Title: Propionic Acidemia *GeneReview* Table 3b
Authors: Shchelochkov O, Carillo N, Venditti C
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Table 3b. Prevalence of Clinical Findings in Propionic Acidemia

System	Symptoms	Prevalence [1]	Source [2]
General	Symptomatic at the time of newborn screen report	57%-63%	Dionisi-Vici et al [2006], Grünert et al [2012]
	Failure to thrive	0%-63%	Touati et al 2006], Rafique [2014]
	Asymptomatic clinical course	7%-19%	Grünert et al [2012], Kölker et al [2015a]
Neurobehavioral	Intellectual disability, IQ<70 [3]	35%-76%	de Baulny et al [2005], Touati et al [2006], Grünert et al [2012]
	Intellectual disability, IQ 70-85	11%	Touati et al [2006]
	Speech delay	55%-60%	Grünert et al [2012], Pena & Burton [2012]
	Hypotonia	38%-51%	Grünert et al [2012], Karimzadeh et al [2014], Kölker et al [2015b]
	Hypertonia	2%-30%	Karimzadeh et al [2014], Kölker et al [2015b]
	Hearing loss [4]	1%-13%	Grünert et al [2012], Kölker et al [2015b]
	Brain atrophy	40%-53%	Haberlandt et al [2009], Karimzadeh et al 2014]
	Basal ganglia abnormality	7%-56%	de Baulny et al [2005], Haberlandt et al [2009], Grünert et al [2012], Pena & Burton [2012], Nizon et al [2013], Karimzadeh et al [2014]
	White matter changes	38%-40%	Nizon et al [2013], Karimzadeh et al [2014]
	Cerebellar abnormalities	11%	Nizon et al [2013]
	Metabolic stroke	6%-18%	Grünert et al [2012], Pena & Burton [2012]
	Seizures	13%-53%	Haberlandt et al [2009], Pena & Burton [2012], Karimzadeh et al [2014], Kölker et al [2015b]
	Movement disorder	13%-30%	Pena & Burton [2012], Karimzadeh et al [2014], Kölker et al [2015b]
	Balance disorder	39%	Kölker et al [2015b]
	Cerebral palsy	13%	Rafique [2014]
	Acute psychosis	8%	Nizon et al [2013]
	Autism	3%-9%	de Baulny et al [2005]
	Attention deficit disorder	15%-21%	Pena & Burton [2012], Nizon et al [2013]
Ophthalmologic	Optic nerve atrophy	11%-25%	Pena & Burton [2012], Martinez Alvarez et al [2016]

System	Symptoms	Prevalence [1]	Source [2]
Cardiovascular	Cardiomyopathy, dilated or hypertrophic	7%-24%	de Baulny et al [2005], Dionisi-Vici et al [2006], Touati et al [2006], Romano et al [2010], Grünert et al [2012], Pena & Burton [2012], Kölker et al [2015b]
	Prolonged QT interval (>440 ms)	33%-70%	Baumgartner et al [2007], Kölker et al [2015b]
	Ventricular dysrhythmia	20%-30%	Baumgartner et al [2007]
Gastrointestinal	Recurrent emesis	6%	Kölker et al [2015b]
	Poor feeding/lack of appetite	76%	Touati et al [2006]
	Recurring diarrhea	6%	Kölker et al [2015b]
	Pancreatitis	3%-18%	Dionisi-Vici et al [2006], Grünert et al [2012], Pena & Burton [2012]
	Elevated ALT and AST	16%-40%	Karimzadeh et al [2014], Kölker et al [2015b]
	Elevated GGT	10%	Kölker et al [2015b]
Renal	Elevated serum creatinine	6%-15%	Grünert et al [2012], Kölker et al [2015b]
	Chronic renal failure	Sporadic	Kölker et al [2015b]
	Renal stones	10%	Karimzadeh et al [2014]
Skeletal	Osteoporosis	0%-6%	Grünert et al [2012]
	Decreased bone density	13%	Pena & Burton [2012]
Hematologic	Pancytopenia	6%-15%	Grünert et al [2012]
	Anemia	22%-89%	Grünert et al [2012], Pena & Burton [2012], Karimzadeh et al [2014], Kölker et al [2015b]
	Leukopenia	18%-31%	Pena & Burton [2012], Kölker et al [2015b]
	Thrombocytopenia	17%-46%	Grünert et al [2012], Pena & Burton [2012], Kölker et al [2015b]
Immune	Immunodeficiency [5]	15%	Pena & Burton [2012]

To facilitate the comparison of data across various studies, the review of literature describing the spectrum and frequency of PA complications has been limited to the decade spanning years 2005-2015.

1. Differences in the reported prevalence of findings may reflect variable sizes of the cohorts, age of the last evaluation, length of follow-up, differences in the therapeutic approaches, availability, turnaround time and sensitivity of the newborn screening, screening method (newborn screen vs selective metabolic screen), overlap of patients in the reported cohorts, ascertainment and recall biases.

2. Pena & Burton [2012] presented self-reported data collected through a survey.

3. The IQ threshold for this clinical category varied among the reports: IQ<75 by de Baulny [2005], IQ<70 by Touati et al [2006] and IQ<69 by Grünert et al [2012].

4. Sensorineural hearing loss in the Grünert et al report [2012] was reported in 6/7 of the patients “impaired hearing ability.”

5. A type of immunodeficiency was not specified.

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