

Caring for Persons with Phenylketonuria

In the United States, PKU occurs in 1 in 10,000 to 15,000 newborns, usually detected by newborn screening as an autosomal recessive disorder. Patients have mutations in the PAH gene on chromosome 12 (region q22–24.1) which provides instructions for making the enzyme, phenylalanine hydroxylase which converts phenylalanine (Phe) to other compounds. There are over 950 variants. Phe occurs in all proteins. If untreated, Phe builds up in the body, causing intellectual disability and other problems. Genetic counseling recommended for family of the proband.

System	Information	Follow-up
Cognition	- Typically, low average or 0.5 SD below mean - Untreated, intellectual disability, autism features. Decrease 4 IQ points per month delay in treatment. - Treated still may have issues with language, memory, learning skills, executive function. - Inc Phe levels in adults lead to dec. attention, slower motor reaction.	Neuropsych testing as needed.
Vision	Subclinical vision issues w/ functional and ocular microstructural defects, some depend on diet.	Yearly full ophthal exam, extra testing as needed.
GI/Nutrition	- Avoid protein (broad recommended range - as low as < 7 gm daily), newborns can breastfeed d/t low Phe levels. Avoid Aspartame & Nutrasweet. - Phe-free L-amino acid (BH₄) supplements include Ca/Vit D and can taste bitter, hyperosmolar & acidic, may cause GI upset and tooth wear.	- Goal Phe 120–360 µmol/l. - Phe levels 360-600 may be treated up to age 12 & in pregnancy (goal <240). - Teens/adults check Phe level monthly. - Periodic amino acid levels. - Risk Fe, Zn, Se, B12 deficiencies.
Obstetric	Excess Phe is teratogenic. Pregnancy with uncontrolled PKU risk fetal loss, offspring intellectual disability, low birth weight, slow growth, aortic coarct, hypoplastic left heart, microcephaly, tracheoesophageal fistula, limb malformations.	- Early contraceptive management in girls. - Dietary or BH₄ Tx (or both) essential pre-conception and in pregnancy. PKU mothers can breastfeed with increased protein in diet.
Infectious Dis	Infections alter metabolism and Phe control.	- Continue BH₄ supplements and high carb drinks w/ infection to decrease muscle protein loss & lessen impact on Phe control. - Use antipyretics to improve food, fluid, energy intake w/ illness.
MSK	Osteopenia if untreated. Early treated have low normal bone density.	Follow and treat vitamin D levels, supplement calcium.
Skin	Lighter skin and hair - inability to make tyrosine and melanin, musty body odor, eczema.	- Avoid sunburn. - Follow and treat zinc levels.
Neurology	Untreated - Parkinson-like-tremor, brisk reflexes, paralysis (dec. brain dopamine), dec. myelin formation, brain MRI w/ patchy or diffuse symmetrical deep periventricular white matter lesions (occipital, parietal, frontal, temporal) as hyperintense T2 / FLAIR sequences.	- Neuro /vision changes & MRI lesions in adults can reverse with resumed diet and/or BH₄ Rx. - Follow and treat B12 levels.
Mental Health	- Food neophobia in children. - Risk anxiety, depression, phobias in teens coming off diet.	- Maintain healthy eating habits and family role modeling. - Routine mental health screening.
Nephrology	Inc calciuria and dec GFR reported.	Monitor renal function
Other	Enzyme co-factor sapropterin lowers Phe for some variants. (BH₄ = tetrahydrobiopterin, Kuvan).	- All patients - lifetime dietician & metabolism support. - Genotypes may predict BH₄ response.

Reference: van Wegberg AMJ, et al. European guidelines on PKU: Dx and Tx. Orphanet J Rare Dis. 2017 Oct 12;12(1):162

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