Disease Name	**Phenylketonuria**
Alternate name(s)	Hyperphenylalaninemia, Phenylalanine hydroxylase deficiency, Følling disease
Acronym	PKU
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	Benign phenylketonuria, Mild phenylketonuria, Variant phenylketonuria, Biopterin-responsive phenylketonuria Tetrahydrobiopterin deficiencies: GTP cyclohydrolase I deficiency, 6-Pyruvoyl-tetrahydropterin synthase deficiency, Dihydropteridine reductase deficiency, Pterin-4_-carbinolamine dehydratase deficiency
Symptom onset	Infancy
Symptoms	Mental delays, decreased pigmentation relative to family members, eczematous rash, seizures, abnormal gait, and unusual “mousy” odor to urine.
Natural history without treatment	Mental delays in the moderate to severe range, hyperactivity, eczema, mild neurologic manifestations, possible abnormal gait microcephaly.
Natural history with treatment	If diet instituted early, normal IQ and development can be expected.
Treatment	Dietary restriction of phenylalanine with supplementary formula for tyrosine and essential amino acids.
Other	“Mousy” or “musky” smelling urine. Females with PKU are at-risk to have children affected by maternal PKU (increased levels of phenylalanine are teratogenic).
Physical phenotype	No abnormalities present at birth. May develop widely-spaced incisors, pes planus, epicanthus and microcephaly.
Inheritance	Autosomal recessive
General population incidence	1:10,000
Ethnic differences	Yes
Population	Turks, Irish
Ethnic incidence	Turks (1:2600), Irish (1:4500)
Enzyme location	Liver
Enzyme Function	Converts phenylalanine to tyrosine
Missing Enzyme	Phenylalanine hydroxylase
Metabolite changes	Increased plasma phenylalanine, increased phenylpyruvic acid in urine, decreased plasma tyrosine.
Prenatal testing	DNA testing is possible if mutations known. RFLP analysis is successful in 75% of families.
MS/MS Profile	N/A
OMIM Link	http://www.ncbi.nlm.nih.gov/omim/261600
Genetests Link	www.geneclinics.org
Support Group	National Urea Cycle Disorders Foundation http://www.nucdf.org National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

Newborn Screening ACT Sheet
[Increased Phenylalanine]
Phenylketonuria (PKU)

Differential Diagnosis: Phenylketonuria (Classical PKU); non-PKU mild hyperphenylalaninemia; pterin defects; transient hyperphenylalaninemia.

Condition Description: In PKU the phenylalanine from ingested protein cannot be metabolized to tyrosine because of deficient liver phenylalanine hydroxylase (PAH). This causes elevated phenylalanine. Pterin defects result from deficiency of tetrahydrobiopterin (BH4), the cofactor for PAH and other hydroxylases. This produces not only increased phenylalanine but also neurotransmitter deficiencies.

YOU SHOULD TAKE THE FOLLOWING ACTIONS IMMEDIATELY:

- Contact family immediately to inform them of the newborn screening result.
- Consult with pediatric metabolic specialist.
- Evaluate the newborn and refer as appropriate.
- Initiate confirmatory/diagnostic tests in consultation with metabolic specialist.
- Provide the family with basic information about PKU and dietary management.
- Report findings to newborn screening program.

Diagnostic Evaluation: Plasma amino acid analysis which shows increased phenylalanine without increased tyrosine (increased phenylalanine:tyrosine ratio). Urine pterin analysis and red blood cell DHPR assay will identify pterin defects. Consider PAH mutation testing.

Clinical Considerations: Asymptomatic in the neonate. If untreated PKU will cause irreversible mental retardation, hyperactivity, autistic-like features, and seizures. Treatment will usually prevent these symptoms. Pterin defects cause early severe neurologic disease (developmental delay/seizures) and require specific therapy.

Additional Information:

Gene Reviews
Genetics Home Reference
Clinical Services
PKU
Tetrahydrobiopterin Deficiency

Referral (local, state, regional and national):

Testing
Clinical Services