Inborn Errors of AA Metabolism

Diseases	Characteristics	Types	Symptom	Treatment
1.**Phenylketonuria (PKU)**	Deficiency of phenylalanine hydroxylase enzyme Most common. Results in hyperphenylalaninemia	**1.Classic PKU:** deficiency of phenylalanine hydroxylase **2.Atypical hyperphenylalaninemia:** deficiency of dihydropteridine reductase, dihydrobiopterin synthetase, carbinolamine dehydratase enzymes **Diagnosis:** Prenatal →detecting gene mutation in fetus Neonatal →measuring levels of blood phe	To Convert Phe to Tyr it requires tetrahydrobiopterin (BH_4) + phenylalanine hydroxylase Or Phe will be accumulated Tyr will not be able to convert to: catecholamies nor serotonin (neurotransmitters) as it requires BH_4 also there will be no melanin →albinism	**Symptoms** CNS symptoms: Mental retardation, failure to walk or talk, seizures. Hypopigmentation. Deficiency of melanin. Hydroxylation of tyrosine by tyrosinase is inhibited by high phe conc. ↑phenylalanine in tissues, plasma, urine. Phe is degraded to phenyllactate, phenylacetate, phenylpyruvate →Gives urine a mousy odor **Treatment:** Life long phe-restricted diet
2.**Maple Syrup Urine Disease**	Deficiency of a-ketoacid dehydrogenase. The enzyme decarboxylates leucine, isoleucine and valine. These aa accumulate in blood	**Classic type**: common, due to little or no activity of a-ketoacid dehydrogenase. **Intermediate and intermittent forms**: Some enzyme activity, symptoms are milder. **Thiamin-responsive form**: High doses of thiamin increases a-ketoacid dehydrogenase activity	**Symptoms:** mental retardation, physical disability, metabolic acidosis. Maple syrup odor of urine.	**Treatment:** Limited intake of leucine, isoleucine and valine
3.**Albinism**	Disease of tyrosine metabolism → tyrosinase deficiency	Tyrosine is involved in melanin production→ no Melanin	Hair, skin, eyes appear white. Vision defects, photophobia.	
4.**Homocystinuria**	Defects in homocysteine metabolism by the deficiency of cystathionine b-synthase that converts homocysteine to cystathione →→ ↑plasma & urine lvls of homocysteine	Homocysteine is a risk factor for Vascular disease (atherosclerosis) & heart disease Skeletal abnormalities, osteoporosis, mental retardation, displacement of eye lens, neural tube defect (spina bifida)		**Treatment:** Oral vit of B_6, B_{12} and folate. Vit B_6 is a cofactor of cystathionine b-synthase. Methionine-restricted diet
5.**Alkaptonuria**	Rare disease of tyrosine degradation →Deficiency of homogentisic acid oxidase. Homogentisic acid is accumulated in tissue and cartilage.	**Symptoms:** Homogentisic aciduria. Oxidized to dark pigment in urine over time Arthritis, black pigmentation of cartilage, tissue Usually asymptomatic until adulthood		**Treatment:** Restricted intake of tyrosine and phenylalanine reduces homogentisic acid and dark pigmentation