

Phenylketonuria: effects, treatment and screening methods



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Phenylketonuria is a single-gene recessive genetic disorder that causes mental retardation along with other physical and behavioral effects. PKU can be screened for shortly after birth and can be treated with diet. There could potentially be drug therapies and/or gene therapies to help treat PKU with more research.

Phenylketonuria is not something new to the field of biology or medicine. This disorder was discovered in the 1930's by a Norwegian biochemist that discovered an excess of phenylpyruvic acid in the urine of a pair of mentally retarded siblings. (Plomin, DeFries, McClearn, & McGuffin, 2008)

Phenylalanine is one of the essential amino acids, which are the building blocks of proteins and is present in many foods in the normal human diet and he suspected that the retardation was due to an increase in the amount of phenylalanine, or an alteration in the metabolism of this protein. It was later discovered that there were more people with this condition. This type of mental retardation came to be known as what we know it now:

phenylketonuria (PKU) (Plomin, 2008).

Although this seems like it would be an uncommon disorder, it is actually fairly common. According to Widaman, 2009, Phenylketonuria is one of the most common inborn errors of metabolism, occurring in 1 in 10, 000 to 15, 000 live births, and is caused by mutations on the gene coding for the enzyme phenylalanine hydroxylase or (PAH). Phenylketonuria is a recessive genetic trait, which means, the offspring has both recessive genes passed down from their “ carrier” parents and the person will only “ express” the disorder if they obtain both defective genes from their parents (i. e. if the offspring only receives one defective gene, they will be a carrier, but they

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will not express the symptoms or have defective phenylalanine metabolism. In a “ normal” person, or a person without the defective genes, phenylalanine is metabolized into tyrosine, which is a nonessential amino acid and is a foundation (or precursor) of several essential hormones, including epinephrine, norepinephrine, and dopamine, etc. In PKU, metabolism of phenylalanine into tyrosine is interrupted, leading to very high levels of phenylalanine and low levels of tyrosine in the blood. (Widaman, 2009).

Research showed that high levels of blood phenylalanine during infancy and childhood lead to serious and permanent brain damage, but the precise nature of the impact on neural function had not been discovered. (Widaman, K, 2009).

Phenylketonuria has devastating effects on health and behavior if not treated. Mental retardation will quickly follow if not screened for or treated and the effects of improper treatment, monitoring, or knowledge are well known. Intellectual function decreases very rapidly when high amounts of phenylalanine are present in a diet of someone with phenylketonuria. This evidence is again presented by Widaman, 2009: “ Apparently normal at birth, such an infant will fall to the level of severe mental retardation (mean IQ of 50) by age 2-a decline that cannot be reversed. But if an infant with PKU is placed on a low phenylalanine diet early in life and continues strictly on such a diet until age 20 years or later, he or she will exhibit normal or near-normal development “(Widaman, K, 2009).

Today, screening for phenylketonuria is part of routine newborn screenings at hospitals around the United States when a newborn is screened for various other genetic disorders. Such screenings can aid in preventing the severe mental retardation that comes along with the lack of a correct diagnosis of PKU. Brosco 2008 states: “ Universal newborn screening for phenylketonuria (PKU) is typically described as one of the most successful public health programs in the history of modern medicine. Since their introduction in the early 1960s, state programs to identify and treat infants with PKU have prevented intellectual disability (formerly “ mental retardation”) in thousands of children” (Brosco, J2008). Tests do need to be regulated and accuracy of these tests needs to be determined. If a newborn is screened for PKU and the outcome produces a false-positive, the newborn will be put on a restrictive diet, which in turn could harm the otherwise healthy infant as a restricted diet in a healthy, growing baby could result in a failure to thrive. For a PKU baby, a restrictive diet is necessary for the developing brain function. While a restrictive diet will benefit a PKU baby, a restrictive diet in healthy babies could produce life-threatening consequences. An excerpt from Brosco, 2008 points out how the false positive could be detrimental to a healthy newborn and re-screening and accuracy of screenings is very important:

“ In 1966 ... 2 children who were admitted to the pediatric hospital at the University of Texas (Galveston, TX) for failure to thrive. Both children had initial results suggesting PKU but no follow-up testing to confirm the diagnosis; it is not clear from “ the researcher’s” report if the confusion began with results from a state NBS (new born screening) program. Texas

implemented a pilot PKU program in 1964, and statewide screening became law in 1965. After several months of receiving formulas low in phenylalanine, both infants developed the known effects of restricting this essential amino acid: they became listless, had poor gain weight, and developed severe eczematous rashes. Their symptoms resolved within days of starting a whole-milk formula, but both infants continued to demonstrate developmental delay at the time of publication. “ The researcher” concluded that “ these cases reflect the fallacy of institution of phenylalanine restriction before a definitive diagnosis of phenylketonuria is established.” (Brosco, J 2008)”

The timing of the tests also needs to be considered; for example if the test is being done in utero to determine the levels of phenylalanine if the mother and/or father is a known carrier or has both defective genes. This type of testing can be further explored in family genetic counseling. Preferably, screenings should be done at an age or point when the “ biomarker abnormalities are significant enough to be detectable and reflect neonatal rather than maternal values or transitional effects.” (Sahai, I, & Marsden, D. 2009).

The treatment and management of phenylketonuria is essential to a successful outcome after an infant is diagnosed. The clinical problems associated with treatment and management can be catastrophic to this persons health. If left untreated, PKU leads to the development of a variety of clinical problems including mental retardation, microcephaly, autistic behavior, eczema, and seizures (Blau, N, Bélanger-Quintana, A, Demirkol, M, Feillet, F, & Giovannini, M. 2009). The management of PKU is mostly based <https://assignbuster.com/phenylketonuria-effects-treatment-and-screening-methods/>

on restriction of foods containing phenylalanine. According to Blau, 2009 Dietary Phe restriction, ideally begun within 1-2 weeks after birth, is effective in protecting the developing central nervous system from the toxic effects of hyperphenylalaninemia, [or high levels of phenylalanine in the blood].

The pharmaceutical industry could have a large profit if they can manufacture a drug that will control levels of phenylalanine or replace mimic the metabolism of phenylalanine. There is currently one drug study that is currently being conducted. The drug in question is called drug sapropterin (brand name Kuvan). Overall, the results of these trials indicated that about 20-50% of patients with PKU achieved a reduction in blood Phe of greater than 30% (Blau, 2009).

Gene therapy is an emerging subject and option of treatment in today's society and is another area of research for those living with phenylketonuria and according to Widaman 2009:

Gene therapy and other forms of medical therapy (e. g., medication) have potential for correcting disordered phenylalanine metabolism by persons with PKU. If such therapies were to become reality, they might solve problems of both PKU and maternal PKU by restoring normal phenylalanine metabolism. Early screening would still be needed to identify infants needing gene therapy, and phenylalanine levels in persons with PKU would still need to be monitored to verify success of therapy. Unfortunately, medical therapies are probably many years away . (Widaman, 2009).

Phenylketonuria is a complicated genetic disorder and more research needs to be done regarding treatment and cures. From studying research available, it seems that there is a long way to go in not only the treatment, prevention, and effects of phenylketonuria, but also the understanding of the pathogenesis of PKU. There are not a lot of studies on diverse populations of individuals with PKU. Studies with large sample sizes of adolescents with high phenylalanine concentrations could improve the statistical credibility of the expected outcome in this age group (Albrecht, Garbade, & Burgard). Much more research needs to be done on this single-gene disorder. Not only screening and treatment options need to be improved, but potentially a cure could be found using gene-therapy, drug therapy or both.