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COMMENTARY

Methyl balance and transmethylation fluxes in humans^{1, 2, 3, 4}

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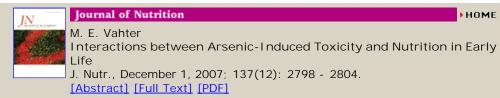
Various questions have been raised about labile methyl balance and total transmethylation fluxes, and further discussion has been encouraged. This report reviews and discusses some of the relevant evidence now available. The fact that, if needed, labile methyl balance is maintained by methylneogenesis appears to be established, but several aspects of transmethylation remain uncertain: definitive measurements of the rate of total transmethylation in humans of both sexes on various diets and at various ages; the extent to which synthesis of phosphatidylcholine has been underestimated; and the relative contributions of the 2 pathways for the formation of sarcosine (ie, *N*-methylglycine). The available evidence indicates that the quantitatively most important pathways for S-adenosylmethionine- dependent transmethylation in mammals are the syntheses of creatine by guanidinoacetate

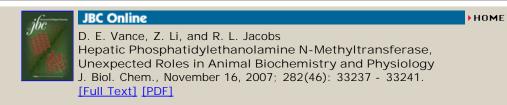
methyl transferase, of phosphatidyl choline by phosphatidyl ethanol amine methyl transferase, and of sarcosine by glycine N-methyltransferase. Data presented in this report show that S-adenosylmethionine and methionine accumulate abnormally in the plasma of humans with glycine N-methyltransferase deficiency but not of those with guanidinoacetate N-methyltransferase deficiency or in the plasma or livers of mice devoid of phosphatidylethanolamine Nmethyltransferase activity. The absence of such accumulations in the latter 2 conditions may be due to removal of Sadenosylmethionine by synthesis of sarcosine. Steps that may help clarify the remaining issues include the determination of the relative rates of synthesis of sarcosine, creatine, and phosphatidylcholine by rapid measurement

of the rates of radiolabel incorporation into these compounds from L-[methyl-³H]methionine administered intraportally to an experimental animal; clarification of the intracellular hepatic isotope enrichment value during stable-isotope infusion studies to enhance the certainty of methyl flux estimates during such studies; and definitive measurement of the dietary betaine intake from various diets.

Key Words: Transmethylation • labile methyl balance • phosphatidylcholine • creatine • sarcosine

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