DOCTOR'S DATA INC

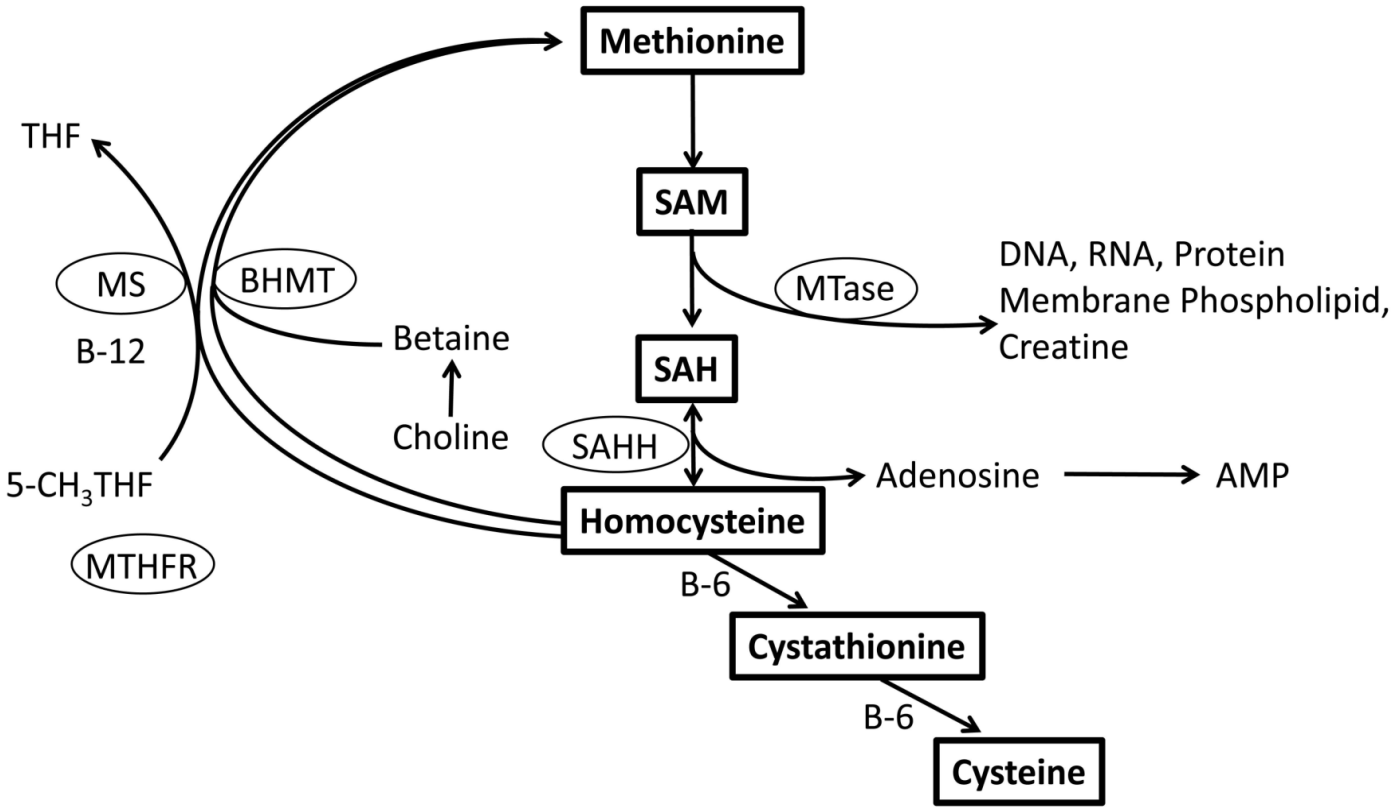
LAB #: B231220-2360-1
PATIENT: Kara Mitchell
ID: MITCHELL-K-01547
SEX: Female
DOB: 03/18/1988 **AGE:** 35

CLIENT #: 31417
DOCTOR:
Rn Labs
18 / 93 Rivergate Pl
Murarrie, Qld, 4172 AUSTRALIA

Methylation Profile; plasma

PRIMARY & INTERMEDIATE METABOLITES	RESULT/UNIT	REFERENCE INTERVAL	PERCENTILE (2.5th, 16th, 50th, 84th, 97.5th)
Methionine	**1.6 µmol/dL**	1.6 - 3.6	
Cysteine	**23 µmol/dL**	20 - 38	
S-adenosylmethionine (SAM)	**75 nmol/L**	86 - 145	
S-adenosylhomocysteine (SAH)	**13.5 nmol/L**	10 - 22	
			68th, 95th
Homocysteine	**5.0 µmol/L**	< 11	
Cystathionine	**0.01 µmol/dL**	< 0.05	

METHYLATION INDEX	RESULT	REFERENCE INTERVAL	PERCENTILE (68th, 95th)
SAM : SAH	**5.6**	> 4	



SPECIMEN DATA

Comments:

Date Collected: **12/11/2023**
Date Received: **12/20/2023**
Date Reported: **12/27/2023**
Method: **LCMS**

<dl: **less than detection limit**

v02.11

Introduction

This test assesses metabolism of the essential amino acid methionine (Met). Methionine is paramount in two metabolic processes; (1) transmethylation that is critical for the methylation of hundreds of important molecules such as DNA, RNA, proteins, neurotransmitters and membrane phosphatidylcholine, and (2) transsulfuration that leads to the biosynthesis of cysteine and hence glutathione , both of which have many important protective / detoxification functions. Aberrant Met metabolism can be caused by nutritional deficiencies, exposures to environmental toxicants and/or genetic polymorphisms and can have significant adverse health consequences. Identification of such abnormalities can guide appropriate nutritional intervention towards normalization of methionine metabolism and decreased risk and incidence of adverse health effects.

The amino acids and intermediary amino acid metabolites were measured by liquid chromatography - mass spectrometry. Reference values are age and sex specific. If patient values deviate from normal, comprehensive descriptive paragraphs will be presented as part of the test report.

S-adenosylmethionine low

S-adenosylmethionine (SAM), the first direct metabolite of normal methionine metabolism, is lower than expected. Up to half of daily methionine uptake is enzymatically converted in the liver to SAM by methionine-adenosyl transferase in the presence of ATP and magnesium. Therefore SAM may be low due to (1) low availability of methionine (check plasma methionine) (2) magnesium deficiency (check whole blood or red blood cell magnesium levels), (3) inhibition of methionine synthase activity, or (4) genetic or chemical inhibition of methionine adenosyltransferase activity. In the latter case, severe depletion of SAM can be associated with DNA hypomethylation and demyelination in the central nervous system. When dietary methionine and choline are insufficient, the folate-dependent pathway for regeneration of methionine from homocysteine is upregulated increasing the cellular requirement for folate. A potential consequence of the diversion of folate 1-carbon methyl groups towards regeneration of methionine (and SAM) may be functional depletion of folate methyl groups for DNA metabolism and integrity with potential for genetically significant consequences (e.g . genomic DNA hypomethylation). It is uncertain whether physiological decreases in SAM alone induced by nutritional deficiencies are causally related to cellular hypomethylation (J Biol Chem 2000;275:29318-23).

SAM is the principal biological methyl donor and participates in three important pathways in the liver; (1) polyamine synthesis (cell growth), (2) transmethylation, and (3) transsulfurration. Normally most of SAM is used in transmethylation reactions as a donor of its methyl group to a diverse group of hundreds of important molecules via the catalytic activity of methyl transferases. Molecules that require methylation for normal biological activity include, but are not limited to, DNA, RNA, proteins, choline, membrane phosphatidylcholine, creatine (liver), neurotransmitters and neurotransmitter receptors. Potential consequences of low SAM and compromised methylation include aberrant neurotransmitter metabolism, abnormal gene expression and silencing, immune dysregulation (autoimmunity), cancer, cardiovascular disease and vascular occlusion, congenital heart disease/birth defects, neurodegenerative disease, poor response to environmental toxins (e.g. endogenous detoxification of arsenic), and increased risk for Down Syndrome and perhaps autism spectrum disorder. While low SAM can be associated with under methylation, it has been suggeted that the most sensitive indicator of poor methylation is the relative plasma concentrations of SAM to S-adenysylhomocysteine (methylation index). If SAM and methionine are low but the reported methylation index is normal, the condition may be remedied with appropriate intake/supplementation with methionine, folate, B-12, B-6, betaine and magnesium. Cheeses, fish, poultry, meats and some nuts (e.g. Brazil nuts, almonds and cashews) are good dietary sources of Met.

Supplementation with Met should be accompanied by magnesium, B-6, folate, betaine and B-12.

References

1. James SJ, Melnyk S, Pogribna M et al. Elevation in S-adenosylhomocysteine and DNA hypomethylation: potential epigenetic mechanism for homocysteine-related pathology. J Nutr 2002;132:2361S-66S.

2. Yi P, Melnyk S, Pogribna M et al. Increase in plasma homocysteine associated with parallel increase in plasma S-andenosylhomocysteine and lymphocyte DNA hypomethylation. JBC 2000;275:29318-23.

3. James SJ, Melnyk S, Jernigan S et al. Abnormal transmethylation/transsulfuration metabolism and DNA hypomethylation among parents of children with autism. J Autism Dev Disord 2008;38:1966-75.

4. Lu SC. Regulation of glutathione synthesis. Mol Aspects Med 2009;30:42-59.