

**Nutrition Guidelines Project: OA Workgroup  
Focus on Propionic Acidemia (PROP<sup>1</sup>)**

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The development of nutrition guidelines for PROP is needed as there are multiple approaches for the nutrition treatment of patients living with PROP but no clear consensus on best practices to promote outcomes<sup>2,3</sup>. PROP due to the non-working propionyl Co-A carboxylase gene, is one of the rarer inborn errors of metabolism (IEMs), with an estimated incidence of 1:100,000<sup>4</sup>. With 4.1 million births per year in the US, there are approximately 41 infants with PROP born per year<sup>5</sup>. Despite the fact that PROP was first described over 50 years ago in 1961<sup>6</sup>, there is still much that we do not know about the natural history of PROP. Medical nutrition therapy (MNT) is a key therapy for patients living with PROP but there are many reports of poor neurologic outcomes. There remains a high rate of morbidity and mortality from either cardiomyopathy and/or from episodes of metabolic instability due to intercurrent illnesses<sup>6</sup>.

Due to the rarity of IEMs, there is a lack of published evidence-based literature standardizing the MNT of any of these disorders<sup>8</sup> including PROP<sup>2,9</sup>. The Southeast newborn screening and Genetics Collaborative (SERC<sup>10</sup>) funded through the Maternal and Child Health Bureau Health Resources and Services Administration (HRSA), Department of Health and Human Services administered the Nutrition Guidelines Project in collaboration with Genetic Metabolic Dietitians (GMDI) to address this national gap. The purpose of the project is to develop nutrition guidelines for the management of genetic metabolic disorders where there is limited published scientific evidence. As a pilot five workgroups were formed to represent the following groupings of IEMs: aminoacidopathies, fatty acid oxidation disorders, organic acidemias (OA), phenylketonuria and urea cycle disorders. PROP was chosen as the first disorder to focus the efforts of the OA workgroup based on a GMDI metabolic dietitians' needs assessment survey; other workgroups are focusing on maple syrup urine disease (MSUD), Phenylketonuria (PKU), and validating the previously developed nutrition guidelines for medium chain acyl Co-A dehydrogenase deficiency (MCADD) and very long chain acyl Co-A dehydrogenase deficiency (VLCADD). Workgroup chairs were chosen by project primary investigators based on their experience in the field. A core group, including the primary investigators, study coordinators and workgroup chairs, oversee the progress of the workgroups. The OA workgroup includes nine metabolic dietitians with a combined 102 years (average 11 years per dietitian) of clinical IEM patient experience. Dietitians were recruited from the professional group, Genetics Metabolic Dietitians International (GMDI)<sup>11</sup>. A nutrition guidelines project website was developed to facilitate workgroup member communications and the systematic sharing and editing of documents.

The OA workgroup summarized a list of 74 questions to address the unanswered or ambiguous MNT questions for PROP. The ultimate goal is to develop a standard of care for the MNT of PROP. The four main areas of MNT to establish consensus include:

1. Establishing the dietary amino acid and nutritional goals when starting diet therapy,
2. Illness nutrition management guidelines,
3. Impact of biotin and L-carnitine use on MNT,
4. Optimal nutrition therapy for patients living with PROP and cardiomyopathy, diabetes, pancreatitis or receiving a liver transplant.

A systematic and transparent process was developed to review published medical literature and to identify and address IEM specific MNT concerns utilizing a combination of evidence based analysis<sup>12</sup> and consensus methods. Evidence-based analysis methods provide workgroups with unbiased and critical assessment of the quality and relevance of published literature for MNT in PROP. Published literature in MNT of PROP is limited. For this reason, the workgroup will also solicit feedback on common clinical practices from expert metabolic physicians and dietitians chosen from the seven US HRSA regions<sup>13</sup>. When gathering clinical practices the workgroup will use established consensus methods such as delphi surveys and nominal group meetings<sup>14</sup>. Delphi surveys will be mailed to participants and include PROP MNT clinical practice statements that invite comments. Moderated face-to-face nominal group meetings will be held to clarify ambiguous MNT practices. The consensus techniques will invite comments from expert metabolic dietitians, physicians, other healthcare providers and patient and family community stakeholders. The goal is to incorporate feedback from a large group of health care providers who are taking care of PROP patients. The PROP and other IEM nutrition guidelines will be field-tested and once finalized will be published on the SERC and GMDI websites and subject to future revisions.

Developing a consensus on nutrition therapy for PROP and nutrition guidelines for other IEM's is timely given the expansion of state public health newborn screening programs. These programs identify patients who require diagnosis and treatment as early in life as possible. Development of an evidence-based and consensus-validated PROP medical nutrition guideline will help to: standardize PROP MNT, improve consistency in PROP nutritional therapy and management, allow for future PROP guideline revisions, and support the main goals of improving the quality of medical care and patient outcomes. A PROP nutrition guideline will focus future directions in MNT, medical and nutrition professional and patient continuing education, and clinical nutrition research for PROP.

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