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Commentary

Propionic acidemia consensus conference summary

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ABSTRACT

In January 2011, Children's National Medical Center in Washington, D.C. hosted a consensus conference to discuss and develop recommendations for the diagnosis and management of propionic acidemia. Several resulting manuscripts from this conference are included in this issue. Topics covered include recommendations for acute management of metabolic decompensations, recommendations for chronic management and health monitoring, natural history of disease in patients with propionic acidemia, and neurologic complications in propionic acidemia.

Propionic acidemia (PA, OMIM ID: 606054) is an organic acidopathy, also known as propionic aciduria and ketotic hyperglycinemia. Advances in treatment and chronic management have improved survival, however patients continue to have neurologic and other organ system complications. Due to its rarity (estimated to be 1 in 100,000 overall to 1 in 3000 in Saudi Arabia), single center clinical reports dominate the literature, with few large multiple center studies. This comparison of treatments is difficult since different institutions use variable approaches to chronic health monitoring and acute management [1–3]. Moreover, complications from PA have been difficult to characterize due to the presence of few multiple center cohorts.

To better describe treatment approaches, identify complications, and provide baseline treatment recommendations based on the best literature available and expert opinion, Children's National Medical Center convened an international group representing clinical biochemistry, neurology, transplant surgery, metabolic nutrition, public policy, basic science, and family support groups to provide a series of recommendations from which further studies can be based. In addition, these recommendations can assist non-biochemical clinicians in care of patients with propionic acidemia, especially in the acute and chronic monitoring setting. The recommendations come from an exhaustive search of the English-language literature which informed expert opinion and allowed for debate of controversial issues. These discussions resulted in two articles with recommendations for acute treatment and chronic health monitoring and two reviews of the natural history of PA and neurological complications.

"Acute management of propionic acidemia" (Chapman et al. in this issue [4]) focuses on the initial identification and treatment of a previously undiagnosed individual or known PA patient. It walks the reader through interventions from presentation (to a non-metabolic center or metabolic center), to transfer to a metabolic center (if necessary), to accelerations of therapies (if necessary), to appropriate discharge planning. In addition, it provides the literature basis for the recommendations.

"Natural history of propionic acidemia" (Pena et al. in this issue [5]) is a review article summarizing the known literature combining multiple case reports to highlight the known complications and outcomes of patients with PA during their lifespan. It also provides a short overview of the genetics of PA and known mutations.

"Chronic management and health supervision of individuals with propionic acidemia" (Sutton et al. in this issue [6]) provides bullet point recommendations, based on known natural history and best evidence summarizing health screening and treatment of chronic complications. It reviews specific complications, timing of screening, and approach to treatment.

"Neurologic complications in propionic acidemia" (Schreiber et al. in this issue [7]) focuses only on the potentially most damaging component of long term morbidity and mortality in patients with PA. It discusses the state of knowledge about the pathophysiology of neurologic complications including metabolic stroke in PA. It also discusses common MRI and magnetic resonance spectroscopy findings in PA. It makes recommendations concerning the present state of imaging and neurologic screening.

During this conference and preparation of the various manuscripts, several scientific needs were identified. These include the need for longitudinal studies into the natural history of PA. As of the time of writing for this manuscript, a longitudinal study in Europe has been launched examining multiple inborn errors of metabolism (including

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PA) and the Region 4 consortium in the United States has begun a study of patients with IEMs detected by newborn screening (including PA). It also identified that better biomarkers were necessary to follow disease progression and for study end-points. Finally multi-center studies for potential clinical interventions are necessary to maximize therapeutic outcomes.

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