

**Newborn Screen & Development**  
**Facts about the genetic diseases new since March 2006**  
**(Excluding Cystic Fibrosis)**

**1) Argininosuccinic acidemia (ASA)**

- a) Incidence: ~1 in 70,000
- b) Deficiency in an enzyme of the urea cycle leading to hyperammonemia
- c) May appear normal at birth
- d) Without treatment: symptoms of lethargy, vomiting, poor appetite, seizures, hypotonia and muscle weakness, breathing problems, coma and death
- e) Treatment: low protein diet and a special medical formula
- f) With early treatment (before symptoms occur): may develop normally, however, more often children have some mental retardation despite treatment
- g) Autosomal recessive

**2) Beta-Ketothiolase deficiency (BKT)**

- a) Unknown incidence
- b) Deficiency mitochondrial acetoacetyl-CoA thiolase leading to build up in isoleucine
- c) May appear normal at birth (symptoms occur 6-24 mo)
- d) Without treatment: vomiting, dehydration, trouble breathing, extreme tiredness, occasionally convulsions, and can sometimes lead to coma or mental retardation
- e) NOTE: some with BKT never have symptoms
- f) Treatment: L-Carnitine & possibly low protein diet
- g) With early treatment (before symptoms): probable normal growth and intelligence, however, even with treatment, some children still symptoms (metabolic crises) which can cause brain damage leading to learning disabilities, mental retardation or other problems (although after age 10 symptoms/crises are rare)
- h) Autosomal recessive

**3) Carnitine uptake defect (CUD)**

- a) Unknown incidence
- b) Deficiency of carnitine uptake leads to in the tissues impaired ability to use fats to produce energy and ketone bodies.
- c) Without treatment: cardiomyopathy, muscle weakness, hypotonia and with repeat episodes brain damage leading to learning disabilities and mental retardation, heart failure, death.
- d) NOTE: some children never have symptoms
- e) Treatment: supplementation with carnitine & frequent feedings
- f) Treatment before symptoms or early: typical growth and development
- g) Treatment with continuing symptoms: repeat metabolic episodes can cause neurological damage over time leading to learning disabilities and mental retardation
- h) Autosomal recessive

**4) Citrullinemia (CIT)**

- a) Incidence: ~1 in 57,000
- b) Deficiency in an enzyme of the urea cycle leading to hyperammonemia

- c) Without treatment: symptoms of lethargy, vomiting, poor appetite, seizures, hypotonia and muscle weakness, breathing problems, cerebral edema, coma and death
- d) Treatment: Dietary restriction of protein & oral dosage of sodium phenylbutyrate and arginine
- e) With early treatment (before symptoms occur): may develop normally, however, some children may have some neurological impairment despite treatment
- f) Possibility of brain damage leading to learning disabilities and mental retardation correlates to severity of initial presentation and amount of recurrent episodes
- g) Recurrent episodes often occur with illnesses (e.g., common cold)
- h) Autosomal recessive

**5) Glutaric acidemia type I (GA I)**

- a) Incidence: ~1 in 30,000/40,000
- b) Deficiency in Glutaryl-coenzyme A dehydrogenase leading to excessive levels of amino acids and their intermediate breakdown products
- c) Without treatment: brain damage (particularly the basal ganglia which helps control movement) leading to hypotonia, spasticity, involuntary movement disorder, delays in motor skills, speech problems and mental retardation
- d) Treatment: Prompt treatment of catabolic events and prevention of fasting during illnesses; diet modifications
- e) With treatment (even early treatment): up to 35% will have neurological insult and disability
- f) Autosomal recessive

**6) Isovaleric Acidemia**

- a) Incidence: ~1 in 100,000 live births
- b) Enzyme deficiency in isovaleryl-CoA dehydrogenase, involved in catabolism of Leu
- c) Without treatment: vomiting, lethargy, severe metabolic ketoacidosis progressing to coma and death (50% with the acute neonatal form will die during their first episode); some may have neurological damage though several make complete recoveries. The majority of patients are developmentally normal.
- d) Treatment: protein-restricted diet, special formula and carnitine supplementation
- e) With treatment: Most will have normal development (especially early treatment)
- f) Autosomal recessive

**7) Long chain hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)**

- a) Incidence: ~1 in 75,000 births
- b) Enzyme defect that prevents the body from breaking down fatty acids into an energy source
- c) Without treatment: lethargy, hypoglycemia, hypotonia, liver dysfunction, cardiomyopathy. Acute symptoms may be difficult to manage and resistant to therapeutic attempts (with high mortality) because the presentations may involve a lethal acute liver failure, a rapidly evolving cardiomyopathy, or hypoketotic hypoglycemic encephalopathy
- d) Treatment: avoid fasting, high carbohydrate and low fat diet supplemented with MCT oil

- e) With treatment: Normal development and learning abilities (if no damage from crises). Peripheral neuropathy, if present, may not improve and prevention of ophthalmological changes (pigmentary retinopathy\*) may not occur with treatment.
- f) Autosomal recessive

**8) Methylmalonic acidemia (mutase deficiency) (MUT)**

- a) Incidence: ~1 in 50,000-100,000
- b) Deficiency of the adenosylcobalamin-dependent enzyme methylmalonyl-CoA mutase leading to an inability to process certain proteins and fats properly
- c) Without treatment: lethargy, failure to thrive, recurrent vomiting, profound metabolic acidosis, respiratory distress, hypotonia, and later on renal failure. Complications of these episodes can include metabolic stroke, extrapyramidal signs, dystonia and brain damage leading to neurological damage.
- d) NOTE: Disease varies from fatal neonatal disease to asymptomatic & age of onset of symptoms can help prognosticate – those with later onset tend to have a more benign course.
- e) Treatment: Protein-restricted diet and special formula diet, OH-Cbl injections, carnitine supplementation, may need other medications
- f) With treatment: most serious of the methylmalonic acedemias up to 60% of patients die within the first year of life and of those that survive, 40% are developmentally impaired
- g) Autosomal recessive

**9) Methylmalonic acidemia (Cbl A,B)**

- a) Incidence: ~1 in 50,000-100,000
- b) Defect in intracellular cobalamin metabolism leading to an inability to process certain proteins and fats properly
- c) Without treatment: Episodic ketoacidosis with vomiting, lethargy and coma which can lead to death. Survivors can have developmental delays, growth retardation, spastic quadriparesis, dystonia and seizures, neutropenia, thrombocytopenia and osteoporosis
- d) Treatment: Protein-restricted diet, OH-Cbl injections, Vitamin B12
- e) With treatment: Children who respond to vitamin B12 treatment tend to do very well as long as treatment is continued. Cb1A has a far better prognosis than Cb1B. Cb1B has ~33% of patients with neurologic impairment.
- f) Autosomal recessive

**10) Multiple carboxylase deficiency (MCD)**

- a) Incidence: ~1 in 87,000
- b) Defect in cellular biotin transport or metabolism leading to impaired activity of three enzymes that are dependent on the vitamin biotin: propionyl CoA carboxylase, beta-methylcrotonyl CoA carboxylase, and pyruvate carboxylase
- c) Mimics biotinidase deficiency

**11) Propionic acidemia (PROP)**

- a) Incidence: ~1 in 100,000
- b) Deficiency of propionyl CoA carboxylase leading to acidosis and hyperammonia

- c) Without treatment: tachypnea, vomiting, lethargy, irritability, shock, coma, and death. Death is very likely if symptomatic in infancy. Repeated episodes leading to mental retardation
- d) Treatment: Diet modifications with special formulas without specific amino acids that make propionyl CoA
- e) With treatment: If had symptoms before treatment (or difficulty maintaining treatment), high probability of brain damage leading to developmental delay. Also optic nerve atrophy may occur.
- f) Autosomal Recessive

**12) Tyrosinemia type I (TYR I)**

- a) Incidence: ~1 in 100,000
- b) Deficient enzyme in catabolism of tyrosine
- c) Without treatment: Symptom onset as early as 2-6 wks with FTT, chronic liver disease (liver disease can start prenatally)
- d) Treatment: special formula restricted in specific amino acids, the medication Orfadin, and typically liver transplant
- e) With treatment: Risks with liver transplant including infections or rejection,
- f) Autosomal recessive

**13) Trifunctional protein deficiency (TFP)**

- a) Unknown incidence
- b) See LCHAD (mimics disease)
- c) Autosomal recessive

**14) Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)**

- a) Unknown incidence
- b) Defect in very long-chain acyl-CoA dehydrogenase leading to problems breaking down fats to energy
- c) Without treatment: variable, from recurrent episodes of hypoglycemia to cardiomyopathy and liver problems and can progress to coma, cardiac arrest, brain damage, or even death (especially in children who are not eating well)
- d) Treatment: eating frequently and avoiding fasting, and sometimes medication (carnitine)
- e) With treatment: not much data out there but it looks like resolution of cardiomyopathy and normal development and learning abilities especially for later-onset disease
- f) Autosomal Recessive

**15) 3-hydroxy 3-methyl glutaric aciduria (HMG)**

- a) Unknown incidence
- b) A defect in HMG lyase leading to problems breaking down an amino acid (leucine)
- c) Without treatment: vomiting, dehydration, extreme tiredness, seizures, hypoglycemia, metabolic acidosis, and coma
- d) Treatment: a special diet (low leucine), including medical foods and formula, possible medications (carnitine)

- e) With treatment: good chance to have typical growth and development. However, even with treatment, some children still have repeated bouts of hypoglycemia or metabolic crises which may cause brain damage leading to learning problems or mental retardation
- f) Autosomal recessive

**16) 3-Methylcrotonyl-CoA carboxylase deficiency (3MCC)**

- a) Rare
- b) A deficiency in 3-methylcrotonyl CoA carboxylase (3MCC) is leading to problems breaking down an amino acid (leucine)
- c) Without treatment: vomiting, dehydration, extreme tiredness, seizures, hypoglycemia, metabolic acidosis, and coma
- d) Treatment: a special diet (low leucine), including medical foods and formula, possible medications (carnitine)
- e) With treatment: good chance to have typical growth and development. However, even with treatment, some children still have repeated bouts of metabolic crisis which may cause brain damage leading to learning problems or mental retardation
- f) Autosomal recessive

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\* Loss of night vision and peripheral vision in varying degrees