Inborn errors of Amino Acids Metabolism

	Phenylketonuria **(most common)**	Maple syrup urine Disease (rare)	Homocystinurea	Alkaptonuria (rare)	Albinism
Definition	Defect in Phenylalanine Metabolism Phenylalanine → tyrosine → Melanin , tissue proteins , catecholamine tryptophan → serotonin	Failure to decarboxylate alpha-ketoacids : Leucine, isoleucine and valine	Defected Homocysteine metabolism	Defected tyrosine degradation	Defected Tyrosine metabolism
Causes	Classic PKU : deficient Phenyl-alanine hydroxylase Atypical hyperphenyl-alaninemia : Deficient BH4 (coenzyme required for PAH , tyrosine hydroxylase and tryptophan hydroxylase) Caused by deficiency of : . Dihydropteridine reductase . Dihydrobiopterin synthase. . Carbinolamine dehydratase	. Classic type: ↓ or no activity of Branched chain alpha-ketoacids dehydrogenase . Intermediate : some enzyme activity, milder symptoms . . Thiamine responsive : high dose of thiamine ↑enzyme activity	Deficiency of cystathionine beta-synthase which converts homocysteine to cystathionine (an intermediate in the synthesis of cysteine)	Deficiency of homogentisic acid oxidase (homogentisic acid is a tyrosine degradation product will be)	Tyrosinase deficiency which is important to convert tyrosine to melanin (pigment of hair , skin and eyes)

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Characteristics And Symptoms	- ↑ phenylalanine in plasma , tissue , urine and is degraded into ; phenyllactate, phenylacetate and phenylpyruvate → mousy odor urine - CNS symptoms : mental retardation , failure to walk or talk , seizures - Hypopigmentation : ✕ Melanin ↓ Tyrosinase activity by ↑ phenylalanine conc.	Accumulated alpha-ketoacids in blood . Mental retardation . Physical disability . Metabolic acidosis Maple syrup odor of urine.	↑Homocysteine levels in urine and plasma which is a risk factor for vascular diseases .skeletal abnormalities , osteoporosis , mental retardation, displacement of eye lens . Neural tube defect association	.Homogentisic acid is oxidized to dark pigment in urine and gives black pigmentation of tissues and cartilage .Arthritis .Usually stays asymptomatic until adulthood	.White skin and hair . Red eyes with vision defects and photophobia
Diagnosis and Treatment	Diagnosis : Prenatal : detecting gene mutations Neonatal infants : serum Phenylalanine measurement Treatment : Life long phenylalanine restricted diet	Treated with limited intake of leucine , isoleucine and valine.	. Oral administration of VitB6(cofactor enzyme for cystathionine synthase) , VitB12 and folate . . Methionine restricted diet	Restricted intake of tyrosine and phenylalanine	____

Inborn errors of amino acid metabolism caused by enzyme loss or deficiency due to genetic problems and it causes many disorders

Phenylketonuria

It is the most common one and it happens due to deficiency of phenylalanine hydroxylaze (classic type) or due to dificiency in BH4 (atypical type) which is coenzyme.

- Phenylketonuria gives urine mousy odor.

Albinism

Due to deficiency of tyrosinase enzyme, which convert tyrosine to melanin, and melanin.

Alkaptonuria

Rare disease of tyrosin degradation and it is due to deficiency of homogentisic acid oxidase.

Homogentisic usually asymptomatic until adulthood.

Homocyctnuria

Due to deficiency if cyctathionine beta-synthase which converts homocycteine to cyctathione.
High plasma homocyctein will cause atherosclerosis and heart disease.

Maple syrup urine disease

Due to deficiency of branched chain α ketoacid dehydrogenase and It gives maple syrup odor of urine.

It has 3 types:
- classic: due to little or no activity of enzyme.
- intermediate: some enzyme activity.
- thiamin-responsive: high dose of thiamin will cause increase in alpha ketoacid