's mission is to provide early detection of inherited genetic disorders for the prevention of morbidity and mortality attributed to these disorders. Newborn Screening is an essential preventive health function to identify infants at risk in the first few days of life so that early intervention can be implemented to prevent severe mental retardations, chronic disability or death. The cost of these disorders when left untreated is enormous, both in human suffering and in economic terms.



Screening Today for a Safer Tomorrow

Disorder/Incidence	Defect	Indicator	Symptoms	Treatment
3-Methylcrotonyl-CoA carboxylase deficiency (3MCC) 1:50,000	Deficiency of 3-methylcrotonyl-CoA carboxylase in Leucine pathway	Elevated C5-hydroxyacylcarnitine with no elevation of C3-acylcarnitine	Can be asymptomatic, or can have symptoms including acute metabolic acidosis, hypoglycemia, hypotonia, muscle atrophy, seizures, and dermatological changes	L-Carnitine supplementation and restriction of dietary protein. Special formulas and "medical" foods
Argininosuccinic acidemia (ASA) 1:70,000	Deficiency of Argininosuccinate lyase in urea cycle	Elevated citrulline	Progressive lethargy, loss of appetite, vomiting, hypothermia, respiratory alkalosis, coma, seizures, apnea, death or mental retardation	High-caloric, protein-restrictive diet, arginine supplementation, administration of sodium benzoate and sodium phenylacetate, dialysis may be necessary in acute hyperammonemia
Beta-ketothiolase deficiency (BKT) Incidence Unknown	Deficiency of mitochondrial acetoacetyl-CoA thiolase	Elevated C5:1 acylcarnitine and elevated C5	Some are asymptomatic, while others have episodes of severe metabolic acidosis and ketosis	Carnitine supplementation
Biotinidase Deficiency 1:60,000 (general population)	Enzyme deficiency, unable to recycle and produce free biotin	Absent or decreased biotinidase activity	Seizures, hypotonia, apnea, skin rash/ infection, developmental delay, alopecia, deafness, blindness, metabolic acidosis, coma, death	Pharmacological doses of oral biotin (5-20 mg/day).
Carnitine uptake defect (Group of disorders including CPT I, II, translocase) 1:40,000	Defect in Carnitine transporters	Elevated C16, C18:1 (long-chain fatty acid)	Highly progressive hypokinetic dilated cardiomyopathy that is generally associated with muscular weakness, coma or sudden death can also occur	Carnitine supplementation, oil supplementation
Citrullinemia (CIT) 1:200,000	Deficiency in argininosuccinic acid synthetase in urea cycle	Elevated citrulline	Progressive lethargy, loss of appetite, vomiting, hypothermia, respiratory alkalosis, coma, seizures, apnea, death or mental retardation	High-caloric, protein-restrictive diet, arginine supplementation, administration of sodium benzoate and sodium phenylacetate. Potassium supplements. Special formulas and "medical" foods
Congenital Adrenal Hyperplasia (CAH) 1:19,000 (GA)	Deficiency of 21-hydroxylase, unable to make cortisol and aldosterone. Many variant forms exist	Elevated 17-hydroxyprogesterone	Abnormal electrolytes: low sodium, elevated potassium, hypoglycemia, dehydration, cardiac arrhythmia, death, ambiguous genitalia in females, progressive virilization in both sexes	Replace cortisol and aldosterone, salt supplementation in some, surgical correction for females
Cystic Fibrosis (CF) 1:2,500 Caucasians 1:17,000 African Americans	Defect in the Cystic Fibrosis Transmembrane Regulator (CFTR) protein	Immunoreactive Trypsinogen and CFTR mutation analysis	Pulmonary obstruction and exocrine pancreatic dysfunction. Failure to thrive	Chest percussion, antibiotics, pancreatic enzyme replacement, proper nutrition and psychosocial support
Galactosemia 1:40,000 (GA)	Deficiency of Galactose-1-Phosphate Uridyl Transferase (GALT), unable to convert galactose to glucose. Many variant forms exist.	Absent or reduced GALT enzyme activity. Elevated total galactose metabolites	Neonatal jaundice, vomiting, lethargy, diarrhea, liver damage, death from E.Coli sepsis, cataracts development delay, hepatomegaly, Fanconi's syndrome, growth failure	Eliminate galactose and lactose from the diet. Soy formulas in infancy. Lactose and galactose free solid foods and medications
Glutaric acidemia type I (GAI) Fewer than 100 cases in U.S.	Deficiency of Glutaryl-CoA dehydrogenase in Lysine, Hydroxylysine, and Tryptophan pathway	Elevated C5-dicarboxylic acylcarnitine	Hypoglycemia, rigidity of muscles, uncoordinated movements, vomiting, metabolic acidosis, hypotonia, seizures and central nervous system degeneration	Carnitine supplementation, possible restriction of dietary lysine and tryptophan, IV fluids and bicarbonate used to treat acidosis Special formulas and "medical" foods
3-OH 3-CH3 glutaric aciduria (HMG) Rare	Deficiency of 3-Hydroxy-3-methylglutaryl-CoA lyase deficiency in leucine pathway and in ketone body synthesis	C-6 dicarboxylic acylcarnitine and C5-hydroxyacylcarnitine	Severe hypoglycemia, metabolic acidosis, hyperammonemia, vomiting, hypotonia, coma, and death	L-carnitine supplementation, avoid fasting, restriction of dietary protein and fat
Homocystinuria 1:350,000 (GA)	Deficiency of cystathionine synthetase, unable to metabolize methionine and homocystine	Elevated methionine	Mental retardation, seizures, behavior disorder, thromboses, dislocated lenses, tall/thin stature	Life long low methionine diet with cystine supplementation. Pyridoxine supplementation also if responsive. Special formulas and "medical" foods.

Disorder/Incidence	Defect	Indicator	Symptoms	Treatment
Hypothyroidism 1:4,000 (GA)	Absent, hypoplastic, or dysfunctional thyroid gland. About 20% are genetic in origin	Low or normal thyroxine (T4) with elevated thyroid stimulating hormone (TSH)	Prolonged neonatal jaundice, poor muscle tone, constipation, lethargy, feeding problems, large tongue, dry and mottled skin, distended abdomen, umbilical hernia	Thyroid hormone replacement (L-Thyroxine)
Isovaleric acidemia (IVA) 1:50,000	Deficiency of Isovaleryl-CoA dehydrogenase, unable to metabolize leucine	Elevated C5-acylcarnitine (isovalerylcarnitine)	Vomiting, acidosis, ketosis, mild hyperammonemia, hypocalcemia, transient bone marrow suppression, lethargy, coma, "Sweaty feet" odor	Life long restriction of dietary protein, L-Carnitine supplementation Special formulas and "medical" foods
Long-chain L-3-OH acyl-CoA dehydrogenase deficiency (LCHAD) 1:200,000	Enzyme deficiency that breaks down long-chain fatty acids	Elevated OH-C16 (longchain fatty acid)	Hypoglycemia, lethargy, failure to thrive, and developmental delay, often accompanied by hypotonia and cardiomyopathy, some SIDS cases are caused by LCHAD	Avoid fasting and follow high-carbohydrate diet. Special formulas and "medical" foods
Maple Syrup Urine Disease (MSUD) 1:130,000 (GA)	Deficiency of the BCKD enzyme complex, unable to metabolize the branched chain amino acids (leucine, isoleucine, and valine)	Elevated branched chain amino acids	Acidosis, hypertonia, seizures, vomiting, apnea, coma, severe mental retardation, neurological impairment, death. Ear wax/urine smells like maple syrup	Life long diet low in leucine, isoleucine, and valine. Thiamine supplementation if responsive. Special formulas and "medical" foods
Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD) 1:15,000 (US)	Enzyme deficiency, unable to metabolize fat for energy in the absence of glucose	Abnormal medium chain acylcarnitines	Hypoglycemia, hyperammonemia, vomiting, lethargy, coma, apnea, cardiac arrest, sudden unexplained death	Regular feedings to avoid fasting, low fat diet, oral L-carnitine supplementation
Methylmalonic acidemias (Mutase deficiency or Cbl A,B) 1:50,000 to 1:100,000	Deficiency of Methylmalonyl-CoA mutase required in the oxidation of amino acids	Elevated C3-acylcarnitine, usually with no elevation of C4-dicarboxylic	Neonatal metabolic acidosis and ketosis with hyperammonemia, lethargy, failure to thrive, vomiting, respiratory distress, hypotonia, and can develop chronic renal failure	Low-protein regimen and/or restriction of isoleucine, valine, and threonine, L-carnitine supplementation, Vitamin B-12 treatment. Special formulas and "medical" foods
Multiple carboxylase deficiency (MCD) 1:87,000	Deficiency of biotin, part of the Vitamin B complex	Biotinidase enzyme assay	Seizures, hypotonia, immune system impairment, skin rashes, hair loss, hearing loss, and mental retardation	Biotin supplementation
Phenylketonuria (PKU) 1:17,000 (GA)	Deficiency of phenylalanine hydroxylase, unable to convert phenylalanine to tyrosine	Elevated phenylalanine	Severe Mental Retardation, eczema, seizures, decreased pigmentation, behavior disorder, "mousey" odor	Life long low phenylalanine diet, tyrosine supplementation. Special formulas and "medical" foods
Propionic acidemia (PROP) 1:100,000	Deficiency of Propionyl-CoA carboxylase	C3 acylcarnitine and possible elevated glycine	Neonatal severe metabolic acidosis and ketosis with hyperammonemia, refusal to feed, vomiting lethargy, hypotonia, developmental delay, seizures, and death	L-Carnitine supplementation and restriction of dietary protein. Special formulas and "medical" foods
Trifunctional protein deficiency (TFP) Rare	Deficiency of trifunctional protein involved in mitochondrial long chain fatty acid oxidation	Elevated OH-C16 (longchain fatty acid)	Hypoketotic hypoglycemia in infancy or early childhood, along with hypotonia and often fatal hypertrophic cardiomyopathy, or sudden unexplained death.	Avoid fasting, avoid extreme dietary fat, and may require Carnitine supplementation. Special formulas and "medical" foods
Tyrosinemia 1:400,000 (GA)	Deficiency of Fumarylacetoacetate hydrolase (FAH), unable to metabolize tyrosine Other variant forms.	Elevated Tyrosine	Hepatic damage, liver cirrhosis and failure, Fanconi syndrome, growth failure, hepatomegaly, hepatic carcinoma, thrombocytopenia	Life long low phenylalanine and tyrosine diet. Special formulas and "medical" foods.
Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)	Enzyme deficiency that breaks down very long-chain fatty acids	Elevated C14:1 (longchain fatty acid)	Hypoketotic hypoglycemia, hepatocellular disease, cardiomyopathy, fatal infantile encephalopathy	Avoid fasting. Dietary supplements with MCT oil. Possible carnitine supplements

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