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## Homocysteine: The Amino Acid Toxin.

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### ABSTRACT

Homocysteine is an amino acid formed by metabolism of essential amino acid, methionine. Its role in body functionality has been relatively underestimated in comparison to cholesterol. New scenario has come up in regards to critical risks of Homocysteine. The elevated level of Homocysteine in blood arises due to its improper depletion from the body and poses high risk factor for vascular diseases, stroke, complications of diabetes and improper functioning of neurotransmitters. The Homocysteine level can be measured by simple blood test. Folic acid, vitamin B12 and B6 can substantially reduce the risk of elevated Homocysteine levels.

**Key words:** Homocysteine, amino acid, toxin.

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## INTRODUCTION

Amino acids are biologically important organic compound which are the building blocks of the protein. They contain amino and carboxylic as main functional groups. For proper body functioning twenty amino acids are required. Out of these nine are essentials i.e. the human body cannot synthesize and external supplement is needed for them.

The nine essential amino acids are histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine. Out of these essential amino acids methionine is sulphur containing i.e. it possess sulphur besides carbon, nitrogen, oxygen and hydrogen. In the class of sulphur containing amino acids cysteine is also there but it is non- essential amino acid.

Homocysteine is an amino acid which is formed in the body from the metabolism of the methionine. Nowadays, there has been upsurge of concern regarding toxicity of the elevated levels of Homocysteine and in comparison to cholesterol its role in vascular diseases has been under estimated. In this paper, we have summarised some of emerging scenario regarding Homocysteine and its toxic effects.

### Structure of Homocysteine:

The structure of Homocysteine quite resembles to structure of cysteine (Figure.1)

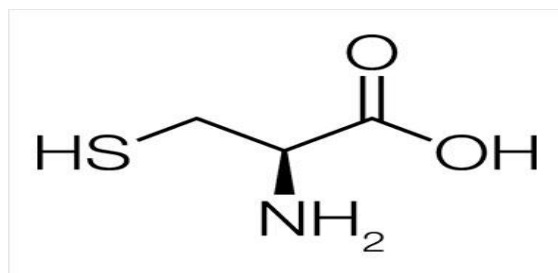


Figure 1: Cysteine amino acid

Homocysteine (Figure 2) is a homologue of cysteine and contains an additional methylene group than cysteine.

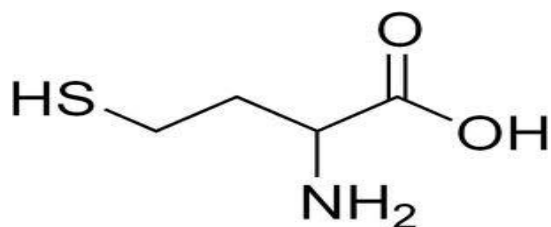


Figure 2: Homocysteine molecule

### Bodily formation and metabolism of Homocysteine:

In human body, Homocysteine is formed by the metabolism of methionine molecule (Figure 3).

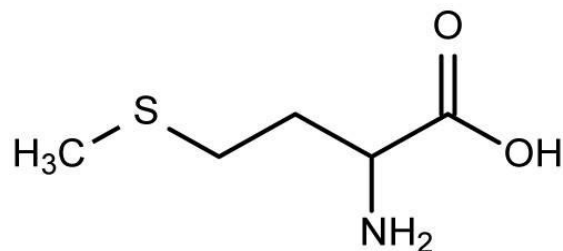


Figure 3: Methionine amino acid

The essential amino acid methionine contains one methyl group attached to the sulphur atom. This methyl group gets removed during metabolism of methionine. A schematic presentation of methionine metabolism and its regeneration is given in Figure 4:

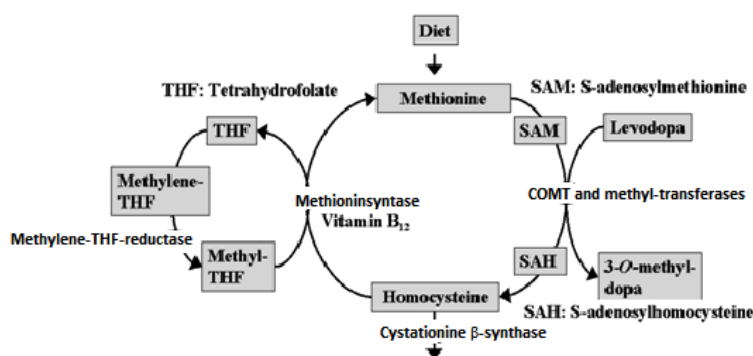


Figure 4: Metabolism and regeneration of methionine, and formation of Homocysteine

In this pathway, the formation of S-adenosylmethionine (SAM) transfers a methyl group to any methyl acceptor molecule (such as neurotransmitter, protein, DNA etc.) and forms S-adenosylhomocysteine (SAH) which is converted to Homocysteine.

Homocysteine re-methylation occurs via methyl-tetrahydrofolate (MTHF) which is the active form of folic acid and is converted back to methionine molecule. The concentration of Homocysteine formed by the metabolism of methionine gets depleted by its reverse conversion to methionine viz. with the help of vitamin B<sub>6</sub>, B<sub>12</sub> and folic acid.

### Risks of Homocysteine:

A normal Homocysteine level is between 4.4 and 10.9 micromoles per litre of blood. The concentration of Homocysteine in male-female age is presented in Table 1.

**Table1: Male-Female Homocysteine levels at different age[1]**

Sex	Age	Lower limit	Upper limit	Unit	Elevated
Female	12–19 years	3.3	7.2	μmol/L	> 10.4 μmol/L or > 140 μg/dL
		45	100	μg/dL	
	>60 years	4.9	11.6	μmol/L	> 150 μg/dL
		66	160	μg/dL	
Male	12–19 years	4.3	9.9	μmol/L	> 11.4 μmol/L or > 150 μg/dL
		60	130	μg/dL	
	>60 years	5.9	15.3	μmol/L	> 150 μg/dL
		80	210	μg/dL	

Homocysteine levels are typically higher in men than women, and increase with age.

Homocysteine, when present in high concentration promotes mortality, and causes risk of cardiovascular disease[2,3] (CVD), stroke, complications of diabetes, improper functioning of neurotransmitters, Alzheimer's disease, birth defects, recurrent pregnancy loss, and many more disorders. A reference to dependency of mortality rate[4] on Homocysteine concentration level is given in Table 2.

**Table2: Mortality ratio dependency on Homocysteine levels**

Concentration of Homocysteine	Mortality Ratio
5.1-8.9 μmole/lit.	1
9.0-11.9 μmole/lit.	1.33
12.0-14.9 μmole/lit.	2.02
15.0-19.9 μmole/lit.	2.48
>20 μmole/lit.	3.56

A reference to disease risk[5] due to elevated Homocysteine levels has been summarised in Table 3.

**Table3: Disease risk due to elevated Homocysteine levels[6]**

Name of disease	Homocysteine level
Coronary artery disease(CAD)	>6.5 μmole/lit.
Kidney Disorders	Thirty times higher risk than CAD
Acute coronary syndrome	>12.0 μmole/lit.
Stroke	>14.24 μmole/lit.
Diabetes	>5 μmole/lit.
Hyperhomocystenemia	>14μmole/lit.
Dementia	>14 μmole/lit.

High Homocysteine level has high risk factor in comparison to “good” HDL cholesterol due to depression of cardiac copper levels. The copper levels have a protective effect on the heart against oxidative damage. That is why Homocysteine increases the risk of arteriosclerosis [8] and have more damaging effect than cholesterol.

**Factors affecting Homocysteine level:**

There are several factors affecting Homocysteine level, some of them are presented in Table 4.

**Table 4: Factors affecting Homocysteine levels**

<b>Diet</b>	Low consumption of foods and vegetables Low intake of folic acid, Vitamin B6, B12 and other multivitamins. High intake of methionine containing proteins
<b>Life Style</b>	Alcohol consumption, High consumption of coffee Smoking
<b>Disease or inherited causes</b>	Diabetes, Hyperthyroidism, Psoriasis, Rheumatoid arthritis, Certain malignancies, renal failure, Malabsorption syndrome Methionine synthase deficiencies, Cystathionine $\beta$ - synthase deficiencies
<b>General</b>	Male gender, increased age, menopause
<b>Drugs increasing Homocysteine level</b>	Estrogens containing oral contraceptives Some antiepileptic drugs Niacin, Sulfasalazine, Diuretic therapy etc.

**Prevention of elevated Homocysteine level:**

Elevated Homocysteine level is a risk factors for several diseases or initiation of diseases. Prevention provides a cheap way to cure. The lowering of Homocysteine can be achieved by a change in life style, regular check up, and intake of diet full of green vegetables, beans and multivitamins. The vitamins which are especially useful in controlling the Homocysteine levels are Folic acid, Vitamin B6 and Vitamin B12. These vitamins help in reverse conversion of Homocysteine into methionine. Adequate amounts of vitamin B6, B12, and folic acid intake is required for keeping Homocysteine at levels associated with lower rates of the diseases. Supplementation with one or more of these vitamins can lower plasma levels of Homocysteine, regardless of the cause of the elevation. Although the doses of these vitamin has not been clearly established yet, but 0.3-1 mg Folic acid, 2-25 mg Vitamin B6 and 0.01-0.1 mg Vitamin B12 may serve the purpose. Higher doses may be required in patients with other complaints.

**CONCLUSION**

Homocysteine is an amino acid toxin, formed in the body from metabolism of methionine. Elevated Homocysteine levels promote mortality, and cause risks of cardiovascular disease (CVD), stroke, complications of diabetes, improper functioning of neurotransmitters, Alzheimer's disease, birth defects, recurrent pregnancy loss, and many more disorders. The risks of initiation of vascular diseases by Homocysteine may be more prominent than cholesterol. Its levels should be watched carefully. Folic acid, vitamin B6 and vitamin B12 are helpful in lowering the blood Homocysteine levels.



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