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Drs. Talwar and St. JO’Reilly respond:

To the Editor:

Dr. McLaren Howard makes an interesting observation relating to the biochemical assessment of thiamin status in people supplemented with the vitamin. In his experience, the indirect measurement of thiamin status using the transketolase (ETK) activation assay is clinically more useful than direct measurement of thiamin diphosphate (TDP) concentrations in red cells in people repleted with thiamin. Unfortunately, we are unable to comment on his observation because no relevant data are presented.

Discrepancies between the ETK activation test and clinical signs of thiamin deficiency have been reported previously, with several studies reporting no relationship between ETK activation results and thiamin intake (1–5). These discrepant findings have raised questions about the usefulness of the ETK activation test as a sole indicator of thiamin status.

Because a valid ETK activation response depends on a kinetically normal enzyme (1, 6), certain disease states may affect enzyme cofactor binding and hence the TDP activation effect (6). Because of the potential difficulty in interpretation of ETK activation effect in some disease states and the limitations of enzyme activation tests in general, several authors have suggested the use of more direct measures of thiamin status, such as TDP in whole blood or plasma (4, 6, 7).

We would agree with Dr. McLaren Howard that further discussion is required on the merits of other direct and indirect measures of thiamin status in patients repleted with thiamin. Meanwhile, our experience with the HPLC assay suggests that measurement of TDP in red cells is the single most useful biochemical measurement for assessing thiamin status in patients who are at risk of thiamin deficiency.

References


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Transient Hyperphosphatasemia of Infancy and Childhood: Study of 194 Cases

To the Editor:

Transient hyperphosphatasemia of infancy and childhood (TH) is a temporary and isolated increase of serum alkaline phosphatase (ALP; EC 3.1.3.1) activity occurring without obvious cause during the first years of life. Despite several reports about this phenomenon, the origin of TH remains obscure.

Over a period of 8 years (1992–1999), we detected 194 cases of TH in 106 boys and 88 girls. The hyperphosphatasemia was discovered fortuitously during routine investigations in outpatient and inpatient departments of a children’s hospital with a capacity of 500 beds. A wide variety of clinical disorders was associated with this condition (gastrointestinal diseases, 24%; respiratory infections, 21%; congenital anomalies and inborn errors of metabolism, 15%; anemia, 10%; malignancies, 7%; neurological disorders, 5% others, 18%).

We measured total ALP activity using the IFCC-recommended method at 37 °C with Elan (Eppendorf) and Cobas Integra (Roche) analyzers. Our reference interval for children was 0.85–6.80 μkat/L (51–408 U/L). Adult reference intervals are 0.54–1.7 μkat/L (32–104 U/L) for women and 0.76–2.0 μkat/L (45–122 U/L) for men. In each TH case, we saw the characteristic two-band ALP isoenzyme pattern on Cellogel zonal electrophoresis as described by Stein et al. (1) and Behúlova et al. (2).

Although markedly increased ALP activities may occur in TH, frequently only slightly or moderately increased activities are observed, depending on the timing of the blood sample in relation to the natural course of TH. Markedly increased activities, therefore, are not necessary to reach a diagnosis of TH. The peak ALP activity in our series was 2- to 20-fold higher than the pediatric upper reference limit, with the median being a 4-fold increase.

In this series, 49% of cases were detected in the second year of life, and 96% of affected children were younger than 5 years (Fig. 1). We speculate that immaturity of the mechanisms responsible for ALP clearance allows increases of plasma ALP, triggered by an exogenous insult.

We observed a marked seasonal clustering of cases from September to November (43%); the lowest incidence was from January to March