

Early detection and treatment important in managing inborn errors of metabolism



Inborn errors of metabolism or IEMs are a group of genetically determined disorders in which a specific enzyme defect produces an abnormality in the body's ability to carry out normal metabolism, which can have serious and immediate health consequences.

Individually, IEMs are rare. However, because there are hundreds of these disorders, they collectively have a broad impact, by some estimates affecting 1 in 1,500 infants. Moreover, IEMs can manifest less frequently as adult-onset, with some patients being in their 60s and 70s.

The UCLA Metabolic Clinic provides diagnostic evaluation and therapeutic management of infants, children and adults in whom an inherited metabolic disorder is known or suspected. The clinic is staffed by a team of physicians, nurse practitioners, dietitians, genetic counselors and social workers, offering one of the largest and most comprehensive IEM programs in the country. Of just 150 metabolic physicians in the U.S. who specialize in these disorders, four are at UCLA.

Defective enzymes

Infants with IEMs can appear perfectly healthy, but if not properly treated an IEM can lead to intellectual disability, organ damage, immunodeficiency, coma and death, sometimes within hours of birth.

Seeing IEM children thrive

Newborn screening detects critical inborn errors of metabolism (IEMs) prior to any signs or symptoms of the disorder.

"If the problem is not detected before discharge from the hospital, these babies are at risk for quickly becoming seriously ill or even dying at home," says Derek Wong, MD, associate clinical professor of medical genetics and director of the UCLA Metabolic Center and Area Service Center.

"In 2011, we saw two neonates with severe methylene tetrahydrofolate reductase (MTHFR) deficiency, an IEM that previously resulted in early deaths or severe intellectual disability. These were the first patients worldwide with MTHFR to be diagnosed by newborn screening," says Dr. Wong. "And we recently celebrated the first birthday of one of our patients who has a urea-cycle disorder. Watching him smile and interact with all of the guests was an incredibly emotional and uplifting experience.

"As a result of early interventions, these children are thriving."

Each inborn error of metabolism has its own pattern of long-term effects. Depending on the particular enzyme that may be defective, IEMs can cause the inability to normally metabolize certain foods and lead to the buildup of metabolites in harmful amounts. IEMs typically fall into categories, including disorders of carbohydrate metabolism, fat metabolism and protein metabolism.

For example, two disorders of protein metabolism are phenylketonuria (PKU), an inability to properly process the amino acid phenylalanine, which can cause severe intellectual disability; and the urea-cycle disorder, ornithine transcarbamylase (OTCD), a deficiency in one of the enzymes responsible for removing ammonia from the blood. Elevated levels of ammonia (hyperammonemia) can cause irreversible brain damage, coma and/or death.

One of Southern California's largest and busiest metabolic centers

To help ensure early detection and intervention, newborns nationwide are screened for IEMs shortly after birth through a cooperative effort among state labs, newborn-screening program area service centers, metabolic-treatment centers, primary-care providers and parents. UCLA has a dual role as both an area service center and a metabolic-treatment center. UCLA's area service center is an independent resource with five dedicated staff members that facilitates referrals within a large region of California to metabolic centers for evaluation and treatment.

UCLA is one of the largest and busiest metabolic centers in Southern California, treating approximately 500 children and adults with confirmed IEMs each year. Some are diagnosed by the newborn-screening program, but others — with several hundred additional types of rare disorders — are seen from both local and international referrals.

Significant advances in diagnosis and research

Routine metabolic disorder screening began in the 1960s when a tiny blood sample taken from the baby's heel was tested for PKU. New technology known as tandem mass spectrometry now enables simultaneous detection of dozens of metabolic disorders from a comparable, small blood sample, greatly expanding the number of children that can be helped.

California screens for more than 50 IEMs. With careful diet and nutrient monitoring customized for the specific disorder and individualized for each patient, the risk of intellectual and other disabilities resulting from IEMs is now often reduced or eliminated.

UCLA is conducting multiple internationally recognized research initiatives to advance understanding of inborn errors of metabolism.

Among current IEM research pursuits is the Urea Cycle Disorders Consortium (UCDC), a multicenter National Institutes of Health-funded group studying the link between various UCD biomarkers and disease progression and severity. The UCDC involves the largest cohort of urea-cycle patients in the world.

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