

Methylation, Detoxification and S_AMe

homocysteine, and the balance of this relationship can quite literally make the difference between life and death.

The Relationship between Homocysteine and Methylation

It is impossible to properly define homocysteine without clearly defining methylation, such is the relationship between the two. Biochemically speaking, methylation is a metabolic process that involves the addition of methyl groups to various molecules. That process begins with the amino acid methionine.

Methylation is one of the most fundamental biological functions of the human body. It occurs at the rate of approximately one billion times per second, affecting everything from fetal development to the immune system to nerve transmission. It is also essential for over 100 different metabolic reactions involving critical molecules such as nucleic acids, DNA, RNA, proteins, phospholipids, myelin, polysaccharides, creatine, and catecholamines to name a few. Methylation has an acute relationship with

1 Methionine: an essential yet relatively ubiquitous amino acid found in most sources of dietary protein. It is the building block of all polypeptide (multiple-amino acid chain) proteins, containing both sulfur and methyl groups.

2 Methionine Bonds with ATP: ATP is adenosine triphosphate, a nucleotide that is the primary energy currency of the cell – and therefore the source of all immediate short-term energy for the human body. This bonding then creates S_AMe.

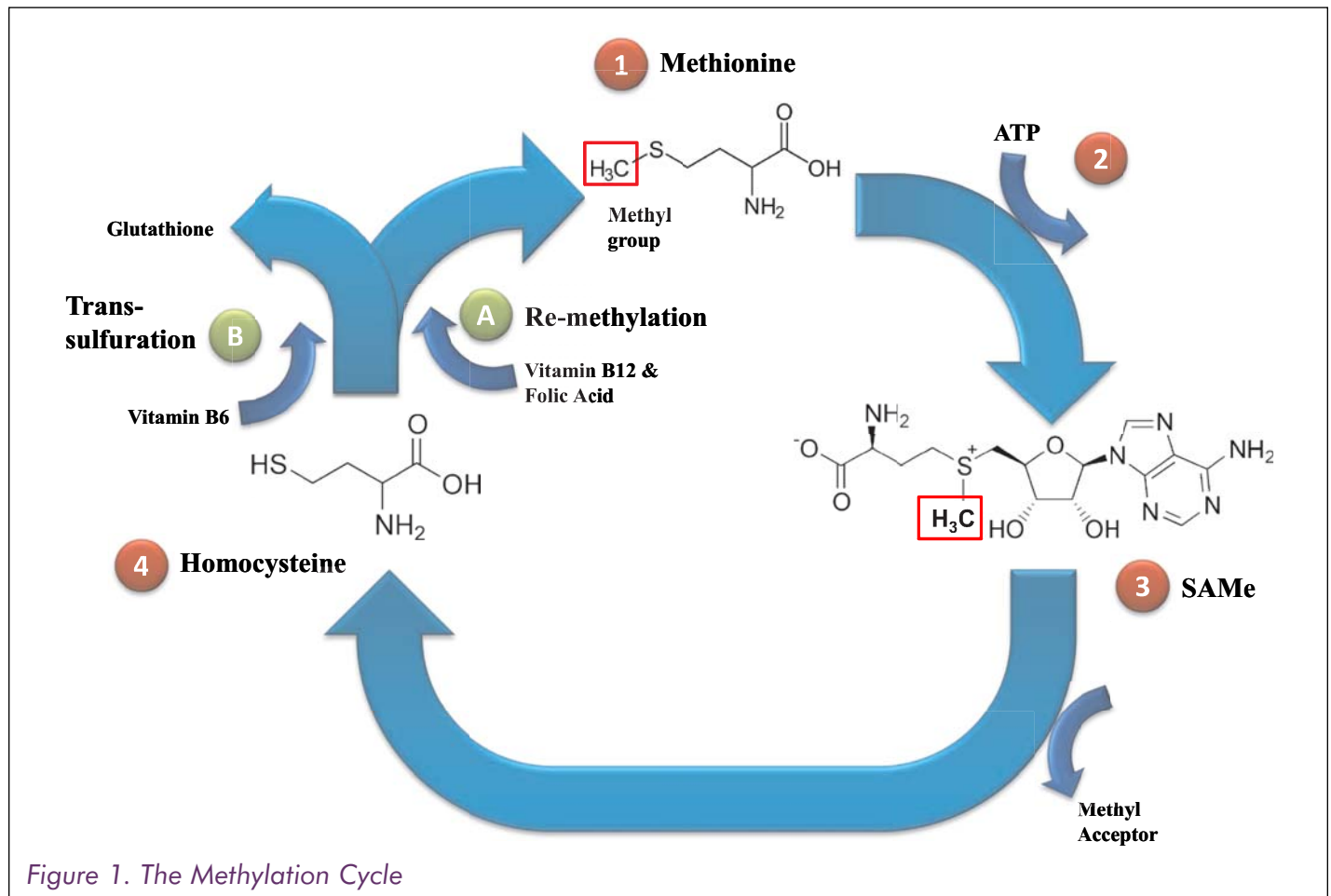
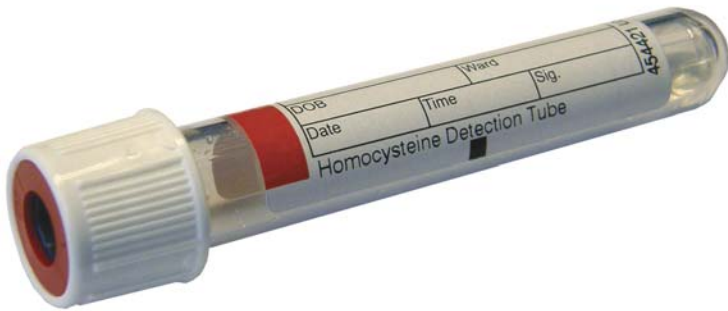


Figure 1. The Methylation Cycle

3 SAME (s-adenosylmethionine): SAME is a coenzyme whose creation results in the chemical reaction of donating its methyl group inherited from methionine to a methyl receptor. The transfer of methyl groups is the reactive process that sparks the entire methylation cycle. After SAME donates its methyl group to a methyl acceptor (which can include folate or vitamin B12), it becomes s-adenosylhomocysteine (SAH). SAH then is rapidly transformed into homocysteine.

4 Homocysteine: This is the critical stage of the methylation cycle. Although technically an amino acid, homocysteine is in effect a by-product of protein metabolism, to which the methylation cycle is intrinsically connected via methionine. This by-product, left unconverted, can accumulate and become toxic. Elevated homocysteine levels have been linked to cardiovascular disease and a myriad of other ailments.



The Critical Juncture

It is at this point where the alternatives to homocysteine accumulation become critical. These alternatives consist of two metabolic pathways: A) the “re-methylation” pathway or B) the “trans-sulfuration” pathway.

A The “re-methylation” pathway is where homocysteine is converted back to methionine. This process is dependent on adequate serum levels of folate and vitamin B12, which will safely recycle homocysteine back into methionine. They will do this by donating methyl groups that they themselves have accepted.

B The “trans-sulfuration” pathway is vitamin B6-dependent, and if adequate levels of this nutrient are present, then it (among other substances) will actually transform homocysteine into either the non-toxic amino acid cysteine or the ubiquitous glutathione, the most important antioxidant produced by the body.

Supplemental SAME, Homocysteine, and Detoxification

Upon first examining SAME’s biological ‘place’, one can be forgiven for failing to make the immediate connection between it and the health conditions for which supplemental SAME is clinically demonstrated to be effective, namely mood, joint and (to a lesser extent) liver health. The connection, however, does exist and is based on detoxification.

Homocysteine can be described as a naturally occurring toxic agent. High levels of homocysteine have been connected to correspondingly high levels of inflammation, and both have a long-established inverse relationship with joint health and a more recently established one with mood health. In this context, the value of lowering homocysteine levels becomes apparent, and since homocysteine is a by-product of the methylation process, improving the methylation process is key to lowering homocysteine levels. In effect, homocysteine can be thought of as a “waste product” of methylation, and thus improving the efficiency of the methylation process is a form of detoxification. The question now becomes: how does SAME, which is an integral part of methylation, contribute to detoxification?

SAME, Mood and Detoxification



It is important to emphasize the difference between the presence of high levels of homocysteine in people suffering from conditions such as depression (and other mood disorders) and determining those levels to be causative factors in such condition(s). While it is still a subject of some speculation, it is believed that elevated homocysteine may cause depression by

altering the function of neurotransmitters.¹ Mood health is one of the areas where SAME has been clinically proven (and officially recognized) to be effective. At least a dozen clinical trials involving hundreds of patients diagnosed with major depression have experienced significant alleviation of their symptoms with supplemental SAME.² While the precise mechanism of action for this remains elusive, an inverse relationship between plasma levels of homocysteine and SAME has been established.³

SAME, Joint Health and Detoxification



Homocysteine has recently been identified as both a risk indicator of osteoporosis as well as a factor in bone metabolism.⁴ Less conclusive but ongoing research is connecting elevated homocysteine levels to osteoarthritis as well.⁵ Supplemental SAME has been successfully used to treat the latter, with numerous clinical studies demonstrating both efficacy and safety to its credit.⁶ Among the mechanisms of action behind this efficacy are increased glutathione production and DNA methylation (assuming B-vitamin levels are adequate).⁷

SAME, Liver Health and Detoxification

SAME also has an established reputation in the treatment of liver health, and this is due in large part to its role as a glutathione precursor (once again, dependent on sufficient levels of B-vitamins). Furthermore, the enzyme that acts as the catalyst to combine methionine with ATP to produce SAME is severely inhibited in cases of liver dysfunction.⁸

The Bottom Line

In summary, healthy methylation will have a high ratio of glutathione production and remethylation compared to homocysteine production. This is the essence of detoxification in the context of methylation. While the effects of supplemental SAME alone are relatively neutral with respect to homocysteine levels⁹, combining it with a synergistic B-complex amounts to strong theoretical evidence for enhanced cardiovascular health. Healthy levels of SAME help ensure that the methylation process remains robust, and concurrently adequate levels of B12, Folic acid, and B-6 help ensure that it remains efficient.

References

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