Phenylketonuria (PKU) is a spectrum of disorders that result in elevated levels of the amino acid phenylalanine with an incidence ranging from 1:13,500 to 1:19,000 births. It is an autosomal recessive metabolic disorder, most commonly the result of deficiency of the enzyme phenylalanine hydroxylase, which converts phenylalanine to tyrosine; however, in a minority of cases it is the result of a deficiency of the cofactor tetrahydrabiopterin. Enzyme deficiency can range from complete (“Classic PKU”) with untreated phenylalanine levels >20 mg/dL (>1200micromol/L) to “Mild PKU” where some enzyme is present and untreated phenylalanine levels range from 10-20 mg/dL (600-1200 micromol/L). “Non-PKU Mild Hyperphenylalaninemia” results in mildly elevated untreated levels of 2-10 mg/dL (120-600 micromol/L) and often does not require dietary modification.

The teratogenic effect of maternal PKU is actually a testament to the success of the newborn screening program and dietary modification for affected newborns. This early intervention has allowed normal growth and development in those affected by this inborn error of metabolism. Prior to the introduction of newborn screening and institution of a phenylalanine free diet, elevated levels of phenylalanine resulted in devastating effects on affected children, preventing them from ever achieving their intellectual, developmental, and reproductive potential. Strict adherence to the “PKU diet” is advised for all affected infants and children, as it prevents the profound mental retardation seen in uncontrolled hyperphenylalaninemia. However, many young women discontinue the cumbersome diet restrictions as they gain increased...
independence in their teenage years. Unfortunately, this is a time period when many unplanned pregnancies occur. The teratogenic effects of high phenylalanine levels on a developing pregnancy are profound with increased risk of fetal loss, fetal congenital anomalies (most commonly cardiac defects, microcephaly, and mental retardation), and abnormal fetal growth. Most important, the untoward outcomes of poorly controlled maternal PKU are preventable!

- Primary care physicians, geneticists, nutrition specialists, and others who care for adolescents and women with PKU are in a unique position to assist them in optimizing their pregnancy preparation and preventing these significant birth defects. Here, we endeavor to provide front-line practitioners who care for adolescents and women affected by PKU with evidence based preconception guidelines with a goal of enabling the pregnant woman to present for her first prenatal visit with optimized phenylalanine levels allowing for the greatest reduction in risk of congenital anomalies and other related poor pregnancy outcomes.

Counseling and Care Guidance

- Family Planning is crucial. At each visit, from before menarche until sterilization is induced or menopause is complete, female patients should be evaluated for risk of pregnancy, and effective contraception should be encouraged and offered.
- Smoking cessation
- Assess alcohol consumption
- Folic acid supplementation should be prescribed. Primary prevention of neural tube abnormalities involves supplementation with 1mg of folic acid each day for 3 months prior to conception. Women with a previously affected fetus, those with a family history, and women with seizure disorder treated with valproic acid or carbamazepine should supplement with 4mg folic acid per day.
- Referral to a genetic counselor to discuss the inheritance of PKU.
- Referral to a nutrition specialist who is familiar with PKU to provide counseling on the PKU diet and assist in obtaining nutritional supplement formula and monitoring overall maternal nutritional status.
- **Three months prior to conception**, assure strict adherence to the PKU diet, which is phenylalanine free, with a goal phenylalanine level of <6 mg/dL (360micromol/L). Once dietary compliance is initiated, phenylalanine levels should fall within the goal range in 5-7 days. Phenylalanine levels should be maintained within the goal range of 2-6 mg/dL (120-360 micromol/L) throughout pregnancy.
- Tyrosine supplementation should be provided if levels are below the goal of 0.9-1.8 mg/dL.
• Aside from the genetic implication of potentially affected offspring (PKU follows an autosomal recessive inheritance pattern) paternal PKU does not result in congenital defects.
• Per ACOG bulletin 230 – “Ideally, pregnant women with PKU should be managed in consultation with practitioners from experienced PKU centers.”


• Women of reproductive age with phenyletonuria should be counseled about the importance of maintaining low phenylalanine during their child-bearing years and should be encouraged to resume a low phenylalanine diet, particularly when they are planning to become pregnant, to avoid adverse outcomes for the offspring. Women who do not desire a pregnancy should be encouraged to use contraception.

Strength of recommendation: A; quality of evidence: II-1.

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