Inborn Errors of Amino Acid Metabolism : Caused by enzyme loss or deficiency due to gene loss or gene mutation					
Diseases	**Phenylketonuria (PKU)** *most common*	**Maple Syrup Urine Disease** ***rare***	**Albinism**	**Homocystinuria**	**Alkaptonuria** ***rare***
Definition	**(Defect in phenylalanine metabolism)** , conversion of phenylalanine to tyrosine require : - phenylalanine hydroxylase -tetrahydrobiopterin	**(failure of decarboxylates alpha ketoacid :leucine, isoleucine and valine)**	**Defect in tyrosine metabolism**	**defects in homocysteine metabolism**	**Defect in tyrosine degradation**
Causes	**1-Classic PKU:** Due to deficiency of phenylalanine hydroxylase enzyme, so phenylalanine accumulation. **2-Atypical hyperphenylalaninemia :** Due to deficiency of BH_4. Caused by the deficiency of: - Dihydropteridine reductase - Dihydrobiopterin synthetase - Carbinolamine dehydratase	**1-Classic type:** Most common, due to little or no activity of a-ketoacid dehydrogenase **2-ntermediate and intermittent forms**: higher enzyme activity, symptoms are milder **3-Thiamin-responsive form**: High doses of thiamin increases a-ketoacid dehydrogenase activity	Due to tyrosinase deficiency which is **important** to convert tyrosine to melanin. Tyrosine is involved in melanin production. Melanin is a pigment of hair, skin, eyes Melanin is absent in albino patients.	Deficiency of cystathionine beta-synthase (which convert homocysteine to cystathionine.) lead to: -**homocystinuria** -**homocysteinemia**.	Due to deficiency of homogentisic acid oxidase

Characteristic And Symptom	-Tyrosine will not converted to catecholamine , tryptophan will not converted to serotonin Because both are require BH_4. -↑ phenylalanine in tissue , plasma and urine → Phenylalanine is degraded to phenyllactate, phenylacetate, and phenylpyruvate → Gives urine a **mousy color**. **CNS symptoms**: Mental retardation, failure to walk or talk , seizures, etc. **Hypopigmentation:** .fair hair , light skin color and blue eyes -Deficiency of melanin -Hydroxylation of tyrosine by **tyrosinase** is inhibited by high phenylalanine conc.	These amino acids and their alpha ketoacid accumulate in blood. **Symptoms**: Mental retardation, physical disability, metabolic acidosis, etc. **Maple syrup odor of urine.**	- Hair and skin appear **white** - Vision defects, **photophobia**.	↑homocysteine and methionine and ↓level of cysteine in plasma and urine. → homocysteine is a risk factor for **vascular disease** (atherosclerosis and heart disease) and skeletal abnormalities , osteoporosis, mental retardation, displacement of eye lens. - Can associated with Neural tube defect (spina bifida)	- Homogentisic aciduria: ↑ homogentisic acid in urine which is oxidized to dark pigment over time. - Arthritis, - black pigmentation of cartilage and tissue - Usually **asymptomatic** until adulthood.
Enzymes Deficiency	**phenylalanine hydroxylase**	**Branched chain alpha ketoacid dehydrogenase**	**Tyrosinase**	**cystathionine beta-synthase**	**homogentisic acid oxidase**
Accumulation (substrate)	**phenylalanine**	**leucine, isoleucine and valine**	**Tyrosine and DOPA**	**Methionine and homocysteine**	**homogentisic acid**
deficient (product)	**tyrosine**	-	**Melanin**	**Cysteine**	-

Diagnosis	**Prenatal:** detecting gene mutation in fetus. **Neonatal** in infants: measuring blood phenylalanine levels	-			
Treatment	Life long phenylalanine restricted diet and tyrosine supplementation.	Limited intake of leucine, isoleucine and valine.	-	-oral administration of vitamins B6 (co factor for cystathionine b-synthase) and vitamins B12 and folate -methionine restricted diet.	Restricted intake of tyrosine and phenylalanine