Genetic Diseases of Phenylalanine Metabolism

Phenylketonuria (PKU)
12q22-q24
OMIM 261600
• 1/12,000 births
• irreversible psychomotor retardation
• autistic behavior
• seizures
• microcephaly
• mousy odor to urine

Tyrosinemia Type II (Richner-Hanahart Syndrome)
16q22.1-q22.3
OMIM 276600
• high levels of tyrosine in urine and blood
• oculocutaneous symptoms in early infancy: corneal erosions, ulcerations, opacities, and plaques
• blisters and erosions on palms and soles
• some have psychomotor retardation

Tyrosinemia Type III
12q24-qter
OMIM 276710
• elevated levels of tyrosine in blood
• massive excretion of tyrosine and derivatives in urine
• mild retardation
• possible convulsions
• no liver damage
• autosomal recessive but there is also a dominant HPD mutant that causes Hawkinsinuria

Hawkinsinuria
12q24-qter
OMIM 140350
• dominant mutation of HPD
• appearance of a novel sulfur aminoacid (hawkinsin) in urine
• “swimming pool” odor to urine
• failure to thrive

Transient Neonatal Tyrosinemia, Scurvy
• 10% of premature births
• more common in pop with low breast feeding and increased formula use
• physiological immaturity of enzyme
• lethargy
• prolonged jaundice
• feeding problems
• many patients respond to vitamin C and low protein

Alkaptonuria (AKU)
3q21-q23
OMIM 203500
• 1/200,000 births
• excess homogenistic acid in urine, turns black upon oxidization
• ochronosis - pigment derived from homogenistic acid polymer deposited in cartilage, joints, sclera (age 20-30)
• arthritis-like stiffness mistaken for rheumatoid arthritis and osteoarthritis
• narrowing and increased calcification of intervertebral disk space

Tyrosinemia Type I
15q23-q25
OMIM 276700
• 1/100,000-1/120,000 births
• progressive liver dysfunction
• cabbage odor to urine
• treat with lower phe, tyr

Albinism