To the Editor:

The critical review of cobalamin-folate interrelations by Chanarin et al. provided an excellent guide through the intricacies of the "methyl trap" hypothesis. However, our interest in patients with inborn defects in the metabolism of sulfur-containing amino acids prompts us to challenge the phrase "the maintenance of near-normal serum methionine levels in children with hereditary MTHFR deficiency" (page 486). The authors are perpetuating an error that crept into the literature and has been repeated by a widely respected reference. The truth is that most patients with MTHFR deficiency have significant hypomethioninemia and the two references cited by Chanarin et al are probably unusual cases. Erbe, to our knowledge, was the first to emphasize hypomethioninemia in his review of 1979, which pointed out its significance in the causation of the CNS manifestations of MTHFR deficiency. Since then other patients with the infantile form of the disease have been described as having low blood methionine levels, although it now appears that older children and patients with a milder form of MTHFR deficiency can present with "near normal" values. We have cared for 2 infants with the disease, and both had hypomethioninemia. One also had low CSF methionine levels. The other infant worsened after four and one half hours of N2O anesthesia—before the diagnosis was made. In both, the major neuropathology was marked demyelination, which included the spinal cord. Smith et al. have recently described subacute combined degeneration in MTHFR deficiency. Despite the fact that infants with the disease also have homocystinemia, low 5 methyl THF, and low neurotransmitter metabolites in the CSF, we suspect that it is the CNS hypomethioninemia that is most devastating. And it is this biochemical parameter that requires early identification and energetic treatment if our dismal record in the therapy of this disorder is to improve.

Incidentally, it should be pointed out that megaloblastic anemia has not been reported in MTHFR deficiency, although the search for it has not always been rigorous.

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REFERENCES


ANNOUNCEMENTS

EXECUTIVE DIRECTOR

An Executive Director is being sought for the Puget Sound Blood Center in Seattle, Washington. The PSBC is a centralized regional blood banking facility that employs 240 people, including seven physicians, and is responsible for the distribution of 250,000 units of blood components annually. Candidates must have an MD degree and have demonstrated administrative skills in transfusion medicine and the ability to contribute to and broaden the ongoing research activities of the Center. The position carries a senior faculty appointment in the School of Medicine at the University of Washington. Interested candidates should send their CV and bibliography as well as the names of three references to Dr. Daniel H. Coleman, c/o Search Committee, Puget Sound Blood Center, Terry and Madison Streets, Seattle, Washington 98104. The PSBC is an Equal Opportunity Employer.
Critical review of cobalamin-folate interrelations [letter]

S Berlow