Inborn Errors of Metabolism

Periodically, the MRNTP is requested to transport from a referral facility a neonate with a suspected inborn error of metabolism. Due to the number and complexity of inborn errors, diagnosis can be challenging. However, early diagnosis has resulted in an improved prognosis for not all but some of these conditions. Approximately 4% of infants born in the United States have a genetic or partly genetic disorder of which inborn errors contribute substantially to this figure. Although figures vary in the literature, the incidence of inborn errors is approximately 1 in 1000-5000 newborns. Inborn errors are single gene disorders with almost all being inherited in an autosomal recessive or X-linked recessive manner. There are approximately 70 genetically distinct inborn errors that can occur from early to later infancy. Newborn screening programs administered at the state level have prompted early detection in many instances if clinical symptoms do not present sooner. For those conditions for which treatment is available, immediate early intervention will yield the best results. Listed below are inborn errors of metabolism that are tested for in the Maryland Newborn Screening Panel:

1) CAH-Congenital Adrenal Hyperplasia refers to any of several autosomal recessive diseases resulting from mutation of genes for enzymes mediating the biochemical steps of production of cortisol from cholesterol by the adrenal glands (steroidogenesis). Most of these conditions involve excessive or deficient production of sex steroids and can alter development of primary or secondary sex characteristics in some affected infants. CAH is treated with hormone replacement, replacing one or both of the hormones missing, generally with Cortef and Florinef.

2) MSUD-Maple Syrup Urine Disease is caused by a deficiency of the branched-chain alpha-keto acid dehydrogenase complex (BCKDH), leading to a buildup of the branched-chain amino acids (leucine, isoleucine, and valine) and their toxic by-products in the blood and urine. The disease is characterized in an infant by the presence of sweet-smelling urine, with an odor similar to that of maple syrup. Infants with this disease seem healthy at birth but if left untreated suffer severe brain damage, and eventually die. From early infancy, symptoms of the condition include poor feeding, vomiting, dehydration, lethargy, hypertonia, seizures, ketoacidosis, opisthotonus, pancreatitis and neurological decline.

3) PKU-Phenylketonuria is an autosomal recessive genetic disorder characterized by a deficiency in the enzyme phenylalanine hydroxylase (PAH). This enzyme is necessary to metabolize the amino acid phenylalanine to the amino acid tyrosine. When PAH is deficient, phenylalanine accumulates and is converted into phenylpyruvate (also known as phenylketone), which is detected in the urine. Left untreated, this condition can cause problems with brain development, leading to progressive mental retardation and seizures. However, PKU is one of the few genetic diseases that can be controlled by diet. A diet low in phenylalanine and high in tyrosine can be a very effective treatment. There is no cure. Damage done is irreversible so early detection is crucial.
4) Homocystinuria is an inherited disorder of the metabolism of the amino acid methionine, often involving cystathionine beta synthase. It is an inherited autosomal recessive trait, which means a child needs to inherit the defective gene from both parents to be affected. This defect leads to a multisystem disorder of the connective tissue, muscles, CNS, and cardiovascular system. Homocystinuria represents a group of hereditary metabolic disorders characterized by an accumulation of homocysteine in the serum and an increased excretion of homocysteine in the urine. Infants appear to be normal and early symptoms, if any are present, are vague.

5) Tyrosinemia is an error of metabolism, usually inborn, in which the body cannot effectively break down the amino acid tyrosine. Symptoms include liver and kidney disturbances and mental retardation. Most inborn forms of tyrosinemia produce hypertyrosinemia (high levels of tyrosine). Treatment varies depending on the specific type. A low protein diet may be required in the management of tyrosinemia. The most effective treatment in patients with tyrosinemia type I seems to be full or partial liver transplant.

6) Galactosemia is a rare genetic metabolic disorder which affects an individual’s ability to properly metabolize the sugar galactose. Its incidence is about 1 per 55,000 births (classic type). Galactosemia is also very common within the Irish Traveller population. This is attributed to consanguinity within a relatively small gene pool.

7) Biotinidase deficiency is caused by the lack of an enzyme called biotinidase. Without treatment, this disorder can lead to seizures, developmental delay, eczema, and hearing loss. Infants with biotinidase deficiency appear normal at birth, but develop critical symptoms after the first weeks or months of life. Symptoms include hypotonia, ataxia, seizures, developmental delay, alopecia, seborrheic dermatitis, hearing loss and optic nerve atrophy. Metabolic acidosis can result in coma and death.

Laboratory studies that should be performed on a neonate suspected of having an inborn error of metabolism (IEM) include:
• Complete blood count with differential
• Urinalysis
• Blood gas
• Serum electrolytes
• Blood glucose
• Plasma ammonia
• Urine reducing substances
• Urine ketones
• Plasma and urine amino acids
• Plasma lactate

In general, symptoms indicating the possibilities of an inborn error of metabolism are:
• Infant becomes acutely ill after normal behavior and feeding; may occur in hours or days
• Seizures and/or hypotonia, especially if seizures are intractable
• Has an unusual odor - common in PKU & MSUD
• Dysmorphism including skin or hair
• Unstable body temperature

Symptoms indicating strong probability of IEM:
• Persistent or recurrent vomiting
• Jaundice or hepatomegaly
• Lethargy
• Comatose
• Family history of neonatal deaths
• Parental consanguinity
• Apnea in term neonate
• Tachypnea unrelated to pulmonary disease
Since symptoms can develop quickly, the referral hospital staff and the transport team must address in the infant with suspected inborn error the fundamental ABCS (airway, breathing, circulation) along with hypoglycemia and metabolic acidosis. Be prepared for the development of seizures, IVH, and rapidly deteriorating neurological status caused by brain swelling that can result in coma. Infants with Galactosemia are prone to develop E. coli sepsis.

References

Parent Resources:

Transport X-ray request
Most hospitals have converted to various systems for X-ray archival. While many vendors claim to have universal application, this has not always been the case. When infants are transported, we ask that a hard copy of radiographs be available to the transport staff for use during their assessment and to accompany the infant on transport.

Welcome Baby Joseph
Personnel News

Congratulations to Johns Hopkins Hospital NNPI/NTN Jennifer Wilson who delivered a healthy baby boy on January 7th, 2009 named Joseph Wilson Matkins. He was 19 ½ inches long and weighed 7 lbs and 10 ozs.
MRNTP Community Initiatives

Polar Bear Plunge 2009

Once again, members of the MRNTP participated in the Maryland Special Olympics Polar Bear Plunge. The event was held on January 23, 2009 at Sandy Point State Park. The team was able to raise $980.00 to help physically and mentally challenged athletes from the State of Maryland. Team members Bill Tippet, his wife Wendy, Kathy Mallamo, Browyn Willett, Bryan Picarello and Shawn Loomis braved the chilly waters of the Chesapeake Bay and served as our frigid ambassadors. Thanks to all who supported our team in this endeavor!

From Left to Right: Bill & Wendy, Colby & Mike, Shawn & Floyd, Floyd & Kathy Bronwyn & Kathy

Welcome New Employee Shawn Loomis

Shawn Loomis has recently become a member of the MRNTP as a medic. Shawn graduated from Liberty High School in Carroll County. He previously worked for the May ambulance company transporting adults. He is currently a part time volunteer for Sykesville fire department as a firefighter/EMT. In his spare time, he plays ice hockey in the winter and roller hockey in the summer. He also enjoys playing with his dog, Cinder, a lab/corgi mix. Please join the MRNTP in welcoming him to the neonatal team.