PKU
Phenylketonuria

REGISTRY POWERED BY NORD
My name is Alex Baker and I am a 22-year-old college student with PKU. I have an associate degree in music performance and I currently study physics at Rutgers University, which I plan to see through to a PhD. I’m an avid musician playing guitar, piano, bass, drums, and vocals. I’m a linguaphile and love studying world languages, and the outdoors is my favorite place. In my free time I’m a server at a local restaurant and for 6 years I’ve been a lifeguard every summer. I’m fascinated by my experience with PKU and frequently ask questions that stimulate a conversation. To today my friends are fascinated by my experience with PKU and frequently ask questions that stimulate a conversation. To them I am a PKU Warrior.

Alex

Meet PKU Warrior ALEX

Alex

What is PKU?

PHENYLKETONURIA

Overview

Phenylketonuria (PKU) is an inborn error of metabolism detectable during the first days of life via routine newborn screening. PKU is characterized by the absence or deficiency of an enzyme called phenylalanine hydroxylase (PAH), responsible for processing the amino acid phenylalanine. Amino acids are the chemical building blocks of proteins and are essential for proper growth and development. With normal PAH activity, phenylalanine is converted to another amino acid, tyrosine. When PAH is absent or deficient, however, phenylalanine accumulates and toxic to the brain. Without treatment, most people with PKU would develop severe intellectual disability. To prevent intellectual disability, treatment consists of a carefully controlled phenylalanine-restricted diet beginning during the first days or weeks of life.

Signs and Symptoms

Infants with PKU typically appear normal at birth. With early screening and dietary treatment, affected individuals may never show symptoms of PKU. Those newborns not diagnosed in the first days of life and therefore not treated properly, may be weak and feed poorly. Other symptoms may include vomiting, irritability, and/or a red skin rash with small pimples. Developmental delay may become obvious at several months of age. The average IQ of untreated children is usually less than 50, and intellectual disability in PKU is a direct result of elevated levels of phenylalanine in the brain that causes the destruction of the fatty covering (myelin) of individual nerve fibers. It can also cause depression by reducing brain levels of dopamine and serotonin (neurotransmitters).

Untreated infants with PKU tend to have unusually light eyes, skin, and hair color due to high phenylalanine levels interfering with production of melanin, a substance that causes pigmentation. They may also have a musty or “mousy” body odor caused by phenylacetic acid in the urine and sweat.

Neurological symptoms are present in some untreated patients with PKU, including seizures, abnormal muscle movements, tight muscles, increased reflexes, involuntary movements, or tremor.

Untreated females with PKU who become pregnant are at high risk for having a miscarriage or problems with fetal growth (intraterine growth retardation). Children of women with untreated PKU may have an abnormally small head (microcephaly), congenital heart disease, developmental abnormalities, and/or fetal abnormalities. There is a strong relationship between the severity of these symptoms and high levels of phenylalanine in the mother. As a result, all women with PKU who have stopped treatment should resume treatment before conception and continue it throughout the pregnancy, which should be managed by a metabolic geneticist and dietician.
Meet PKU Warrior DIONE

My name is Dione Goodreau. I'm a 32-year-old female with PKU working as a Transportation Manager for Pepsi Beverages Company. I have been in the field of logistics and supply chain since graduation college in 2008. I'm a board member for the Michigan PKU Organization as well, and have been spending a lot of time commuting with other adults with PKU who have stepped out from home to be a voice among many.

I was born in Germany in 1986, and the fact that newborn screening was being practiced there at that time is an incredible blessing. I wouldn't be here today without my parents who did something even then. I've worked hard to make sure I grew up healthy. Growing up in my family I was the only one with PKU, and I didn't even let that bother me, so the fact that I'm here is 'different.' I didn't care and never let it stop me. I grew up to be a very successful athlete and participated in the 2004 World Synchronized Skating Championships and represented Team USA overseas in many competitions. I studied hard and got a degree in my field of supply chain, and have been working in upper management for 10 years. I got to where I am because I was always represented.

I believe that finding a cure would be an incredible blessing. After your PKU diagnosis, and you're told your phe levels are critical to assure normal development and cognition. The goal of treatment for PKU is to keep plasma phenylalanine levels within 120 μmol/L to 360 μmol/L (2-6 mg/dL). This is generally achieved through a carefully planned and monitored diet. Limiting the child’s intake of phenylalanine must be done cautiously because it’s an essential amino acid. A judiciously maintained diet can prevent intellectual disability as well as neurological, behavioral, and dermatological problems. Treatment must be started at a very young age or some degree of intellectual disability may be expected, although some late-treated children have done quite well. Studies have shown that timely initiation of dietary therapy following the diagnosis of PKU in a newborn infant AND long-term control of plasma phe levels are critical to assure normal development and cognition.

The biggest struggle is formula. Newer options have been available in recent years which is incredible, but none of them come with insurance coverage. And (even) when they do get covered, the other added issue is calorie content. PKU has the highest caloric content of any low protein foods and formulas, it's difficult to manage a healthy diet, calorically speaking, while still managing to keep my phe under control. A healthy caloric content. With the high-calorie content of so many low protein foods and formulas, it's difficult to manage a healthy diet, calorically speaking, while still managing to keep my phe under control.

Lower calorie options for all foods and formulas, and having more of these options covered with the passing of the Medical Nutrition Equity Act. Obviously another thing that would help is to look for a cure, completely eliminating the need for medical foods and formulas all together.

What would help?

1. Lower calorie options for all foods and formulas, and having more of these options covered with the passing of the Medical Nutrition Equity Act.
2. A cure, completely eliminating the need for medical foods and formulas all together.

The reported incidence of PKU from newborn screening programs ranges from one in 13,500 to 19,000 newborns in the United States. PKU affects people from most ethnic backgrounds, although it is rare in Americans of African descent and Jews of Ashkenazi ancestry.

What is PKU?

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Causes

PKU is inherited in an autosomal recessive pattern. Recessive genetic disorders occur when an individual inherits an abnormal gene from each parent. If an individual receives one normal gene copy and one abnormal gene copy, they will be a carrier for the condition, but will not have symptoms. The risk for two carrier parents to both pass the abnormal gene and, therefore, have an affected child, is 25% with each pregnancy. The risk is the same for males and females.

More than 1,000 different changes (mutations) in the PKU gene have been identified. Because the different mutations result in varying degrees of PAH enzyme activity, and therefore varying degrees of phenylalanine elevation in blood, the diet of each child must be adjusted to the individual’s specific phenylalanine tolerance.

Affected Populations

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Standard Therapies

TREATMENT

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If people with PKU stop controlling their dietary intake of phenylalanine, neurological changes usually occur. IQs may decline. Other problems that may appear and become severe once dietary regulation is stopped include difficulties in school, behavioral problems, mood changes, poor visual-motor coordination, poor memory, poor problem-solving skills, fatigue, tremors, poor concentration, and depression, to name a few.

After years of controversy, today there is nearly universal acceptance among clinicians that the diet needs to be continued indefinitely, and that adults with PKU who stopped the diet in childhood or beyond should return to the diet. Many adults have restarted the diet and found improvement in mental clarity as a result of lowered phenylalanine levels in their blood.

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Meet PKU Warrior KAY

KAY

I am Kay Mueller Emerson and I have PKU. My older brother, Keith, and I were born before newborn screening. Keith was diagnosed with PKU a few months before I was born, which is why the doctors were waiting to test me as soon as I was born. I was put on the diet from birth until I was 10 years of age. I was the first person treated for PKU in the state of Wisconsin and one of the first early treated in the United States. It is for this reason my diet was very closely monitored and extremely strict. Yet with all this I felt very blessed. I was getting the very best care available at the time. My mother always made me feel proud of my PKU and my diet. She took what little she had to work with and made it quite spectacular. The cookies I took to school for milk-and-cookie time were always nicely decorated and very memorable. It was when I returned to the diet 32 years later that I realized how much love and care she put in all that she did.

I was an active child who loved ballet, tap, and swimming. I attended day camp every summer, both on and off the diet. I had very few problems with the diet while growing up; my problems occurred when I was taken off the diet. I was always a fussy eater, but the high-protein food was even harder for me to eat. When it came to drinking cow’s milk, I hit a few bumps along the way because I really hated it. My mother and I fought over it every day. We discovered a solution when I was sick around Christmas one year. My mother offered me egg nog and I loved it. She even found egg nog crystals to add to my milk. As a teen I started giving speeches and demonstrations to my peers about PKU. This started my education at the clinic on how to be in the public eye and prepare me for a future where I can represent the PKU community.

After graduating high school I entered the Edgewood College education program. While in college, I discovered I have a real gift for foreign language and a natural talent for the piano. On May 15, 1982 I graduated Edgewood with a BS in education and a minor in psychology. Soon after I graduated college I met David Emerson and we married a year later. I taught in the Madison, Wisconsin area preschool systems for more than 20 years. In 2011 I returned to the diet for life. I am now an administrator of two blogs on Facebook: Glass Half Full, a blog about the positive side of life and the world around us and Katie’s Kitchen, featuring PKU and non-PKU recipes and menus. I enjoy sewing by hand, needlework, and reading.

What is PKU?

Because phenylalanine occurs in practically all natural proteins, it is impossible to adequately restrict the diet using natural foods alone without compromising health. For this reason, special phenylalanine-free food preparations are helpful. Foods high in protein, such as meat, milk, fish, and cheese are typically not allowed on the diet. Naturally low-protein foods such as fruits, vegetables, and some cereals are allowed in limited quantities.

In 2007 Kuvan® (sapropterin dihydrochloride) was approved by the FDA to treat PKU. Kuvan, an oral pharmaceutical formulation of BH4, is the natural cofactor for the PAH enzyme. It stimulates activity of the residual PAH enzyme to metabolize phenylalanine into tyrosine, and should be used in conjunction with a phenylalanine-restricted diet. Kuvan is manufactured by BioMarin Pharmaceutical Inc.

In 2018, Palynziq® (pegvaliase-pqpz) was approved by the FDA for adults with PKU. Palynziq is an injectable enzyme therapy for patients who have uncontrolled blood phenylalanine concentrations on current treatment; it is also manufactured by BioMarin Pharmaceutical Inc.

Investigational Therapies

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov. All studies receiving US government funding, and some supported by private industry, are posted on this government web site.

For information about current clinical trials being conducted at the NIH Clinical Center in Bethesda, MD, contact the National Institutes of Health (NIH) Patient Recruitment Office:

Toll-free: (800) 415-1222
TTY: (866) 415-1010
Email: prpl@cc.nih.gov

Current clinical trials are also posted on the NORD website:

www.rarediseases.org

For information about clinical trials sponsored by private sources, contact: www.centerwatch.com

For information about clinical trials conducted in Europe, contact: www.clinicaltrialsregister.eu
Meet PKU Warrior DAVID

My name is David Van Buren. I am 59 years old and I have classic PKU. I have a 61-year-old brother and two grandchildren, ages 5 and 7, and they have it, too.

When I was born in 1959 the medical community didn’t know what PKU was, let alone how to test for it. In 1961 my sister was born and the doctors tested her using the wet diaper test because the Guthrie test did not exist. She was negative and everyone was relieved. The doctors had observed me many times and said I was not exhibiting any symptoms of PKU and that I didn’t need to be tested, but my mother had me tested and I was positive. I was put on the PKU diet.

I was taken off the diet when I was 5; at that point I ate anything a non-PKU kid would eat and I remained untreated for 47 years! I returned to the diet and began to manage my PKU when my granddaughter was born; I wondered how my life would have been if I had stayed on the diet all those years.

Today I am living life as an adult with PKU. I am struggling with the same things we all struggle with and I am seeking ways to support anyone with PKU. I hope my story can encourage and enlighten because NO ONE IS IN THIS ALONE!

Who we are: THE NATIONAL PKU ALLIANCE (NPKUA)

The National PKU Alliance (NPKUA) works to improve the lives of individuals with PKU and to pursue a cure. The organization was created in 2008 by local groups of PKU families all over the country who recognized the importance of a national agenda to serve the PKU community in research, advocacy, education, and support.

IN THE LAST DECADE, THE NPKUA HAS:

- Invested more than $3 million in research, which has led to new scientific knowledge about PKU and accelerated the development of new treatments and a potential cure
- Connected the PKU community through a biennial patient conference, which attracts more than 600 attendees each year
- Launched the PKU Patient Registry to accelerate research and understanding of PKU
- Provided support to adults wanting to return to treatment
- Assisted women with PKU with the maternal PKU mentoring program and emergency assistance program
- Advocated successfully with the FDA and NIH on the unmet medical needs in PKU and the importance of new treatments and a cure
- Advanced technological innovation in the development of a home phenylalanine meter to improve treatment
- Acted as the central source of scientifically based information on PKU for the patient community

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**Clinical Story**

The PKU Patient Registry, powered by Nord, was designed to facilitate further research into PKU by providing insight into patient demographics, family history, genetics, diagnosis, treatment, clinical results, and disease burden. The 525 patients contributing to the registry as of September 2018 resided in 43 US states, Conada, China, the United Kingdom, Australia, Germany, Belarus, Belgium, France, Ireland, Japan, Mexico, the Netherlands, Norway, Paraguay, Switzerland, Turkey, or Uruguay. The registry population averaged 17 years old, with a range in age from newborn to 66 years, and was predominantly female (59%) and Caucasian (96%). Most (82%) patients had commercial insurance coverage and the rest were covered by government-sponsored plans.

When left untreated, patients with PKU are at risk of developing severe neurological complications, including IQ loss, memory loss, concentration problems, mood disorders, and, in some cases, significant intellectual delay. Damage is irreversible, so early detection is crucial. Patients in the registry were largely diagnosed via newborn screening, with only 5% (19/389) detected later in life. Common comorbidities include anxiety (43%) and depression (26%). 53% of those with anxiety stated it is a current problem, while 47% of those with depression said that is a current problem.

PKU may be treated by a diet low in phenylalanine and high in tyrosine. When treatment is begun early (within the first few weeks of life) and rigorously adhered to, affected children can expect good development and a normal life span. Of those in the registry, 76% of patients rated their health as very good or excellent, and 92% reported they are currently on a PKU diet, the most common of which was low protein (82%). Challenges in insurance coverage, however, for medical and low-protein foods, is a current problem, while 47% of those with depression said that is a current problem.

Prior to pregnancy, my levels were not 2-6 mg/dl and I often wondered if having healthy children was even a possibility for me. Through the support of my family and wonderful doctors, together with my own self-discipline and dedication, I was able to lower my levels and have my Healthy babies. My PKU diet on top of that and it took my pregnancies to another level. Because my PKU was so well controlled, I was able to have a baby and wasn’t on bedrest, and hospitalizations to prevent preterm labor, my pregnancies were far from easy. Throw managing my PKU diet on top of all that and it took my pregnancies to another level.

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Meet PKU Warrior LINDA

Hello, my name is Linda Cywin. I am 1 of 4 children and 3 of us have PKU. I was 6 months old when I was diagnosed with PKU and I was put on the diet until I was 8 years old. Back then the diet was very hard because everything had to be counted and the (milk) formula tasted so nasty. My father used to put maple syrup in it to get me to drink it. It’s amazing all the different things to treat PKU and all the research being done to help us to treat it the way that is best for us.

I had a huge issue with my levels when I was first on the study; they were very high (30), and it was extremely difficult to deal with. So I was well worth the energy to do this. I once told a patient I spoke in the FDA about getting Palynziq approved, and I am proud to say that it was approved on May 4, 2018. It was an honor to tell the FDA that those of us with PKU need and deserve to have something that would allow us to live a normal life.

I had the pleasure of being in a study for Palynziq® for 7 years to help those of us with PKU be able to live a more normal life. We were taught that if we were given the medication a little at a time, it was much better than giving it all in one dose, as I had once experienced a 10-day reaction which included hives, itching, swelling, and pain in both my hands and feet. It was easily fixed by Benadryl and a week’s respite from the meds before slowly re-introducing them back into my body so it was not such a shock to my immune system.

Linda

NPKUA is a vital voice within, and on behalf of, the PKU community. We serve a dual mission: to improve the daily lives of those individuals and families affected by PKU, and to accelerate the timeline for a cure by investing in peer-reviewed and targeted research.

With continued data collection from the NPKUA registry, awareness of issues around insurance coverage and the burden of disease will increase.

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