Clinical and Laboratory Study of Methylmalonic Acidemia

NCT00078078

Status	RECRUITING
Sponsor	National Human Genome Research Institute (NHGRI)
Enrollment	2,275 participants

Key Eligibility Criteria

Inclusion (1)

• Patients of any sex, ethnicity, and over 1 month of age with biochemical or genetic diagnosis of methylmalonic acidemia or cobalamin disorders are eligible to enroll in this protocol. The primary reason for expanding enrollment to young children is because individuals with cobalamin C deficiency (cblC) develop a maculopathy often in utero or early infancy yet the natural history of the disease progression in these early years has not been well defined. Our colleagues at the National Eye Institute have documented the retinal findings in the largest cohort of individuals with cblC and have developed an expertise in this disorder. A recent report suggests that early treatment may significantly improve the retinal disease and will be the focus of a future clinical trial at the NIH Clinical Center requiring a need for more natural history data from birth to early childhood. Children ages 1 month to 2 years or under 12 kg will be reviewed by the Pediatric Consult Service prior to scheduling and if approved will be evaluated in the outpatient clinic for limited evaluations blood draw, eye exam, consults. Affected infants that are not approved by the Pediatric Consult Service or are not stable enough to travel may enroll remotely by telemedicine to include in natural history data collection, such as medical history and laboratory result sharing and interpretation, molecular genetic testing, genetic counseling, nutrition consult with dietary food log analysis, neurocognitive assessments. Affected individuals of any of the other disorders under study, younger than 2 years may be evaluated at Children s National Medical Center (CNMC) as part of an evolving agreement in the Translational Program in Pediatrics, if they are deemed eligible for participation by the NIH team and the CNMC team. Patients will be diagnosed based on a determination of MMA and homocysteine levels in plasma and urine. Most will have their complementation class known or pending. Molecular genetic analyses to determine mutations will be expected to have been performed prior to acceptance into the study. Some patients who have not yet had these laboratory tests will be admitted to the protocol based upon metabolic parameters and clinical history. This latter category of patients might include individuals with a suspected genetic but unknown type of MMA.

Exclusion (4)

• The PI/AI may decline to enroll a patient for reasons such as being medically unstable, residing in a hospital, sub-optimal metabolic control or for any concerns arising after review of the laboratory and clinical data; any patient who requires dialysis once or more/week and weighs \<40 kg; any patient who is being treated for an intercurrent infection with antibiotics or has evidence of an acute infection and has metabolic symptoms; any patient who does not have a regular/local metabolic, genetic or endocrine physician and/or a family physician, pediatrician, or internist; any patient who may be metabolically unstable but not acutely ill; and any patient or family who may not be able to institute recommendations for appropriate testing and care before visiting the NIH. Each family may be contacted by the NIH team prior to a pending admission to confirm that the patient is metabolically stable and ready to visit the NIH in a state of relative health, with an adequate supply of special formulas, medications, supplements, and if needed, medical equipment such as feeding pumps and replacement parts for feeding tubes. A subset of participants will be enrolled in the tissue collection part of the study only (i.e. if they are too sick to travel).

• Pregnant women may be eligible to enroll in the study if they are affected with methylmalonic acidemia or a cobalamin disorder or are family members of an affected subject. Pregnant women are not excluded because it is important to learn more about the effects of these disorders in pregnant participants and the fetus. This research involves no more than minimal risk to the fetus. Affected subjects who are pregnant or become pregnant during their participation on the study will not be withdrawn, but will be excluded from some procedures until the pregnancy is concluded. Affected subjects who are pregnant may undergo procedures as part of their clinical care, including blood draws, genetic studies, and consultations, according to the clinical judgement of the clinical team. Pregnant participants will be excluded from some procedures such as stable isotope, GFR testing, and MRI until the pregnancy is concluded.

• Patients with methylmalonic acidemia or cobalamin disorders of any age, sex and ethnicity, undergoing a transplantation surgery at UPMC Children s Hospital of Pittsburgh, are eligible to participate in the tissue collection arm of the study. Pregnant women will be excluded from tissue collection at the UPMC Children s Hospital of Pittsburgh.

• For the healthy volunteers, eligibility criteria include individuals that are age 18 and over.

Locations (3 total)

Children's National Medical Center, Washington D.C., District of Columbia, United States
National Institutes of Health Clinical Center, Bethesda, Maryland, United States
UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania, United States