Published in final edited form as:

Pediatr Nephrol. 2018 July ; 33(7): 1133–1143. doi:10.1007/s00467-017-3751-z.

Vitamin and trace element deficiencies in the pediatric dialysis patient

Lyndsay A. Harshman, Kathy Lee-Son, and Jennifer G. Jetton

Stead Family Department of Pediatrics, Division of Nephrology, Dialysis & Transplantation,
University of Iowa Stead Family Children's Hospital

Abstract

Pediatric dialysis patients are at risk of nutritional illness secondary to deficiencies in water soluble vitamins and trace elements. Unlike 25-OH vitamin D, most other vitamins and trace elements are not routinely monitored in the blood and detection of deficiency may not occur until significant complications develop. Causes of deficiency in patients on maintenance dialysis are multifactorial, ranging from diminished nutritional intake to altered metabolism as well as dialysate-driven losses of water soluble vitamins and select trace elements. This review summarizes the nutritional sources of key water soluble vitamins and trace elements with a focus on the biological roles and clinical manifestations of deficiency to augment awareness of potential nutritional illness in the maintenance pediatric dialysis patient. The limited pediatric data on the topic of clearance of water soluble vitamins and trace elements by individual dialysis modality will be reviewed, including a brief discussion on clearance of water-soluble vitamins and trace elements with continuous renal replacement therapy.

Keywords

nutritional illness; water-soluble vitamins; Wernicke encephalopathy; zinc; selenium; clearance

Introduction

Pediatric patients with end stage renal disease (ESRD) on maintenance dialysis (e.g., hemodialysis and peritoneal dialysis) risk development of vitamin and trace element deficiencies, despite a strong focus on nutritional adequacy in this patient population. Development of nutritional illness due to vitamin and trace element deficiency is often multifactorial in nature. Children with ESRD on dialysis have decreased appetite and lower spontaneous food intake compared to children not requiring dialysis [1], as appetite often declines concomitantly with decreasing glomerular filtration rate [2]. Increased dialysate losses of water soluble vitamins and higher metabolic needs compound the potential for vitamin deficiencies [3, 4]. Risk of nutritional illness is heightened for pediatric patients with an acute on chronic illness associated with hypercatabolic states, increased caloric

Address correspondence to: Lyndsay A. Harshman, M.D., Stead Family Department of Pediatrics, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, 4037 Boyd Tower, Iowa City, Iowa 52242-1053, 319-356-7249 (phone), 319-384-9616 (fax), lyndsay-harshman@uiowa.edu.

Conflict of interest: The authors declare no conflict of interest.

needs requiring exclusive parenteral nutrition, and/or accelerated protein clearance in the setting of more aggressive renal replacement therapy needs – for example, daily hemodialysis requirements or continuous renal replacement therapy (CRRT).

Specific pediatric guidelines for monitoring vitamin and trace element levels are lacking, as are standardized protocols for correcting deficits when they do occur, leaving these patients at risk to develop deficiencies of key nutrients required for optimal growth, development, and cellular metabolism. Given the lack of routine laboratory monitoring, the clinical presentation of nutritional illness may be masked by the medical comorbidities and somatic effects of ESRD experienced by the dialysis patient. Individual assessment and nutritional prescription, in partnership with a skilled renal dietician, is required for optimal nutritional care.

This review describes key water soluble vitamins and trace elements for children on dialysis with a focus on 1) nutritional sources and risk of deficiency, 2) clinical manifestation of deficiency, and 3) clearance of vitamin and trace elements by dialysis modality. Evidence summarized here represents the limited pediatric literature available – mostly single-center studies published before 2000 – and thus is largely derived from adult data.

The medical complexity and risk for nutritional illness within the pediatric dialysis patient population is highlighted with a representative clinical vignette:

Clinical Vignette

A 13-year-old male on maintenance hemodialysis developed new onset, fluid unresponsive intradialytic hypotension. Other symptoms included tremulousness, disorientation, ataxia, and garbled speech. His past medical history included recent bone marrow transplant and prolonged requirement for exclusive parenteral nutrition due to severe graft-versus-host disease of his gastrointestinal tract. Extensive laboratory evaluation revealed elevated serum lactate of 12.6 mEq/L without acidosis. No sources of infection, cardiac dysfunction, or cerebrovascular disease were identified. He was eventually found to have severe thiamine deficiency due to inadvertent lack of thiamine in his parenteral nutrition. Further history revealed the patient had been non-adherent with prescribed vitamin B supplementation during the same time period. Both the elevated serum lactate and neurological symptoms quickly resolved within 24 hours of administration of parenteral thiamine.

The clinical vignette illustrates new-onset Wernicke encephalopathy secondary to thiamine deficiency. This patient was at high risk for nutritional deficiency due to his non-adherence with water soluble vitamin supplementation and exclusive dependence on parenteral nutrition. Diagnosis of nutritional illness was initially delayed as his symptoms of hypotension and elevated lactate suggested more commonly considered diagnoses in ill pediatric dialysis patients (e.g., sepsis). This vignette highlights the need for increased awareness of the risk factors and effects of water soluble vitamin and trace nutrient deficiencies in pediatric patients on dialysis.

Vitamin and trace element nutritional sources and risk for deficiency

Overview

Vitamins are organic substances that cannot be synthesized by the human body. Their functions are essential for normal human metabolism. The water soluble vitamins at highest risk for deficiency in the maintenance dialysis (both hemodialysis and peritoneal modalities) population include thiamine (B1), pyridoxine (B6), folate (B9), and vitamin C (ascorbic acid). Trace elements, such as zinc and selenium, are mineral substances that constitute less than 0.01% of the total human body weight. Daily requirements in adults are in the 1–100 mg/day range [5]. Intact renal function is required for trace mineral homeostasis.

To date, there have been no randomized controlled trials examining the intake and/or needs of vitamins and trace elements in pediatric chronic kidney disease (CKD) or ESRD populations. This leads to an absence of data on ideal vitamin and trace element intakes in infants and children with advanced renal disease, in contrast to well-defined standards for healthy children. Guidelines from the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) Clinical Practice Guidelines for Nutrition in Children with CKD detail daily vitamin and trace element needs based on data from the *general pediatric population* [6, 7]. It is suggested that pediatric dialysis patients receive a water-soluble vitamin supplement such that the combination of enteral nutrition and supplemental vitamin provision meet age and gender-based values for daily recommended intake (DRI) accepted in the general pediatric population (see Table 1) to reduce risk for development of adverse health-related conditions associated with vitamin deficiency [5, 6].

Some pediatric dialysis patients who meet daily caloric goals through a combination of general diet and/or enteral formula supplements could actually meet or exceed the recommended 100% DRI for individual vitamins and trace elements through the use of adult multivitamin preparations occasionally given to children on dialysis due to the paucity of commercially available, dialysis-specific multivitamin supplement options available for pediatric use [8, 9]. Care should be taken to not greatly exceed 100% of the DRI for vitamin and trace element intake due to the potential for toxicity with supplementation on dialysis. Furthermore, collaboration and frequent evaluation with a renal dietician should occur to evaluate the total dietary intakes, including vitamin supplementation, to ensure adequacy of vitamin provision. Table 2 provides a comparison of vitamin and trace element content for commonly used renal formulas.

Natural dietary sources of water-soluble vitamins and key trace elements are found in foods such as fruits, legumes, red meat, and dairy, all of which may be limited in the ESRD population on dialysis because of high potassium and phosphorus contents. Reduced oral intakes related to stringent dietary and fluid modifications, combined with losses through dialytic clearance [10], create the potential for nutrient deficit or depletion.

Dietary sources of thiamine include lean pork, legumes, and enriched cereals. Data from adult PD patients suggests that spontaneous intakes of thiamine, as well as pyridoxine, appear to be largely related to reduction in enteral intake in parallel with progression of renal disease [11]. In a truly thiamine-free diet, intrinsic body stores are sufficient for

approximately 10 days prior to development of mild thiamine deficiency, with symptoms of severe thiamine deficiency manifesting at 14–20 days [12]. Basal thiamine requirements are increased in patients with a high metabolic rate (e.g., sepsis) or high carbohydrate intake, for example, in special populations receiving a dextrose-based, parenteral nutrition formula [13, 14] due to the requirement for thiamine in essential carbohydrate metabolism. In addition, the presence of protein energy wasting is a risk factor for effective thiamine deficiency given that thiamine is extensively protein-bound [15].

Green vegetables, fruits, grains, cereals, and liver are natural dietary sources of folate. In contrast to dietary thiamine and pyridoxine, exogenous (supplemented) folate is better-absorbed than naturally occurring folate [5]. Even healthy pediatric patients without kidney disease may have inadequate dietary folate intake if their diets are lacking in fruits and vegetables [16]. For patients on dialysis experiencing medically necessary dietary limitations, the risk for profound folate deficiency is significant [17]. This risk may, however, be attenuated with receipt of goal enteral nutrition in combination with a water soluble multivitamin [9]. Concern for folate deficiency in the dialysis patient should also prompt dietary and clinical evaluation for pyridoxine deficiency, as folate metabolism requires pyridoxine as a co-enzyme.

Bananas and dairy products are two rich sources of pyridoxine although respectively rich in potassium and phosphorus. Alternative sources of pyridoxine include fortified cereals, eggs, and fish. Even for pediatric dialysis patients receiving goal enteral nutrition, pyridoxine intake may be 40% less than the daily-recommended intake without vitamin supplementation [9, 18]. Pyridoxine metabolism functionally requires zinc as a co-factor, and symptomology of pyridoxine deficiency may be exacerbated by comorbid zinc deficiency in the dialysis patient.

Vitamin C deficiency in the maintenance dialysis patient may arise due to dietary restrictions in vitamin C containing foods, such as citrus fruits, that are also likely to contain high levels of potassium. Deficiency is further compounded by dialytic losses of vitamin C and heightened catabolism of vitamin C in inflammatory states associated with dialysis dependence [19]. Adult CAPD patients receiving inconsistent enteral nutrition may have vitamin C intakes that are lower than the DRI [11] and estimated plasma vitamin C levels can be as low as those observed in malnourished, non-dialysis patient populations meeting a clinical diagnosis of scurvy (< 10 micromolar) [20]. Conversely, infants on CCPD receiving appropriate enteral formulas will meet 100% DRI of vitamin C, with total intake approaching 180% if additional vitamin C supplementation is also provided [9]. Toxicity associated with vitamin C excess includes the potential for significant systemic secondary oxalosis. Oligoanuric ESRD patients are at greater risk for over supplementation as Vitamin C is normally excreted via the urine and may not be cleared adequately with dialysis to account for excessive supplementation. Balancing the lack of evidence for vitamin C supplementation in the dialysis population and the known risks associated with excess [21, 22], current NKF-KDOQI guidelines suggest that combined dietary and supplement intake for the pediatric dialysis patient should not significantly exceed the DRI [6].

The main source for trace element intake is the diet. High-protein food sources including poultry, eggs, meats, and whole grains are rich in zinc. Zinc deficiency has been rarely described in otherwise healthy, exclusively breast-fed infants whose mothers have diets lacking in good sources of zinc [23, 24]; thus, general maternal nutrition should be a clinical consideration for infants on dialysis receiving breast milk feeds as a primary source of nutrition. Zinc content may vary by formula type. For example, among infant formulas, phytates found within soy-based formula bind zinc, such that all soy-based formulas offered to infants on dialysis should be zinc-fortified [25, 26].

Selenium deficiency classically occurs in areas with low water and soil selenium, and in populations requiring long-term parenteral nutrition who receive inadequate or no selenium supplementation [27]. Primary sources of food yielding selenium include seafood, meats, and whole grains as well as local water sources. For the youngest ESRD patients, consideration should be given to selenium content based on formula type. Soy-based formula provides less selenium than cow's milk based formulas (typically ranging 0.2–0.6 micrograms per 100 milliliters for soy-based formula versus 0.8–1.2 micrograms per 100 milliliters for cow's milk); similarly, breast milk selenium content is variable according to the selenium dietary intake of the mother, but may be up to 1.5 micrograms per 100 milliliters [5].

Clinical features of vitamin and trace element deficiency

Water soluble vitamins

Of the water soluble vitamins, thiamine deficiency has potential to lead to the most dramatic clinical features. Thiamine plays a pivotal role in carbohydrate metabolism as a coenzyme for the conversion of pyruvate to acetyl coenzyme A (Figure 1, [28]). In acute thiamine deficiency, pyruvate accumulates and is metabolized to lactate without accompanying acidosis [29].

Early symptoms of mild thiamine deficiency may be vague, such as irritability, fatigue, anorexia, peripheral neuropathy, sleep disturbance, and depression. Unfortunately, the clinical diagnosis of thiamine deficiency in a chronically hospitalized patient on dialysis may be delayed if symptoms are mistaken for more common differential diagnoses such as sepsis, seizure, or cerebrovascular injury [30, 31]. Severe thiamine deficiency manifests as “dry Beriberi” with presentation of Wernicke encephalopathy as characterized by the triad of confusion, ophthalmoplegia, and ataxia. The clinical syndrome is further expanded with presentation of confabulation and amnesia, clinically termed Korsakoff syndrome. Thiamine deficiency may also lead to diastolic cardiac dysfunction manifesting in edema and peripheral vasodilation, known as “wet Beriberi.” Recurrent episodes of Wernicke encephalopathy in dialysis patients may be more likely in those who have had a prior episode, even in those with laboratory evidence of replete of thiamine stores and receiving prophylactic thiamine supplementation [30, 32].

Diagnosis of thiamine deficiency can be made via clinical symptomatology and laboratory evaluation using whole blood thiamine testing to quantitate the active form of thiamine (thiamine diphosphate) as an indicator of total body thiamine status. If clinical evidence of

thiamine deficiency exists, repletion should be initiated prior to waiting result of laboratory whole blood thiamine stores. Magnesium is a necessary component for the conversion of thiamine into thiamine pyrophosphate [33]. Thus, thiamine replacement for suspected severe thiamine deficiency should occur with replacement of magnesium as indicated.

Hematological abnormalities are hallmark clinical features of folate and pyridoxine deficiency. Folate is the dietary form of folic acid (B9). Folic acid (B9) functions as a necessary enzymatic cofactor in the synthesis of purine and thymidine nucleotides critical for red blood cell formation [34]. Pyridoxine (B6) is one of three derivatives of the pyridine ring: pyridoxine, pyridoxal, and pyridoxamine. Pyridoxine is a critical coenzyme for erythrocyte transaminase activity, influencing the stability and affinity of oxygen to hemoglobin polymers [35]. Sideroblastic anemia due to severe pyridoxine deficiency has been reported as a rare dialysis complication in adults [36]. Additional clinical features of pyridoxine deficiency include glossitis, cheilosis, and angular stomatitis. Folate deficiency may manifest as erythropoietin resistance in pediatric hemodialysis patients; improvement in serum hemoglobin and reduction in erythropoietin requirement occurs following folate provision [37]. Concern for erythropoietin resistance, in conjunction with megaloblastic anemia, should prompt evaluation for folate deficiency. Severe deficiencies of folate and pyridoxine may lead to seizures, mental status changes, chronic abdominal cramping/discomfort, nausea, and/or diarrhea.

Adequate folate and pyridoxine stores are required for the conversion of homocysteine to methionine [38]. Hyperhomocysteinemia is a well-known complication of ESRD with associated adverse cardiovascular outcomes. Pyridoxine and folate are thought to play key roles in the metabolism of plasma homocysteine. Large-scale clinical trials in adult dialysis and CKD literature have examined the potential effects of folate and pyridoxine supplementation on reduction of plasma homocysteine to improve cardiovascular morbidity and mortality; however, no large trial has yet demonstrated a long-term benefit from folate supplementation despite an absolute reduction in homocysteine level [39, 40]. While the impact of folic acid supplementation and benefit on cardiovascular outcomes in both adult and pediatric dialysis populations is unknown, current pediatric dialysis literature provides support for supplementation with 2.5–5.0 milligrams per day of folic acid in the setting of hyperhomocysteinemia [6, 41].

Vitamin C is an abundant plasma and intracellular antioxidant vitamin. Vitamin C is required as a critical co-factor for prolyl-hydroxylase and lysyl-hydroxylase in synthesis of collagen [42, 43]. This antioxidant vitamin also plays a key role in prevention of chronic-disease related anemia in the ESRD population through increased absorption and utilization of dietary non-heme iron [44], facilitation of erythropoiesis, and enhanced red blood cell stability [45]. The clinical manifestations of vitamin C deficiency may initially be subtle and confused with complaints of chronic uremia – weakness, malaise, fatigue, and minor bleeding. One recent clinical case report describes clinical diagnosis of scurvy in a pediatric peritoneal dialysis patient – including long-bone changes, gingival hyperplasia and bleeding, perifollicular hemorrhage, and bloody dialysate – with full clinical resolution of symptoms following appropriate oral vitamin C supplementation [46]. Aggressive enteral and/or

parenteral iron repletion should be provided in cases of suspected vitamin C deficiency in the dialysis patient given the high likelihood of coexisting, profound iron deficiency anemia.

Trace Elements

Zinc is an essential element required for cellular processes across the spectrum of normal cell growth and proliferation, repair, transport, and immune function [47]. Zinc has the ability to form tight structural bonds to maintain protein structure, for example – the zinc finger proteins that interact with DNA – as well as maintain nuclear stability and histone structure [48]. Up to 78% of adult patients on HD may be zinc deficient [49, 50]. Inadequate zinc levels in adult HD populations have been shown to be independent predictors of both mortality and infection requiring hospitalization [51]. Mild to moderate nutritional zinc deficiency is associated with nonspecific signs and symptoms including anorexia, dysgeusia, and reduced ability to protect against oxidative stress – all of which are commonly observed symptoms in dialysis patients regardless of zinc status [52, 53]. Significant zinc deficiency may lead to clinically significant growth delay/failure, mental status changes, and in males, hypogonadism/oligospermia [54]. In one rare case, Parra et al., describe an adult HD patient with laboratory evidence of zinc deficiency and presentation of acrodermatitis enteropathica-like syndrome – characterized by oral lesions, alopecia, chronic diarrhea, and mental status changes – with complete clinical resolution of symptoms after oral zinc sulfate repletion [55].

Selenium provides key antioxidant properties at the level of the vascular endothelium as a necessary co-factor for the enzyme glutathione peroxidase [56]. Selenium deficiency may present with progressive vascular and coronary disease, theoretically secondary to increased susceptibility to oxidant stress in the dialysis population. Clinical signs of low selenium stores may also include macrocytosis and loss of hair and skin pigmentation. Severe deficiency leads to a nutritional cardiomyopathy (“Keshan disease”) and may accelerate development of neurodegenerative disease [57, 58]. Adequate selenium stores are required for deiodinase conversion of triiodothyronine (T3) to thyroxine (T4) in normal thyroid hormone metabolism. Data support that selenium deficiency in adult hemodialysis patients is correlated with development of euthyroid sick syndrome [59].

Table 3 provides a summary of clinical symptoms associated with deficiency presentation, risk factors for deficiency, suggested diagnostic tests to confirm deficiency, and guidelines for repletion in the general (non-ESRD pediatric population).

Clearance of vitamins and trace elements by dialysis modality

Dialysis may result in depletion of substances that are present within the body but not present within the dialysate (e.g., water-soluble vitamins and/or certain trace elements). Filtration-based modalities of dialysis (e.g., HD and CRRT) provide clearance by allowing the equilibration of plasma water and dialysate across a semi-permeable membrane. In comparison to HD, PD patients are exposed to much lower dialysate volumes, but may have higher peritoneal protein losses leading to excessive loss of protein-bound trace elements [60].

Hemodialysis

In the chronic HD patient, loss of water-soluble vitamins to the dialysate is a well-recognized phenomenon [3]. The molecular weights of serum thiamine, pyridoxine, and folate are in the small to middle molecule range of 135–1400 Daltons, which are cleared readily with both high-flux and low-flux dialyzer membranes [61].

While thiamine is cleared via HD more effectively than via PD [62, 63], thiamine deficiency is a known, rare complication in patients on both modalities [32, 64]. Pyridoxine deficiency is common in the adult HD population [65]. It is unclear what effect the dialyzer membrane (e.g., high flux versus low flux) plays, if any, in removal of pyridoxine to the ultrafiltrate – particularly given that pyridoxine is a protein-bound molecule [61, 66]. Conversely, risk for folic acid deficiency may be directly impacted by use of a high flux dialyzer membrane. Plasma folic acid levels may decrease by approximately 26% during a single maintenance HD session in adults [67] with evidence of reduction in both plasma folate and red blood cell folate concentrations using high flux polysulfone dialyzers.

Vitamin C deficiency has been documented as a complication of both HD and PD in adult patient populations [68, 69]. Vitamin C is a non-protein bound molecule with a small molecular weight that is highly dialyzable. HD is estimated to remove several hundred milligrams of vitamin C per session [70, 71], reducing plasma ascorbic acid levels by 30–50% [20, 72]. As mentioned earlier, this degree of clearance may not be sufficient to prevent toxicity if the patient is receiving vitamin C well in excess of DRI.

Extended-hours home HD is offered at some select pediatric dialysis centers. This therapy option provides the dialysis patient a longer filtration-based treatment over several total treatments per week (e.g., three hours per session, five to six times per week). Limited data suggest that adult nocturnal HD may be associated with a higher risk of deficiency of water-soluble vitamins, specifically thiamine and vitamin C, when providing greater than 15 hours per week of therapy compared to conventional HD therapy [73].

Zinc deficiency is of particular concern in the maintenance HD population secondary to declining dietary intake with progression of renal disease coinciding with dialysate zinc losses on maintenance HD [74, 75]. In a meta-analysis of 128 studies, Tonelli et al. demonstrated that serum levels of zinc were significantly lower in adult HD patients on maintenance therapy [76]. Zinc may be removed by HD at a higher rate than other trace elements due to its lack of protein binding [62].

Selenium levels, like zinc, have been cited as deficient in the adult chronic HD population [76]; however, data are conflicting as to whether lower plasma selenium levels on HD may be more reflective of nutritional status and/or increased inflammatory responses and oxidative stress rather than increased selenium clearance, per se [77, 78].

Peritoneal Dialysis

There can be significant losses of pyridoxine and folic acid through peritoneal dialysis [79, 80]. Pyridoxine may be more readily cleared than folic acid due to increased propensity for protein binding compared to folic acid [15]. CAPD is unlikely to result in significant

clearance of thiamine [81]. Adult data suggest that there is high clearance of vitamin C into peritoneal dialysate and that more intensive dialysis regimens may result in greater dialysate vitamin C losses [82].

Less information is available regarding the removal of trace elements by peritoneal dialysis compared to the removal of water-soluble vitamins. Selenium and zinc losses on peritoneal dialysis do not appear to be significant [83].

Continuous renal replacement therapy (CRRT)

In addition to the maintenance HD and PD populations, acutely ill patients requiring support with high-clearance/high-flow modalities such as continuous renal replacement therapy (CRRT) are at risk for depletion of water-soluble vitamins. Thus, although this form of acute renal replacement therapy is in contrast to the maintenance forms discussed above, it does require brief mention here. Limited data exist to support strategies for targeted supplementation and repletion of trace elements in the adult critical care population on while receiving CRRT; however, there are no similar guidelines for children. Broadly speaking, micronutrients lost in CRRT should be replaced as indicated.

Studies in adult patients demonstrate removal of 68 milligrams vitamin C and 290 micrograms of folic acid per day by CRRT [84]. Pediatric patients on CRRT may be at risk for decreased serum folate levels despite positive daily folate balances, suggesting that standard pediatric folate supplementation may not be adequate on therapies such as CRRT [85]. Prolonged CRRT can result in thiamine losses of ~ 4 mg/24 hours in critically ill adults with the potential for acute thiamine depletion despite standard daily parenteral nutrition provision. Thus, additional thiamine supplementation could be considered in the critically ill patient (both pediatric and adult) on CRRT [12, 86].

Pasko et al. [87] reviewed records of five pediatric patients on CRRT and demonstrated minimal trans-membrane losses of chromium, copper, manganese, and zinc. These data suggest that pediatric patients on short-term CRRT, receiving supplementation with trace elements via standard parenteral nutrition, do not experience clinically significant losses of most trace elements, even at higher effluent rates of 60 ml/min per 1.73 m² [87, 88]. Selenium is most at risk for depletion despite supplementation at standard amounts in critically ill patients [12]; thus additional daily parenteral selenium supplementation may be warranted for those on CRRT [89].

Conclusion

Clinically symptomatic forms of nutrient deficiency are infrequently reported in pediatric maintenance dialysis patients, but consideration to key vitamin and trace element depletion with routine nutritional assessment in the dialysis patient is critical. It is particularly important in the patient with acute on chronic medical illness who may have suboptimal enteral nutrition or additional risk factors for pre-existing nutritional deficiencies. Ultimately the diagnosis of vitamin and trace element deficiency in the pediatric dialysis patient may be made only after severe deficiencies present clinically.

A multidisciplinary approach to care, including routine assessment with a skilled renal dietician, is essential in screening for nutritional disease from vitamin and trace element deficiency. Nutritional illness should be considered in the differential diagnoses for the many variable clinical symptoms that arise in the pediatric dialysis population. Knowledge of signs and symptoms associated with subtle nutritional deficiencies will allow for early evaluation, diagnosis, and treatment of these potentially critical and correctable conditions.

References

1. Ratsch IM, Catassi C, Verrina E, Gusmano R, Appiani A, Bettinelli A, Picca S, Rizzoni G, Fabian-Bach C, Wingen AM, Mehls O, Giorgi PL. Energy and nutrient intake of patients with mild-to-moderate chronic renal failure compared with healthy children: an Italian multicentre study. *Eur J Pediatr.* 1992; 151:701–705. [PubMed: 1396935]
2. Norman LJ, Coleman JE, Macdonald IA, Tomsett AM, Watson AR. Nutrition and growth in relation to severity of renal disease in children. *Pediatr Nephrol.* 2000; 15:259–265. [PubMed: 11149122]
3. Makoff R. Water-soluble vitamin status in patients with renal disease treated with hemodialysis or peritoneal dialysis. *J Renal Nutr.* 1991; 1:56–73.
4. Makoff R, Dwyer J, Rocco MV. Folic acid, pyridoxine, cobalamin, and homocysteine and their relationship to cardiovascular disease in end-stage renal disease. *J Renal Nutr.* 1996; 6:2–11.
5. Kleinman, RE., Greer, FR. *Pediatric Nutrition.* American Academy of Pediatrics; Elk Grove Village: 2013. Trace Elements.
6. National Kidney Foundation. KDOQI Clinical Practice Guideline for Nutrition in Children with CKD: 2008 Update. *Am J Kidney Dis.* 2008; 53(Suppl 2):S11–104.
7. Health Canada. Dietary reference intake: recommended dietary allowance and adequate intake. Minister of Public Works and Government Services; 2010.
8. Kriley M, Warady BA. Vitamin status of pediatric patients receiving long-term peritoneal dialysis. *Am J Clin Nutr.* 1991; 53:1476–1479. [PubMed: 2035477]
9. Warady BA, Kriley M, Alon U, Hellerstein S. Vitamin status of infants receiving long-term peritoneal dialysis. *Pediatr Nephrol.* 1994; 8:354–356. [PubMed: 7917868]
10. Wiesen P, Van Overmeire L, Delanaye P, Dubois B, Preiser JC. Nutrition disorders during acute renal failure and renal replacement therapy. *JPEN J Parenter Enteral Nutr.* 2011; 35:217–222. [PubMed: 21378251]
11. Wang AY, Sea MM, Ip R, Law MC, Chow KM, Lui SF, Li PK, Woo J. Independent effects of residual renal function and dialysis adequacy on dietary micronutrient intakes in patients receiving continuous ambulatory peritoneal dialysis. *Am J Clin Nutr.* 2002; 76:569–576. [PubMed: 12198001]
12. Berger MM, Shenkin A, Revely JP, Roberts E, Cayeux MC, Baines M, Chiolo RL. Copper, selenium, zinc, and thiamine balances during continuous venovenous hemodiafiltration in critically ill patients. *Am J Clin Nutr.* 2004; 80:410–416. [PubMed: 15277163]
13. Sequeira Lopes da Silva JT, Almaraz Velarde R, Olgado Ferrero F, Robles Marcos M, Perez Civantos D, Ramirez Moreno JM, Luengo Perez LM. Wernicke's encephalopathy induced by total parental nutrition. *Nutr Hosp.* 2010; 25:1034–1036. [PubMed: 21519777]
14. Francini-Pesenti F, Brocadello F, Manara R, Santelli L, Laroni A, Caregaro L. Wernicke's syndrome during parenteral feeding: not an unusual complication. *Nutrition.* 2009; 25:142–146. [PubMed: 18929463]
15. Chazot, C., Kopple, JD. Vitamin metabolism and requirements in renal disease and renal failure. In: Kopple, JD., Massry, SG., editors. *Kopple and Massry's Nutritional Management of Renal Disease.* Lippincott Williams & Wilkins; Philadelphia, PA: 2003. p. 415–478.
16. Cavadini C, Siega-Riz AM, Popkin BM. US adolescent food intake trends from 1965 to 1996. *West J Med.* 2000; 173:378–383. [PubMed: 11112748]

17. Jankowska M, Szupryczyńska N, Debska-Slizien A, Borek P, Kaczkan M, Rutkowski B, Malgorzewicz S. Dietary Intake of Vitamins in Different Options of Treatment in Chronic Kidney Disease: Is There a Deficiency? *Transplant Proc.* 2016; 48:1427–1430. [PubMed: 27496421]
18. Foreman JW, Abitbol CL, Trachtman H, Garin EH, Feld LG, Strife CF, Massie MD, Boyle RM, Chan JC. Nutritional intake in children with renal insufficiency: a report of the growth failure in children with renal diseases study. *J Am Coll Nutr.* 1996; 15:579–585. [PubMed: 8951735]
19. Raimann JG, Levin NW, Craig RG, Sirover W, Kotanko P, Handelsman G. Is Vitamin C Intake too Low in Dialysis Patients? *Semin Dial.* 2013; 26:1–5. [PubMed: 23106569]
20. Jackson P, Loughrey CM, Lightbody JH, McNamee PT, Young IS. Effect of hemodialysis on total antioxidant capacity and serum antioxidants in patients with chronic renal failure. *Clin Chem.* 1995; 41:1135–1138. [PubMed: 7628087]
21. Rolton HA, McConnell KM, Modi KS, Macdougall AI. The effect of vitamin C intake on plasma oxalate in patients on regular haemodialysis. *Nephrol Dial Transplant.* 1991; 6:440–443. [PubMed: 1876286]
22. Ono K. Secondary hyperoxalemia caused by vitamin C supplementation in regular hemodialysis patients. *Clin Nephrol.* 1986; 26:239–243. [PubMed: 3802587]
23. Kuramoto Y, Igarashi Y, Tagami H. Acquired zinc deficiency in breast-fed infants. *Semin Dermatol.* 1991; 10:309–312. [PubMed: 1764359]
24. Piela Z, Szuber M, Mach B, Janniger CK. Zinc deficiency in exclusively breast-fed infants. *Cutis.* 1998; 61:197–200. [PubMed: 9564591]
25. Erdman JW Jr, Fordyce EJ. Soy products and the human diet. *Am J Clin Nutr.* 1989; 49:725–737. [PubMed: 2655410]
26. Sandstrom B, Cederblad A, Lonnerdal B. Zinc absorption from human milk, cow's milk, and infant formulas. *Am J Dis Child.* 1983; 137:726–729. [PubMed: 6869328]
27. Vinceti M, Filippini T, Cilloni S, Bargellini A, Vergoni AV, Tsatsakis A, Ferrante M. Health risk assessment of environmental selenium: Emerging evidence and challenges (Review). *Mol Med Rep.* 2017; 15:3323–3335. [PubMed: 28339083]
28. Velez RJ, Myers B, Guber MS. Severe Acute Metabolic-Acidosis (Acute Beriberi) - an Avoidable Complication of Total Parenteral-Nutrition. *J Parenter Enter.* 1985; 9:216–219.
29. Giacalone M, Martinelli R, Abramo A, Rubino A, Pavoni V, Iaconi P, Giunta F, Forfori F. Rapid reversal of severe lactic acidosis after thiamine administration in critically ill adults: a report of 3 cases. *Nutr Clin Pract.* 2015; 30:104–110. [PubMed: 25516536]
30. Hung SC, Hung SH, Tarng DC, Yang WC, Chen TW, Huang TP. Thiamine deficiency and unexplained encephalopathy in hemodialysis and peritoneal dialysis patients. *Am J Kidney Dis.* 2001; 38:941–947. [PubMed: 11684545]
31. Descombes E, Dessibourg CA, Fellay G. Acute encephalopathy due to thiamine deficiency (Wernicke's encephalopathy) in a chronic hemodialyzed patient: a case report. *Clin Nephrol.* 1991; 35:171–175. [PubMed: 1855320]
32. Barbara PG, Manuel B, Elisabetta M, Giorgio S, Fabio T, Valentina C, Emanuela M, Massimo B, Giuseppe S, Paolo SG. The suddenly speechless florist on chronic dialysis: the unexpected threats of a flower shop? Diagnosis: dialysis related Wernicke encephalopathy. *Nephrol Dial Transplant.* 2006; 21:223–225. [PubMed: 16280376]
33. Dyckner T, Ek B, Nyhlin H, Wester PO. Aggravation of thiamine deficiency by magnesium depletion. A case report. *Acta Med Scand.* 1985; 218:129–131. [PubMed: 4050546]
34. Koury MJ, Horne DW. Apoptosis mediates and thymidine prevents erythroblast destruction in folate deficiency anemia. *Proc Natl Acad Sci U S A.* 1994; 91:4067–4071. [PubMed: 8171036]
35. Shenkin, A., Roberts, NB., Chem, C. Vitamins and trace elements. In: Burtis, CA, Ashwood, ER., Bruns, DE., editors. *Teitz Textbook of Clinical Chemistry and Molecular Diagnostics.* Saunders/Elsevier; St. Louis, MO: 2012. p. 895
36. Nankivell BJ. Vitamin B6 deficiency on hemodialysis causing sideroblastic anemia. *Nephron.* 1991; 59:674–675. [PubMed: 1766516]
37. Bamgbola OF, Kaskel F. Role of folate deficiency on erythropoietin resistance in pediatric and adolescent patients on chronic dialysis. *Pediatr Nephrol.* 2005; 20:1622–1629. [PubMed: 16133045]

38. Ducker GS, Rabinowitz JD. One-Carbon Metabolism in Health and Disease. *Cell Metab.* 2016; 25:27–42. [PubMed: 27641100]
39. Jamison RL, Hartigan P, Kaufman JS, Goldfarb DS, Warren SR, Guarino PD, Gaziano JM, Veterans Affairs Site I. Effect of homocysteine lowering on mortality and vascular disease in advanced chronic kidney disease and end-stage renal disease: a randomized controlled trial. *JAMA.* 2007; 298:1163–1170. [PubMed: 17848650]
40. Heinz J, Kropf S, Domrose U, Westphal S, Borucki K, Luley C, Neumann KH, Dierkes J. B vitamins and the risk of total mortality and cardiovascular disease in end-stage renal disease: results of a randomized controlled trial. *Circulation.* 2010; 121:1432–1438. [PubMed: 20231532]
41. Schroder CH, de Boer AW, Giesen AM, Monnens LA, Blom H. Treatment of hyperhomocysteinemia in children on dialysis by folic acid. *Pediatr Nephrol.* 1999; 13:583–585. [PubMed: 10460506]
42. Pinnell SR. Regulation of collagen biosynthesis by ascorbic acid: a review. *Yale J Biol Med.* 1985; 58:553–559. [PubMed: 3008449]
43. Murad S, Grove D, Lindberg KA, Reynolds G, Sivarajah A, Pinnell SR. Regulation of collagen synthesis by ascorbic acid. *Proc Natl Acad Sci U S A.* 1981; 78:2879–2882. [PubMed: 6265920]
44. Fidler MC, Davidsson L, Zeder C, Walczyk T, Hurrell RF. Iron absorption from ferrous fumarate in adult women is influenced by ascorbic acid but not by Na2EDTA. *Br J Nutr.* 2003; 90:1081–1085. [PubMed: 14641967]
45. Handelman GJ. New insight on vitamin C in patients with chronic kidney disease. *J Ren Nutr.* 2011; 21:110–112. [PubMed: 21195931]
46. Kittisakmontri K, Swangtrakul N, Padungmaneeb W, Charoenkwan P. Gingival Bleeding and Bloody Dialysate: A Case Report of Scurvy in a Child With End-Stage Renal Disease Receiving Peritoneal Dialysis. *J Ren Nutr.* 2016; 26:407–411. [PubMed: 27118080]
47. Stefanidou M, Maravelias C, Dona A, Spiliopoulou C. Zinc: a multipurpose trace element. *Arch Toxicol.* 2006; 80:1–9. [PubMed: 16187101]
48. Berg JM, Shi Y. The galvanization of biology: a growing appreciation for the roles of zinc. *Science.* 1996; 271:1081–1085. [PubMed: 8599083]
49. Lee SH, Huang JW, Hung KY, Leu LJ, Kan YT, Yang CS, Wu DC, Huang CL, Chen PY, Chen JS, Chen WY. Trace metals' abnormalities in hemodialysis patients: Relationship with medications. *Artif Organs.* 2000; 24:841–844. [PubMed: 11119069]
50. Vanholder R, Cornelis R, Dhondt A, Lameire N. The role of trace elements in uraemic toxicity. *Nephrol Dial Transplant.* 2002; 17(Suppl 2):2–8.
51. Yang CY, Wu ML, Chou YY, Li SY, Deng JF, Yang WC, Ng YY. Essential trace element status and clinical outcomes in long-term dialysis patients: a two-year prospective observational cohort study. *Clin Nutr.* 2012; 31:630–636. [PubMed: 22405403]
52. Shankar AH, Prasad AS. Zinc and immune function: the biological basis of altered resistance to infection. *Am J Clin Nutr.* 1998; 68:447S–463S. [PubMed: 9701160]
53. Chen J, Wang S, Luo M, Zhang Z, Dai X, Kong M, Cai L, Wang Y, Shi B, Tan Y. Zinc deficiency worsens and supplementation prevents high-fat diet induced vascular inflammation, oxidative stress, and pathological remodeling. *Toxicol Sci.* 2016
54. Prasad AS. Clinical manifestations of zinc deficiency. *Annu Rev Nutr.* 1985; 5:341–363. [PubMed: 3896271]
55. Parra E, Campistol JM, Soy D, Deulofeu R. Acrodermatitis enteropathica-like syndrome in a dialysis patient. *Nephron.* 1995; 70:389–390. [PubMed: 7477640]
56. Turan B, Delilbasi E, Dalay N, Sert S, Afrasyap L, Sayal A. Serum Selenium and Glutathione-Peroxidase Activities and Their Interaction with Toxic Metals in Dialysis and Renal-Transplantation Patients. *Biol Trace Elem Res.* 1992; 33:95–102. [PubMed: 1379465]
57. Chen J, Berry MJ. Selenium and selenoproteins in the brain and brain diseases. *J Neurochem.* 2003; 86:1–12. [PubMed: 12807419]
58. Rederstorff M, Krol A, Lescure A. Understanding the importance of selenium and selenoproteins in muscle function. *Cell Mol Life Sci.* 2006; 63:52–59. [PubMed: 16314926]

59. Liu ML, Xu G, Huang ZY, Zhong XC, Liu SH, Jiang TY. Euthyroid sick syndrome and nutritional status are correlated with hyposelenemia in hemodialysis patients. *Int J Artif Organs*. 2011; 34:577–583. [PubMed: 21786251]
60. D'Haese PC, De Broe ME. Adequacy of dialysis: trace elements in dialysis fluids. *Nephrol Dial Transplant*. 1996; 11(Suppl 2):92–97. [PubMed: 8804004]
61. Heinz J, Domrose U, Westphal S, Luley C, Neumann KH, Dierkes J. Washout of water-soluble vitamins and of homocysteine during haemodialysis: Effect of high-flux and low-flux dialyser membranes. *Nephrology*. 2008; 13:384–389. [PubMed: 18518942]
62. Vanrenterghem D, Cornelis R, Vanholder R. Behavior of 12 Trace-Elements in Serum of Uremic Patients on Hemodiafiltration. *J Trace Elem Electrolytes Health Dis*. 1992; 6:169–174. [PubMed: 1483035]
63. Fouque D, Vennegoor M, ter Wee P, Wanner C, Basci A, Canaud B, Haage P, Konner K, Kooman J, Martin-Malo A, Pedrini L, Pizzarelli F, Tattersall J, Tordoir J, Vanholder R. EBPG guideline on nutrition. *Nephrol Dial Transplant*. 2007; 22(suppl 2):Sii45–Sii87.
64. Ueda K, Takada D, Mii A, Tsuzuku Y, Saito SK, Kaneko T, Utsumi K, Iino Y, Katayama Y. Severe thiamine deficiency resulted in Wernicke's encephalopathy in a chronic dialysis patient. *Clin Exp Nephrol*. 2006; 10:290–293. [PubMed: 17186335]
65. Corken M, Porter J. Is vitamin B(6) deficiency an under-recognized risk in patients receiving haemodialysis? A systematic review: 2000–2010. *Nephrology (Carlton)*. 2011; 16:619–625. [PubMed: 21609363]
66. Kasama R, Koch T, Canals-Navas C, Pitone JM. Vitamin B6 and hemodialysis: the impact of high-flux/high-efficiency dialysis and review of the literature. *Am J Kidney Dis*. 1996; 27:680–686. [PubMed: 8629628]
67. Leblanc M, Pichette V, Geadah D, Ouimet D. Folic acid and pyridoxal-5'-phosphate losses during high-efficiency hemodialysis in patients without hydrosoluble vitamin supplementation. *J Ren Nutr*. 2000; 10:196–201. [PubMed: 11070147]
68. Richter A, Kuhlmann MK, Seibert E, Kotanko P, Levin NW, Handelsman GJ. Vitamin C deficiency and secondary hyperparathyroidism in chronic haemodialysis patients. *Nephrol Dial Transplant*. 2008; 23:2058–2063. [PubMed: 18353890]
69. Zhang KY, Dong J, Cheng XY, Bai WY, Guo WY, Wu LY, Zuo L. Association between vitamin C deficiency and dialysis modalities. *Nephrology*. 2012; 17:452–457. [PubMed: 22404236]
70. Morena M, Cristol JP, Bosc JY, Tetta C, Forret G, Leger CL, Delcourt C, Papoz L, Descamps B, Canaud B. Convective and diffusive losses of vitamin C during haemodiafiltration session: a contributive factor to oxidative stress in haemodialysis patients. *Nephrol Dial Transplant*. 2002; 17:422–427. [PubMed: 11865087]
71. Bohm V, Tiroke K, Schneider S, Sperschneider H, Stein G, Bitsch R. Vitamin C status of patients with chronic renal failure, dialysis patients and patients after renal transplantation. *Int J Vitam Nutr Res*. 1997; 67:262–266. [PubMed: 9285256]
72. Sullivan JF, Eisenstein AB. Ascorbic acid depletion during hemodialysis. *JAMA*. 1972; 220:1697–1699. [PubMed: 5067604]
73. Coveney N, Polkinghorne KR, Linehan L, Corradini A, Kerr PG. Water-soluble vitamin levels in extended hours hemodialysis. *Hemodial Int*. 2011; 15:30–38. [PubMed: 21105994]
74. Bhogade RB, Suryakar AN, Joshi NG. Effect of hemodialysis on serum copper and zinc levels in renal failure patients. *EJGM*. 2013; 10:154–157.
75. Guo CH, Wang CL. Effects of zinc supplementation on plasma copper/zinc ratios, oxidative stress, and immunological status in hemodialysis patients. *Int J Med Sci*. 2013; 10:79–89. [PubMed: 23289009]
76. Tonelli M, Wiebe N, Hemmelgarn B, Klarenbach S, Field C, Manns B, Thadhani R, Gill J. Alberta Kidney Disease N. Trace elements in hemodialysis patients: a systematic review and meta-analysis. *BMC Med*. 2009; 7:25. [PubMed: 19454005]
77. Bober J, Kwiatkowska E, Kedzierska K, Olszewska M, Golebiewska E, Stachowska E, Kucharska E, Ciechanowski K, Chlubek D. Influence of glucose in the dialysate on the activity of erythrocyte-glutathione-peroxidase and blood selenium concentration in hemodialyzed patients. *Arch Med Res*. 2007; 38:330–336. [PubMed: 17350485]

78. Iglesias SB, Leite HP, Paes AT, Oliveira SV, Sarni RO. Low plasma selenium concentrations in critically ill children: the interaction effect between inflammation and selenium deficiency. *Crit Care*. 2014; 18:R101. [PubMed: 24886623]
79. Blumberg A, Hanck A, Sander G. Vitamin Nutrition in Patients on Continuous Ambulatory Peritoneal-Dialysis (Capd). *Clin Nephrol*. 1983; 20:244–250. [PubMed: 6652978]
80. Boeschoten EW, Schrijver J, Krediet RT, Schreurs WH, Arisz L. Deficiencies of vitamins in CAPD patients: the effect of supplementation. *Nephrol Dial Transplant*. 1988; 3:187–193. [PubMed: 3140085]
81. Makoff R. Vitamin replacement therapy in renal failure patients. *Miner Electrolyte Metab*. 1999; 25:349–351. [PubMed: 10681665]
82. Tsapas G, Magoula I, Paletas K, Concouris L. Effect of peritoneal dialysis on plasma levels of ascorbic acid. *Nephron*. 1983; 33:34–37. [PubMed: 6835452]
83. Sriram K, Abraham G. Loss of zinc and selenium does not occur through peritoneal dialysis. *Nutrition*. 2000; 16:1047–1051. [PubMed: 11118823]
84. Story DA, Ronco C, Bellomo R. Trace element and vitamin concentrations and losses in critically ill patients treated with continuous venovenous hemofiltration. *Crit Care Med*. 1999; 27:220–223. [PubMed: 9934919]
85. Zappitelli M, Juarez M, Castillo L, Coss-Bu J, Goldstein SL. Continuous renal replacement therapy amino acid, trace metal and folate clearance in critically ill children. *Intensive Care Med*. 2009; 35:698–706. [PubMed: 19183946]
86. Honore PM, De Waele E, Jacobs R, Mattens S, Rose T, Joannes-Boyau O, De Regt J, Verfaillie L, Van Gorp V, Boer W, Collin V, Spapen HD. Nutritional and metabolic alterations during continuous renal replacement therapy. *Blood Purif*. 2013; 35:279–284. [PubMed: 23689499]
87. Pasko DA, Churchwell MD, Btaiche IF, Jain JC, Mueller BA. Renal Replacement Therapy Kinetics Study G. Continuous venovenous hemodiafiltration trace element clearance in pediatric patients: a case series. *Pediatr Nephrol*. 2009; 24:807–813. [PubMed: 19156445]
88. Churchwell MD, Pasko DA, Btaiche IF, Jain JC, Mueller BA. Trace element removal during in vitro and in vivo continuous haemodialysis. *Nephrol Dial Transplant*. 2007; 22:2970–2977. [PubMed: 17556411]
89. Martinez JL, Riera JASI, Jimenez FJJ. Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Acute renal failure. *Nutr Hosp*. 2011; 26:21–26. [PubMed: 22411514]
90. Kliegman, RM. Stanton, BMD. St Geme, J., Schnor, NF., editors. *Nelson's Textbook of Pediatrics*. Saunders Elsevier; Philadelphia, PA: 2016.
91. Weinstein M, Babyn P, Zlotkin S. An orange a day keeps the doctor away: scurvy in the year 2000. *Pediatrics*. 2001; 108:E55. [PubMed: 11533373]
92. Hotz C, Brown KH. Identifying populations at risk of zinc deficiency: The use of supplementation trials. *Nutr Rev*. 2001; 59:80–84. [PubMed: 11330625]
93. Vinton NE, Dahlstrom KA, Strobel CT, Ament ME. Macrocytosis and Pseudoalbinism - Manifestations of Selenium Deficiency. *J Pediatr-Us*. 1987; 111:711–717.

Summary Points

1. Symptoms of water-soluble vitamin and trace element deficiency may be confused with pre-existing/evolving symptoms of ESRD. Consideration to underlying nutritional deficiency should be given for those patients who are unable to tolerate full enteral nutrition or are dependent on parenteral nutrition for prolonged periods of time.
2. Thiamine (vitamin B1) is a key water-soluble vitamin that is cleared more readily by hemodialysis than peritoneal dialysis. Risk for thiamine deficiency is highest in critically ill dialysis patients (particularly those requiring HD or CRRT) with pre-existent malnutrition and are those requiring long-term, high-carbohydrate, parenteral nutrition.
3. Vitamin C is cleared by both hemodialysis and peritoneal dialysis. Adult data demonstrate a tendency for low vitamin C levels, particularly in the maintenance HD population; however, pediatric data suggest that childhood ESRD vitamin C intakes may be adequate if receiving appropriate, well-tolerated enteral nutrition in combination with water soluble vitamin supplementation.
4. Zinc levels are more likely to be lower in the maintenance HD population given that zinc is a non-protein bound element and may be more readily removed by filtration-based dialysis methods. Zinc deficiency is an independent risk factor for hospitalization overall mortality in the dialysis population.
5. Maintenance HD and prolonged CRRT patients may be at risk for lower selenium levels. Significant selenium depletion can lead to nutritional cardiomyopathy and thyroid disease.

Figure 1.
Thiamine requirements in the metabolic pathways of glucose*

Suggested dietary allowance and adequate intake for water-soluble vitamins and trace elements in the general pediatric population [6–7]. *Note – recommended daily allowances (RDA) are in bold with adequate intakes in standard font.*

Table 1

	Infants 0–6 mo	Infants 7–12 mo	Children 1–3 y	Children 4–8 y	Males 9–13 y	Males 14–18 y	Females 9–13 y	Females 14–18 y
Vitamin A ($\mu\text{g/d}$)	400	500	300	400	600	900	600	700
Vitamin C (mg/d)	40	50	15	25	45	75	45	65
Vitamin E (mg/d)	4	5	6	7	11	15	11	15
Vitamin K ($\mu\text{g/d}$)	2.0	2.5	30	55	60	75	60	75
Thiamin (mg/d)	0.2	0.3	0.5	0.6	0.9	1.2	0.9	1.0
Riboflavin (mg/d)	0.3	0.4	0.5	0.6	0.9	1.3	0.9	1.0
Niacin (mg/d; NE)	2 ⁺	4	6	8	12	16	12	14
Vitamin B ₆ (mg/d)	0.1	0.3	0.5	0.6	1.0	1.3	1.0	1.2
Folate ($\mu\text{g/d}$)	65	80	150	200	300	400	300	400
Vitamin B ₁₂ ($\mu\text{g/d}$)	0.4	0.5	0.9	1.2	1.8	2.4	1.8	2.4
Pantothenic Acid (mg/d)	1.7	1.8	2	3	4	5	4	5
Biotin ($\mu\text{g/d}$)	5	6	8	12	20	25	20	25
Copper ($\mu\text{g/d}$)	200	220	340	440	700	890	700	890
Selenium ($\mu\text{g/d}$)	15	20	20	30	40	55	40	55
Zinc (mg/d)	2	3	3	5	8	11	8	9

Vitamin and Trace Element Content of Commonly Used Enteral Formulas in Pediatric Dialysis Patients
Content value from individual formula can be compared to percent daily recommended intake needs for patient age and gender as seen on Table 1.

Table 2

<i>Content per 100 mL</i>	<u>Thiamine (B1)</u>	<u>Pyridoxine (B6)</u>	<u>Folate (B9)</u>	<u>Vitamin C</u>	<u>Zinc</u>	<u>Selenium</u>
Similac Standard	0.07 mg	0.04 mg	10.7 mcg	6 mg	0.5 mg	1.67 mcg
Gerber GoodStart Gentle	0.07 mg	0.05 mg	10 mcg	6.7 mg	0.5 mg	2 mcg
Similac PM 60/40	0.07 mg	0.04 mg	10 mcg	6 mg	0.5 mg	1.2 mcg
Calcilo	0.07 mg	0.04 mg	10 mcg	6 mg	0.5 mg	1.67 mcg
Suplena[*]	0.23 mg	0.8 mg	104 mcg	10.4 mg	4.2 mg	12 mcg
Nepro[*]	0.23 mg	0.8 mg	104 mcg	10.4 mg	4.2 mg	12 mcg

* Denotes a formula often used in adult dialysis populations but can be utilized in the pediatric setting as indicated by nutritional needs.

Table 3

3a - Overview of water soluble vitamin and trace minerals at risk for deficiency in the pediatric dialysis population			
Nutrient	Symptoms of Deficiency	Dietary Sources	Diagnostic Tests
Thiamine (B1)	“Wernicke encephalopathy” – peripheral neuropathy, ophthalmoplegia, nystagmus, ataxia, edema	dairy, nuts, legumes, fruits, egg, unrefined grains, pork, vegetables	Thiamine pyrophosphate level, whole blood/red blood cell transketolase activation test
Pyridoxine (B6)	Facial seborrhea, glossitis, angular stomatitis, cheilosis, mental status changes	Fortified cereals	Pyridoxal 5'-phosphate 4-pyridoxic acid
Folate (B9)	Abdominal cramps, nausea, diarrhea, irritability, poor sleep, seizures, megaloblastic anemia	Green vegetables, liver, grains, some fruits	Acute deficiency – low serum folate Chronic deficiency – low red blood cell folate
Vitamin C (ascorbic acid)	“Scurvy” – osmotic diarrhea, gingival bleeding, perifollicular hemorrhage, long-bone changes (arthropathy)	Citrus fruits	White blood cell ascorbate concentration, radiographic evidence of long bone widening
Zinc	Clinical phenotype of “Acrodermatitis enteropathica” – anorexia, hypogeusia, growth retardation, diffuse skin lesions with impaired wound healing	Meat, dairy, legumes, whole grains, oysters	Blood zinc level
Selenium	“Keshan disease” – progressive cardiomyopathy, cardiovascular disease with thyroid disease, also with myositis	Meats, seafood, nuts	Blood selenium level

3b – Repletion dosing for vitamin and trace mineral deficiencies in the general pediatric population^{^^}	
Thiamine (B1)	Children:10–25 mg/day parenterally x 1–2 wk, followed by 5 mg PO for 6 weeks [90]
Pyridoxine (B6)	5–25 mg/day of oral pyridoxine x 3 weeks, followed by 2.5–5 mg/day orally via multivitamin
Folate (B9)	Deficiency in infants: 0.1 mg/kg/day oral administration daily Deficiency in children: 1.0 mg oral administration daily, followed by 0.1 to 0.5 mg daily maintenance dosing.
Vitamin C	100 mg orally, intramuscularly, or intravenously 3x per day x 1 week, followed by 100 mg daily [91]
Zinc	Supplementation trial with 1 mg/kg; can increase to 2 mg/kg BID-TID [92]
Selenium	2 mcg/kg/day IV selenium for repletion followed by 1 mcg/kg/day as maintenance therapy for goal of serum level of 50–150 mcg/L [93]

^{^^} Dosing not otherwise established in pediatric CKD/ESRD