7- Sulfur containing Amino Acids includes:

Methionine, Cysteine, and Cystine

Methionine is an essential amino acid that is inactive in this form

C-CH2-S-CH3 + and can be activated by reacting with ATP molecule → S-adenosine-methyl group-CH2-CH-C + PP + Pi

So the active form is involved in transamination reactions by giving methyl group:

Norepinephrine + SAM(methyl group) → Epinephrine

Cystine

-C-CH2-S-S-CH2-C $\xrightarrow{\text{Reductase}}$ 2 Cysteine molecules

Methionine $\xrightarrow{\text{demethylation}}$ Homocystine C-CH2-CH2-SH

Homocystine + Serine $\xrightarrow{\text{Vit.B6}}$ Cystine + Homoserine

Metabolism of Cystine:

-C-CH2-SH $\xrightarrow{\text{Deoxygenase(O2)}}$ Cysteine Sulfinate C-CH2SO2H

$\xrightarrow{\text{Transamination}}$ Pyruvate Sulfinate OOC-C-CH2SO2H By $\xrightarrow{\text{Desulfinase(SO2)}}$ Pyruvic acid

or by decarboxylation(CO2 out) will yield Taurine(part of bile salt).

Metabolic Defects:

1. Cystinuria: An inherited disorder characterized by defect of cystine, ornithine, arginine, and lysine(COAL) of which cystine is the most insoluble one, leads to renal stone formation(cystine stone).

2. Cystinosis(cystine storage disease):

It is a defect in the carrier mediated transport of cystine and leads to accumulation of cystine in the tissues such as kidneys resulting in renal failure.

8- Histidine:

It is a semi-essential amino acid, it can be synthesized in a small amount in the body for short periods that are enough to maintain body health in adult but not adequate for children.

Histidine $\xrightarrow{\text{histidase(NH4 out)}}$ Uroconic acid $\xrightarrow{\text{Uroconase(H2O in)}}$ 4-imidazole-5-propionate

$\xrightarrow{\text{Hydrolase}}$ N-formimino glutamate $\xrightarrow{\text{Transferase(TH4 folate)}}$ Glutamate $\xrightarrow{\text{Aminotransferase}}$

α.ketoglutarate(CAC).

Genetic defects in histidase and uroconase results in histidinemia and uroconic aciduria.

9- Phenylalanine:

Phenylalanine amino acid by hydroxylation(hydroxylase) converted to tyrosine in presence of oxygen and tetrahydrobiopterin(TH4 biopterin) and by TH4 biopterin reductase will reduce TH4 to DH2 biopterin.

By transamination phenylalanine is converted to phenyketonic acid (phenyl pyruvic acid), which in turn can be converted to phenyl lactic acid by NADH dependent dehydrogenase, or can be converted to phenyl acetic acid by decarboxylation reaction(decarboxylase).

10- Tyrosine:

It is a non-essential amino acid formed by hydroxylation of phenylalanine.

Tyrosine $\xrightarrow{\text{Aminotransferase}}$ OH-phenylalanine $\xrightarrow{\text{Hydroxylase, Copper, Vit.C, NADH}}$ Homogentistic acid $\xrightarrow{\text{Oxidase(iron)}}$ fumarylacetoacetate $\xrightarrow{\text{Hydrolase}}$ Fumarate + aa

A. Type 1 Tyrosinosis: deficiency of fumaryl acetoacetate hydrolase leads to increase of tyrosine levels in blood, and tissues. Early death may occurs within 6 months in acute cases due to liver failure. Chronic cases may survive till 10 years.

B. Type 2 tyrosine aminotransferase deficiency (Richiner-hanhart disease).

C. Type 3 Neonatal tyrosinemia

D. Type 4 Genetic defect in homogentistic oxidase resulting in Alkaptinuria, an autosomal recessive trait characterized by dark urine when left in air(brownish-black), later leads to achronosis (pigmentation of connective tissue) and arthritis and it is not a life threatening case.

Tyrosine is a precursor of many substances in the body:

1- Tyrosine $\xrightarrow{\textbf{Hydroxylase}}$ Dopa $\xrightarrow{\text{Decarboxylase(CO2 out), vit.B6}}$ Dopamine - $\xrightarrow{\text{Oxidase(O2, copper, vit.C)}}$ Noradrenaline $\xrightarrow{\text{Methylation (active CH3 SAM)}}$ Adrenaline

2- Dopa can give thyroid hormones T3 and T4

3- Dopa also is a precursor of melanin pigment that secreted by skin melanocytes.

11- Tryptophan:

It is an essential amino acid, a precursor of **Niacin (NAD, NADP**), and it was estimated that each 60mg of tryptophan will give 1mg niacin and by this way the need for niacin in diet is reduced.

Tryptophan Metabolism:

Tryptophan $\xrightarrow{\text{Hydroxylase (O2)}}$ 5-OH Tryptophan $\xrightarrow{\text{Decarboxylase(CO2 out)}}$

5-OH Tryptamine(serotonin) $\xrightarrow{\text{Mono amino oxidase (NH3 out)}}$ 5-OH Indol acetic acid (5HIAA)

- **5HIAA in urine** is used as indicator of **carcinoid tumors**(tumor of intestine)**,** so in such case a large amounts of serotonin are formed about **400mg/dl** so large amounts of 5HIAA will excreted in urine, while the normal value is **7mg/dl.**

Hurtnup disease:

The defects in the transport mechanism of tryptophan amino acid in kidneys and intestine will results in excretion of large amounts of this amino acid in urine and feces, and as it is the precursor of niacin, so this results in low niacin level and affected person will complain symptoms mimics Pellagra disease(niacin def.)(skin lesions, mental changes, and cerebral ataxia)