PHENYLKETONURIA AND PREGNANCY

Part I: General Information

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Update A Fact Sheet
for Practitioners

What Is Phenylketonuria (PKU)?

Phenylketonuria (PKU) is an inborn error in the metabolism of the amino acid phenylalanine (PHE). It results from an absence or decreased activity of the enzyme phenylalanine hydroxylase. Untreated PKU causes mental retardation. However, routine newborn screening and immediate initiation of rigorous treatment with a low phenylalanine diet can prevent disabilities associated with PKU, including mental retardation, ADHD, and seizures.

Dietary treatment requires the use of a synthetic medical food (formula) as the primary source of protein. The formula limits PHE intake, but still provides enough PHE for growth and development. The goal of treatment is to maintain serum PHE levels of 2-6 mg/dl in order to support normal cognitive development and functioning. Lifelong treatment is required for an individual with PKU.

What is Maternal PKU?

An elevated maternal level of Phenylalanine that causes damage to a developing fetus is termed "maternal PKU." The term refers to the cause of the damage, rather than to the features of the damage.

There is a 1:1.5 gradient of PHE across the placenta. Thus, the fetus is exposed to a higher concentration of PHE than that which exists in maternal blood. Because of this gradient, serum PHE levels that are safe for adults are harmful to the fetus. The higher the serum PHE concentration, the greater the degree of damage to the fetus.

What are the effects of untreated or poorly treated Maternal PKU on reproductive outcomes?

Elevated maternal serum PHE levels may cause spontaneous abortion, microcephaly, congenital cardiac anomalies, poor intrauterine growth, and mental retardation. Serum PHE levels at the time of conception and in early pregnancy are the most critical to the organ development of the fetus.

What is the intellectual development of children of women with PKU?

The intellectual development of children whose mothers have PKU appears to be directly related to maternal serum PHE levels. The Maternal PKU Collaborative Study provides some data about intellectual development:

- Almost 100% of the children whose mothers had serum PHE levels of > 20 mg/dl were mentally retarded.
- More than 20% of the children of women who had serum levels between 3-10 mg/dl were mentally retarded. (This is higher than the expected frequency of mental retardation of 3% in the general population.)

There is little data on the intellectual development of children whose mothers had

serum PHE levels of 1-4 mg/dl throughout pregnancy because few women were able to achieve and maintain these low levels.

Who is at increased risk for having a baby damaged because of elevated maternal PHE levels?

Any woman who has serum PHE levels greater than 6 mg/dl—even if she does not herself carry the diagnosis of PKU—is at risk. (This includes women with "hyperphenylalaninemia.")

Can a woman with PKU be treated to improve reproductive outcomes?

Yes. If maternal serum PHE levels are <4 mg/dl prior to conception and during pregnancy, the risk to the fetus is decreased. However, the risk of damage to the fetus cannot be entirely eliminated by treatment during pregnancy.

What is the treatment during pregnancy for women with PKU?

Nutritional management is the key to pregnancy treatment for women with PKU. "Safe" maternal serum PHE levels, combined with adequate nutrition during pregnancy, cannot be achieved without the use of medical food (formula), and formula is essential to healthy maternal weight gain. Formula should provide 80-90% of protein and energy intake during pregnancy.

Optimum management of PKU for a pregnant woman requires huge emotional, physical and financial commitments by the woman and is extremely labor-intensive for her health care providers. Optimum management begins months before conception. It is important for any woman with PKU who is contemplating pregnancy to understand that optimum management will lower the chance that her baby will be born with damage because of her PHE levels, however all babies still have a small risk for birth defects.

What is a Reasonable Management Algorithm for Women with PKU?

If not pregnant and prefers not to become pregnant:

- discuss risks of pregnancy
- provide birth control options
- discuss options for family planning... surrogate mother, adoption

If not pregnant and wishes to become pregnant:

- counsel about reproductive risk
- describe treatment protocol and goals
- discuss costs of medical care
- describe risks to the fetus even with excellent control of serum PHE levels
- consider blood draws for PHE levels and initiate diet to control PHE levels

If pregnant, immediate action is required:

If a woman with PKU is pregnant and the pregnancy is not planned, this is a medical crisis because each day of high maternal serum PHE levels can cause further damage to the developing fetus.

- refer to metabolic genetics clinic for counseling regarding risks and outcome
- refer to high risk pregnancy clinic or perinatologist for coordination of services between metabolic nutritionist and perinatologist for high risk obstetrical care
- discuss cost of formula, maternal medical care, and infant medical care

If pregnancies are not planned and rigorous treatment is not followed, the number of infants born with mental retardation will erase the public health benefit of newborn screening.

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Resources

National PKU News Webpage – *http://www.pkunews.org*

University of Washington PKU Program – *http://depts.washington.edu/pku/*

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