NUTRICIA

MATERNAL PHENYLKETONURIA

FACT SHEET

Elizabeth, Mom with PKU

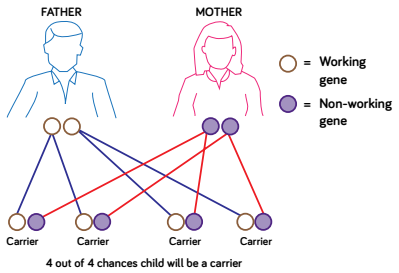
This fact sheet is for educational purposes only. An experienced healthcare professional should be consulted for the management of PKU, both before and during pregnancy.

What is Maternal PKU?

Phenylketonuria (PKU) is an inherited metabolic disorder that causes a person to have high levels of the amino acid phenylalanine (PHE) in the blood. When a person with PKU becomes pregnant this is referred to as maternal PKU. Persons with PKU cannot break down dietary PHE, a component of food proteins. PKU can be screened for at birth through a simple blood test, referred to as newborn screening. Early intervention with a PHE-restricted diet prevents the intellectual and developmental disability seen in individuals who are not managed adequately by diet. It is estimated that one out of 10,000 live births has decreased activity of phenylalanine hydroxylase (PAH),[1] the enzyme deficient in PKU.

Inheritance with Maternal PKU

Possible outcomes for each child if father is **not** a carrier

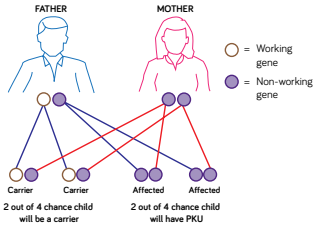


With proper dietary management individuals with PKU can have healthy children. During pregnancy, PHE readily passes from the mother to the developing baby through the placenta. In the baby, high PHE levels interfere with normal growth and development. About 90% of babies born to mothers with prolonged high PHE levels of greater than 600 µmol/L (10 mg/dL) during pregnancy have intellectual and developmental disability. Most have a small head size and low birth weight.[1] Many have heart defects. These findings in an infant are referred to as Maternal PKU Syndrome. Thus, high PHE levels can cause lifelong damage to the baby. It is important for the health of the unborn baby that an individual with PKU is on a strict PKU diet, ideally before conception and throughout pregnancy.

PAH deficiency most accurately describes the range of clinical phenotypes* ranging from classic PKU to hyperphenylalaninemia. Based on the American College of Medical Genetics and Genomics (ACMG) guidelines, PAH deficiency is the term that will be most likely used.

Inheritance with Maternal PKU

Possible outcomes for each child if father **is** a carrier



Can a person with PKU give birth to a healthy baby?

The best outcomes for babies have been in mothers who are on a PHE-restricted diet and in good metabolic control prior to pregnancy.[2] Recommendations are to obtain a maternal PHE level below 360 µmol/L (6 mg/dL) prior to conception and to maintain a PHE level below 360 µmol/L throughout pregnancy.[2] Studies have shown that when PHE levels are within ranges recommended above, babies born to persons with PKU are as likely to be healthy as babies born to persons without PKU.

Should a person with PKU go on a PHE-restricted diet if she is already pregnant?

The sooner a person with PKU starts on a PHE-restricted diet and has PHE levels in the recommended range during pregnancy, the higher the chances are of having a child unaffected with maternal PKU syndrome. For this reason, it is very important for an individual with PKU to reach out immediately to her metabolic team as soon as she finds out she is pregnant. Ideally, a planned pregnancy is best to allow for preconception PHE control.

A PHE-free or low-PHE metabolic formula provides the majority of the body's required protein for patients with PKU. In the first trimester, protein intake is going to be connected to the baby's birth measurements; e.g. head circumference, body length and weight. Protein and calorie intake have a direct relationship to the head circumference of the baby.[3]

Eating too little protein or too few calories can cause the breakdown of protein in the body (i.e. catabolism) which will increase PHE levels. Every PHE-free or low-PHE metabolic formula has a different amount of protein and calories; therefore an individualized diet prescription is necessary.

Nutricia North America provides a range of medical formulas for PKU. Please contact us for more information. Your dietitian will help you decide which products are best for you.

***Phenotype** - observable traits, outward appearances, development or behavior

Will a baby born to a person with PKU also be diagnosed with PKU?

Having maternal PKU does not mean the baby will have PKU. In order for the baby to have PKU, the father must be a carrier of the PKU gene as well. Please refer to the two pictograms on page one.

Does a person with "mild" PKU have to be managed with diet during pregnancy?

Hyperphenylalaninemia, sometimes referred to as "mild PKU" is differentiated from classic PKU in that the genetic defect is milder and more enzyme activity is available. Some individuals with hyperphenylalaninemia can maintain acceptable levels of blood PHE without being on a strict PHE-restricted diet. The reason is that individuals with mild hyperphenylalaninemia may have small amounts of PAH activity that helps break down PHE. However, some individuals with mild hyperphenylalaninemia may have elevated blood PHE levels which require a special PKU diet. It is important to talk with your metabolic team and prenatal care providers (e.g. obstetrician, midwife, family practice physician or general practice physician) about the best course of management for you.

What is the role of the prenatal health care provider in the management of maternal PKU?

It is important for an individual with PKU to share her knowledge of PKU with her prenatal health care provider (HCP), if possible before pregnancy, as many prenatal HCPs are not familiar with PKU. The prenatal HCP will help manage the pregnancy and provide prenatal care. They will work closely with the patient and her metabolic team in order for her to have a healthy baby. Attaining good control of blood PHE levels before and during the pregnancy is ideal; the metabolic team can help provide the necessary guidance to the obstetrician or other prenatal care provider.

The metabolic clinic professionals are able to help people with PKU have healthy babies. It is best to be seen by the metabolic team before pregnancy occurs to help facilitate a healthy pregnancy and outcome. Regular obstetrician visits will be necessary for routine pregnancy care. Before pregnancy it is important to continue birth control until blood PHE levels are considered safe enough to become pregnant.

Are there any special recommendations for maternal PKU from an obstetric point of view?

For any maternal PKU pregnancy, periodic ultrasound examinations and a fetal echocardiogram are recommended given there is a risk of congenital heart disease. Generally the echocardiogram is performed between 18 and 22 weeks of pregnancy. Serial ultrasound examinations to monitor general fetal growth and to check the growth of the head of the unborn baby into the third trimester are also recommended. If there is a problem with growth of the head, it may not be seen until the third trimester of pregnancy. Otherwise prenatal care is no different from that of other pregnant person. Additional routine prenatal testing as suggested for all pregnancies is also recommended.

What should a person with PKU do to plan for a pregnancy?

- Contact the metabolic clinic for consultation.
- Consult with the metabolic dietitian to assess diet management and reduce blood PHE levels.
- Contact the prenatal healthcare provider.

If an individual has been off diet, time and patience may be necessary to initiate dietary care, obtain PHE levels, obtain formula and low protein products and coordinate insurance coverage for all aspects of needed care.

What if there are other questions about maternal PKU? The metabolic clinic staff is the best resource for helping plan for a healthy pregnancy.

Phlexy-10 Tablets only available in the US

Nutricia North America would like to thank Laurie Bernstein, MS RD FADA, Children's Hospital Colorado for her consultation.

Questions about PKU Formula Coverage?

NUTRICIA NAVIGATOR

800-365-7354

Coverage@Nutricia.com

For more information or product samples, please visit **NutriciaMetabolics.com** or call US: **(800) 365-7354**

All products shown are medical foods in the US and foods for special dietary use in Canada for the dietary management of phenylketonuria (PKU) and must be used under medical supervision.

References

1. Vockley, et al. Genet Med. 2014;16(2):188-200. **2**. Koch, et al. Molecular Genetics and Metabolism. 2000;71(1-2):233-9. **3**. Borazjani, et al. J Health Popul Nutr. 2013;31(4):435-445.

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