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Thiamine deficiency, beriberi, and maternal and child health: why pharmacokinetics matter^{1–3}

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In this issue of the Journal, Coats et al (1) describe short-term thiamine pharmacokinetics in nursing women from Cambodia who received a therapeutic course of oral thiamine for 5 d. Before supplementation, the mothers and infants were biochemically thiamine deficient. Treatment normalized thiamine status in the mothers but not in the infants, although thiamine concentrations in breast milk increased rapidly with supplementation. The authors characterized thiamine status in the mothers and their breastfed infants before and after thiamine administration and compared their findings with blood samples from healthy nursing American mothers who were age-matched to their Cambodian counterparts. The data provide important insights on the nutritional pathophysiology of thiamine depletion, repletion, and therapeutics and a sobering reminder that nutritional deficiency disease, including beriberi, persists as an important cause of morbidity and mortality globally. Several aspects of the study are worth further consideration, including the study design, the analytic approach used to assess thiamine status, and implications for global maternal and child health.

This study adds to the limited literature on pharmacokinetic data for thiamine; most of the previously published data come from healthy, well-nourished subjects (2). Coats et al used a standard approach to examine thiamine disposition in 16 healthy nursing Cambodian women from a district in Prey Vang Province, where previous work showed endemic thiamine deficiency among mothers and infants (1, 3). The thiamine dose used (100 mg thiamine hydrochloride tablet/d for 5 d, 500 mg total), although far above the Recommended Dietary Allowance (1.4 mg/d for lactating women) and higher than the usual therapeutic regimen for “mild” thiamine deficiency (5–30 mg/d in single or divided doses for 1 mo), was similar to doses typically used for severe deficiency [300 mg/d (4)] and within the range used in a previous pharmacokinetics study (2). The present study shows high maternal bioavailability of this pharmacologic dose but only modest improvements in the thiamine status of the infants after 5 d of maternal treatment. The authors appropriately note that supplementation

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²The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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for longer periods or with higher or more frequent doses should be considered and, most importantly, that symptomatic infants should be treated directly (1).

The findings of Coats et al indicate rapid normalization of circulating maternal plasma thiamine and thiamine monophosphate by day 6, and rapid normalization of breast-milk thiamine, but slower normalization of blood thiamine diphosphate (1). The information on breast-milk thiamine is of great value in a thiamine-deficient population and provides unique data to estimate the benefit to the infant if only the mother receives supplementation, data that were not available previously. A recent report on a longer-term thiamine supplementation regimen (100 mg/d during pregnancy and lactation) at antenatal clinics in a refugee camp showed that thiamine status in lactating women 12 wk postpartum was within the range observed in well-nourished women and that thiamine measurements in breast milk provided useful information on maternal thiamine status (5).

The analytic approach used to assess thiamine status has evolved over time. The traditional indirect approach, not used in this study but still in use (6), is to measure erythrocyte transketolase activity as a functional test that reflects the adequacy of body stores and is sensitive to marginal thiamine deficiency. However, advances in laboratory techniques and the availability of HPLC instrumentation have facilitated the use of the direct approach to measure thiamine and its phosphate esters by use of sensitive and specific fluorometric detection (1, 5, 7). Furthermore, this direct approach can be applied to a wide range of matrices (serum, whole blood or erythrocytes, urine, and breast milk) that are not all accessible to the functional test. Regardless of the approach, however, tests to assess thiamine status are not conducted widely enough to justify establishing an external proficiency testing program. It is therefore vital that each laboratory establishes its own internal quality assessment program to ensure high-quality measurements (8).

What factors account for the persistence of thiamine deficiency, especially in postpartum women and their breastfed infants? Despite recognition of its public health significance for >100 y, beriberi remains prevalent in Southeast Asia, where it has long been associated with consumption of polished rice and numerous foods containing antithiamine activity as well as alcohol and betel nut use (1, 3, 6, 9, 10). The work of Coats et al (1) serves to remind us, once again, of the persistence of thiamine deficiency as a maternal and child health problem. In 2001 McGready et al (9) reported a 57.7% prevalence of biochemical thiamine deficiency in a population of postpartum refugee women along the Thai-Burmese border. In 2011 Khounnorath et al (10) and Lima et al (11) described biochemical thiamine deficiency in breastfed infants and critically ill children on admission in Vientiane, Laos, and Sao Paulo, Brazil, respectively.

The current study reminds us that the full spectrum of clinical thiamine deficiency, including beriberi, Wernicke encephalopathy, and even death, also occurs in situations other than primary nutritional deficiency or frank alcoholism. Some clinical causes include bariatric surgery (12) and prolonged administration of total parenteral nutrition without thiamine (13), which is a continuing challenge with shortages of parenteral multivitamin solutions (14).

Considering its short biological half-life, limited body reserves, constant metabolic demand particularly during periods of rapid growth, variable content and bioavailability in human diets, the clinically inapparent presentation of deficiency, as well as the profound clinical manifestations and adverse clinical outcomes that can develop quickly during chronic depletion, thiamine will likely continue to serve as a sentinel for nutritional deficiency and a harbinger for deficiency of other nutrients. Coats et al show that acute thiamine treatment, even with a pharmacologic dose, may be insufficient to replete thiamine stores in the maternal and infant dyad. Public health leaders should be alert to identify situations in which mothers and infants are at high risk of thiamine deficiency and ensure prompt initiation of treatment. In treating thiamine deficiency, clinicians can implement evidence-based supplementation protocols to maximize clinical benefit in postpartum women and their breastfed infants. These combined efforts can help to reduce and prevent beriberi worldwide by addressing the root cause, unrecognized thiamine deficiency. Greater recognition of the spectrum of thiamine deficiency should enable the supporting science to move beyond descriptive epidemiology to implement prevention and control in vulnerable populations worldwide.

References

1. Coats D, Frank EL, Reid JM, Ou K, Chea M, Khin M, Preou C, Enders FT, Fischer PR, Topazian M. Thiamine pharmacokinetics in Cambodian mothers and their breastfed infants. *Am J Clin Nutr*. 2013; 98:839–44. [PubMed: 23864540]
2. Smithline HA, Donnino M, Greenblatt DJ. Pharmacokinetics of high-dose oral thiamine hydrochloride in healthy subjects. *BMC Clin Pharmacol*. 2012; 12:4. [PubMed: 22305197]
3. Coats D, Shelton-Dodge K, Ou K, Khun V, Seab S, Sok K, Prou C, Tortorelli S, Moyer TP, Cooper LE, et al. Thiamine deficiency in Cambodian infants with and without beriberi. *J Pediatr*. 2012; 161:843–7. [PubMed: 22703952]
4. US National Library of Medicine. Thiamine (vitamin B1). Available from: <http://www.nlm.nih.gov/medlineplus/druginfo/natural/965.html> (cited 11 July 2013)
5. Stuetz W, Carrara VI, McGready R, Lee SJ, Beisalski HK, Nosten FH. Thiamine diphosphate in whole blood, thiamine and thiamine monophosphate in breast-milk in a refugee population. *PLoS ONE*. 2012; 7:e36280. [PubMed: 22768031]
6. Soukaloun D, Lee SJ, Chamberlain K, Taylor AM, Mayxay M, Sisouk K, Soumphonphakdy B, Latsavong K, Akkhavong K, Phommachanh D, et al. Erythrocyte transketolase activity, markers of cardiac dysfunction and the diagnosis of infantile beriberi. *PLoS Negl Trop Dis*. 2011; 5:e971. [PubMed: 21364976]
7. Lu J, Frank EL. Rapid HPLC measurement of thiamine and its phosphate esters in whole blood. *Clin Chem*. 2008; 54:901–6. [PubMed: 18356241]
8. Pfeiffer, CM.; Schleicher, RL.; Caldwell, KL. Biochemical indices. In: Caballero, B., editor. *Encyclopedia of human nutrition*. 3rd. Vol. 1. Waltham, MA: Academic Press; 2013. p. 156-74.
9. McCready R, Simpson JA, Cho T, Dubowitz L, Changbumrung S, Bohm V, Munger RG, Sauberlich HE, White NJ, Nosten F. Postpartum thiamine deficiency in a Karen displaced population. *Am J Clin Nutr*. 2001; 74:808–13. [PubMed: 11722964]
10. Khounnorath S, Chamberlain K, Taylor AM, Soukaloun D, Mayxay M, Lee SJ, Phengdy B, Luangxay K, Sisouk K, Soumphonphakdy B, et al. Clinically unapparent infantile thiamin deficiency in Vientiane, Laos. *PLoS Negl Trop Dis*. 2011; 5:e969. [PubMed: 21423705]
11. Lima LFP, Leite HP, de AC, Taddei JA. Low blood thiamine concentrations in children upon admission to the intensive care unit: risk factors and prognostic significance. *Am J Clin Nutr*. 2011; 93:57–61. [PubMed: 21068344]
12. Saltzman E, Karl JP. Nutrient deficiencies after gastric bypass surgery. *Ann Rev Nutr*. 2013; 33:19.1–21.

13. Deaths associated with thiamine-deficient total parenteral nutrition. *MMWR Morb Mortal Wkly Rep.* 1989; 38:43–6. [PubMed: 2492074]
14. US Food Drug Administration. Current drug shortages. Available from: <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm314741.htm#mvi> (cited cited 11 July 2013)

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