


**RENAL**

## Nutrition Assessment of Vitamin & Trace Element Status in CKD

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### Learning Objectives

- Identify factors that impact assessment of vitamin and trace element status
- Discuss the signs and symptoms of nutrient deficiencies and toxicities
- Assess the impact of medications on vitamin and trace element status
- Review recommendations for dosing vitamins and trace elements in CKD patients
- Examine the issues surrounding laboratory measurement of vitamins and trace elements

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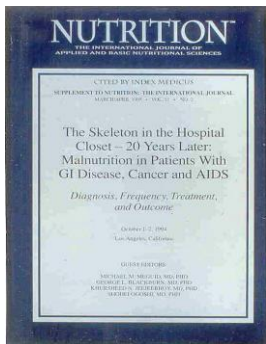
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### Vitamins/Trace Elements and CKD

- Deficiency Risk
  - Zinc, selenium, chromium, copper, manganese, iron
  - B vitamins: pyridoxine, cobalamin, folate
  - Vitamin C
  - Vitamin D
- Toxicity Risk
  - Vitamin A & E
  - Vitamin C
  - Aluminum



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### KDOQI 2020 Clinical Guidelines

- CKD 5D: Consider micronutrient supplementation (water-soluble vitamins/trace elements) to treat deficiency with sustained inadequate intake
- Caution with potential adverse effects of vitamins A, C, E
- No evidence that supplemental zinc or selenium improves nutritional, inflammatory, or micronutrient status



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## Steps to Identifying Nutrient Status

- Evaluate dietary intake
- Review urinary and GI losses or retention
- Identify potential dialysate losses or sources
- Review drug-nutrient interactions
- Determine metabolic demand for nutrients
- Review laboratory data
- Examine patient for signs/symptoms of toxicity/deficiency



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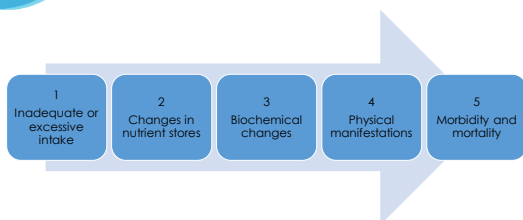
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## Stages of Nutrient Imbalance



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## Signs & Symptoms of Deficiency/Toxicity

Clark SF. Chapter 8 in The A.S.P.E.N. Adult Nutrition Support Core Curriculum, 2012

Vitamin	Deficiency	Toxicity
Vitamin A	Impaired wound healing, night blindness, Bitot's spot	Alopecia, dry mucous membranes, dry/rough skin, anemia, cortical bone loss/fractures, ataxia, renal osteodystrophy, pruritus, conjunctivitis
Vitamin D	Hypocalcemia, osteomalacia, osteoporosis	Hypercalcemia, hyperphosphatemia, suppressed parathyroid levels, hypercalciuria, soft tissue calcification
Vitamin E	↑ platelet aggregation, hemolytic anemia, neuronal degeneration	Impaired neutrophil function, impaired coagulation
Vitamin K	Bleeding, hemorrhage, low bone density	Prolonged bleeding

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## Signs & Symptoms of Deficiency/Toxicity

Clark SF, Chapter 8 in The A.S.P.E.N. Adult Nutrition Support Core Curriculum, 2012

Vitamin	Deficiency	Toxicity
Vitamin C	Anorexia, fatigue, petechiae, bleeding gums, impaired wound healing	Kidney stone risk, rebound scurvy, nausea, vomiting
Thiamin	Dry beriberi: paresthesia, weakness in lower extremities Wet beriberi: cardiac failure, refractory lactic acidosis, Wernicke-Korsakoff syndrome, encephalopathy, ataxia	Uncommon
Riboflavin	Hyperemia/edema pharyngeal & oral mucosa, magenta tongue	Rare
Niacin	Dermatitis, diarrhea, dementia, sunburn-like rash in sun-exposed areas	Flushing of the skin, (3 g/d): vasodilation, itching, GI irritation

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## Signs & Symptoms of Deficiency and Toxicity

Clark SF, Chapter 8 in The A.S.P.E.N. Adult Nutrition Support Core Curriculum, 2012

Nutrient	Deficiency	Toxicity
Folic Acid	Megaloblastic macrocytic anemia, smooth sore tongue, dementia	No toxic effects known
Biotin	Hypotonia, anorexia, pallor, glossitis, lethargy, muscle pain, alopecia	No known toxic effects
Pantothenic Acid	Listlessness, irritability, neuromuscular disturbances, hypoglycemia	Rare – mild GI distress
Cobalamin (B <sub>12</sub> )	Cognitive decline, CVD, bone fractures, megaloblastic macrocytic anemia (pernicious anemia)	None known
Pyridoxine	Seborrheic dermatitis, microcytic anemia, confusion, glossitis	Sensory neuropathy, sensory ataxia, impaired cutaneous & deep sensations

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## Signs & Symptoms of Deficiency and Toxicity

Clark SF, Chapter 8 in The A.S.P.E.N. Adult Nutrition Support Core Curriculum, 2012

Trace Element	Deficiency	Toxicity
Iron	Microcytic, hypochromic anemia, tachycardia, poor capillary refill	Organ damage (liver, heart, pancreas)
Zinc	Inadequate growth, alterations in taste & smell, poor wound healing, anemia, atherosclerosis risk	GI distress, nausea, ↓ immune function, ↓ HDL
Copper	Sensory ataxia, hypochromic microcytic anemia, pancytopenia	Rare – liver damage
Manganese	↓ reproductive performance, ataxia, defects in carb/lipid metabolism	CNS abnormalities, ataxia, hyperirritability, hallucinations
Selenium	Oxidative injury, altered thyroid hormone metabolism, Keshan disease	Nausea, vomiting, alopecia, tooth decay, skin lesions
Iodine	Nodular goiter, tachycardia, muscle weakness	↓ thyroid activity, ↑ TSH
Chromium	Weight loss, refractory hyperglycemia, ↑ plasma free fatty acids	Rhabdomyolysis, liver dysfunction, renal failure
Fluoride	Increased risk for developing dental caries	Nausea, vomiting, diarrhea
Molybdenum	Tachycardia, tachypnea, visual and mental changes, lethargy	Rare – hyperuricemia, gout-like symptoms




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## Goals of Nutrient Limitation/Supplementation

- Alleviate signs & symptoms
- Maintain/correct metabolic pathways
- Improve overall health
- Correct laboratory values



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## Factors Affecting Adequacy

### Deficiency Risk

- Insufficient intake
- Absorption competition
- Increased metabolic demand
- Dialysis losses
- Excessive/ongoing losses
  - Malabsorption
  - Malabsorption
  - Urinary/GI/wound losses
- Medications

### Toxicity Risk

- Excessive intake
- Impaired excretion /absorption
  - Renal insufficiency
  - Hyperbilirubinemia
- Contamination of IV solutions
- Decreased metabolic demand
- Medications



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Medication	Impacted Nutrients
Warfarin	Vitamin K is antagonist
Loop and thiazide diuretics	↑ urinary loss of Na, K, Mg, Zn
Sulfamethoxazole/trimethoprim	Interferes with folate metabolism
Fluoroquinolones	Bind to Mg, Ca, Zn and Fe to form insoluble/non-absorbable complex
Tetracyclines	Bind to Mg, Ca, Zn and Fe to form insoluble/non-absorbable complex; may ↓ vit K production by bacteria; long-term use ↑ risk of B vit def; combining with vit A can ↑ intracranial HTN
Rifampin	May increase metabolism of vit D
Amphotericin B	Causes losses of K, Mg, Ca; nephrotoxic
Biguanide	↓ absorption of B <sub>12</sub> and folic acid
Corticosteroids	↓ Ca absorption, ↑ urinary loss of Ca, K, Zn, Vit C
Bisphosphonates	↓ serum Ca; long-term can cause Zn deficiency
ACE inhibitors/ ARBs	May ↑ K
Calcium acetate	May reduce Fe absorption
Sevelamer carbonate	May interfere with fat soluble vitamin absorption

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## Differential Diagnosis

- Where are losses/excesses occurring?
- Why is the patient losing/gaining nutrient(s)?
- Is nutrition support/diet meeting or exceeding needs?
- What else results in observed signs and symptoms?



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## Name the Nutrient Deficiency

- A. Beriberi
- B. Pellagra
- C. Goiter
- D. Scurvy

Casal's necklace  
Niacin / tryptophan deficiency

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### Name the Nutrient Deficiency

- A. Vitamin C
- B. Zinc
- C. Biotin
- D. Fluoride

**Scurvy**  
Bleeding gums occur in conjunction with poor dentition

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### Name the Nutrient Deficiency

- A. Rickets
- B. Beriberi
- C. Scurvy
- D. Pernicious anemia

The earliest signs of vitamin C deficiency are small ecchymosis and petechiae

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### Name the Nutrient Deficiency

- A. Vitamin D
- B. Thiamin
- C. Folic acid
- D. Zinc

Patients can also present with growth retardation, anorexia, alopecia, diarrhea, apathy, night blindness, poor wound healing and dysgeusia

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## High Risk Patients for Deficiency

- Refeeding syndrome: thiamin
- SBS/steatorrhea: B<sub>12</sub>, FSV, Se, Zn, Fe, riboflavin, choline
- Bariatric surgery: B<sub>12</sub>, Fe, Folate, A, C, B<sub>6</sub>, D, thiamin
- Chronic inflammation: antioxidants (Zn, Se, Cu, A, C, E)
- CKD: D, Fe, Zn, water-soluble vitamins
- Liver disease: Zn, Se, FSV, thiamin, B<sub>12</sub>, folate, niacin, riboflavin, pyridoxine
- ETOH abuse: thiamin, riboflavin, niacin, folate
- Wound healing: A, C, Zn
- Inadequate sun exposure: D



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## Too Much of a Nutrient?

- Vitamin A: CKD
  - Alopecia, muscle/bone pain
- Manganese: long-term PN
  - CNS abnormalities
- Copper: hyperbilirubinemia
  - Liver damage (rare)
- Excess oral zinc = ↓ copper & iron absorption
  - GI distress, decreased immune function
- Vitamin C
  - Avoid excessive doses with CKD (oxalosis), iron overload disease or with anticoagulation therapy
- Pharmacologic doses of niacin for hyperlipidemia
  - vasodilation (flushing)
- Excess iron
  - hemochromatosis



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### Recommendations for Fat-Soluble Vitamins and CKD-5

McCann Pocket Guide 6<sup>th</sup> ed & Byham-Gray et al Clinical Guide 2<sup>nd</sup> ed

Vitamin	Daily Dose	Comments
Vitamin A	none	Levels increased with CKD. Elevated levels can cause anemia and abnormal lipid and calcium metabolism. Do not routinely supplement due to toxicity risk.
Vitamin D	Based on patient need and surrogate markers	Vit D, PTH, calcium, phos involved in bone metabolism: protocols for management per dialysis unit. Provide cholecalciferol or ergocalciferol to correct 25(OH)D deficiency.
Vitamin E	15 mg (DRI: 22.5)	Patients on anticoagulation therapy: vit E can contribute to DVT and a vit K-responsive hemorrhagic condition. Do not routinely supplement due to toxicity risk.
Vitamin K	1 mg with antibiotic therapy	Antibiotics may interfere with vit K production in the GI tract. Avoid supplementation with anticoagulation

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### Recommendations for Water-Soluble Vitamins with CKD-5

Daugirdas et al Handbook of Dialysis 5<sup>th</sup> ed, 2015

Vitamin	Daily Dose	Comments
Thiamin	1.5 mg	ATP production; CHO metabolism
Riboflavin	1.7 mg	Essential for B <sub>6</sub> & niacin functions; component of 2 flavin coenzymes: FMN & FAD
Niacin	20 mg	2 forms: nicotinic acid and nicotinamide (NAD/NADP)
Pantothenic Acid	10 mg	Component of CoA
Pyridoxine	10 mg	3 forms: pyridoxine, pyridoxal, pyridoxamine; conversion of tryptophan to niacin
Cyanocobalamin	4 µg	Coenzyme that transfers H <sub>2</sub> atoms and methyl groups; homocysteine to methionine
Vitamin C	60-100 mg	Reductive protection for folic acid & vit E. Provide at least 75 mg/d (f) or 90 mg/d (m) with deficiency risk
Folic acid	> 1 mg	Transports single carbon fragments - amino acids, purines, pyrimidines (DNA)
Biotin	30 µg	Transports carboxyl units

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### Recommendations for Trace Elements for CKD-5

McCann Pocket Guide 6<sup>th</sup> ed & Byham-Gray et al Clinical Guide 2<sup>nd</sup> ed

Trace Element	Daily Dose	Comments
Selenium	55-70 µg (PD)	No recommendations for HD, renal excretion
Zinc	15 mg (HD) 12-15 mg (PD)	Routine supplementation not recommended. Increase dose with large GI losses, bound to albumin.
Copper*	10 mg (DRI)	Zinc supplementation decreases absorption
Chromium*	DRI not determined	Renal excretion
Iron	10-15 mg (PD) Individualized (HD)	Zinc supplementation decreases absorption
Iodine*	1.1 mg (DRI)	Renal excretion

\* No specific recommendations for CKD

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## Ideal Laboratory Test

Shenkin A Nutrition 1997

- Identify severe micronutrient deficiency and associated clinical risk
- Identify depleted micronutrient status (b/o poor intake/utilization) prior to clinical risk
- Identify adequate micronutrient status and optimal tissue function



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## Micronutrient Laboratory Tests

Mordarski B. *Nutrition Focused Physical Exam*, 3<sup>rd</sup> ed. 2022

Nutrient	Test	*serum/plasma **whole blood	Normal Value	Deficiency	Toxicity
Vitamin A	vitamin A (retinol)*		30-100 µg/dL	< 10 µg/dL	>100 µg/dL
Vitamin D	Calcifediol [25(OH)D]*		≥20 ng/mL	≤ 12 ng/mL	> 50 ng/mL
Vitamin E	Alpha-tocopherol* Alpha-tocopherolipids*		0.5-2.0 mg/dL	<0.5 mg/dL <0.8 mg/g total lipid	>2.0 mg/dL
Vitamin K	Prothrombin time [PT] <small>plasma</small> International normalized ratio (INR)		10-13 seconds ≤1.1 (therapeutic range: 2-3)	elevated elevated	
Thiamine (B1)	Thiamine pyrophosphate (TPP)** Thiamine**		0-14% 3.0-7.7 µg/dL	≥25% (severe) <1.7 µg/dL	
Riboflavin (B2)	Erythrocyte glutathione reductase activity coefficient (EGRAC)**		< 1.2	>1.4	
Niacin (B3)	N-methylnicotinamide <small>(24-hr urine)</small> N-methyl-2-pyridoxine-5-carboximide [2-pyridoxine] <small>(24-hr urine)</small>		17.5-46.7 µmol/d	<5.8 µmol/d <2 mg/g Cr	

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## Micronutrient Laboratory Tests

Mordarski B. *Nutrition Focused Physical Exam*, 3<sup>rd</sup> ed. 2022

Nutrient	Test	*serum/plasma* whole blood**	Normal Value	Deficiency	Toxicity
Pyridoxine (B6)	Pyridoxal 5'-phosphate [PLP] <small>plasma/RBC</small> 4-pyridoxic acid (PA) <small>24hr urine</small> Erythrocyte aspartate aminotransferase (eAST) index** & Erythrocyte alanine aminotransferase (eALT) index**		39-98 nmol/L >3 µmol/d <1.6 <1.25	<20 nmol/L <3 µmol/d	
Cobalamin (B12)	vitamin B <sub>12</sub> * Methylmalonic acid (MMA) <small>serum</small> Homocysteine (Hcy)*		170-250 pg/mL 0.08-0.56 µmol/L 5-15 µmol/L 65 y: <20 µmol/L	<150 pg/mL elevated elevated	
Folate (B9)	RBC erythrocyte Folate*		140-628 ng/mL	<140 ng/mL <3 ng/mL	
Biotin	Biotin <small>serum/whole blood</small> Biotin <small>(24-hr urine)</small> 3-hydroxyisovaleric acid (3-HIA)		<200 pg/mL < 6 µg/d 75-195 µmol/d	<200 pg/mL < 6 µg/d >195 µmol/d	
Vitamin C	ascorbic acid*		> 0.4 mg/dL	≤0.2 mg/dL	

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## Micronutrient Laboratory Tests

Mordarski B. *Nutrition Focused Physical Exam*, 3<sup>rd</sup> ed. 2022

Nutrient	Test serum/plasma* whole blood**	Normal Value	Deficiency	Toxicity
Iron	Ferritin serum	M: 40-300 µg/L F: 20-200 µg/L	<12-30 µg/L	M: >300 µg/L F: >200 µg/L
	TIBC		>400 µg/dL	
	Transferrin saturation(%) serum	15-45%	≤ 15%	
	Mean corpuscular volume (MCV) Hemoglobin**	80-95 fL	≤ 80 fL M: <13 g/dL F: <12 g/dL	
Zinc	Zinc* Zinc 14 hr urine	80-120 µg/dL 0.2-1.3 mg/d	<30 µg/dL	
Copper	Copper*	70-140 µg/dL	<50 µg/dL	>140 µg/dL
	Ceruloplasmin serum	20-35 mg/dL	< 20 mg/dL	
	Copper 24-hr urine	< 60 µg/d	>60 µg/d	
Manganese	Manganese**	5-15 µg/L		

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## Micronutrient Laboratory Tests

Mordarski B. *Nutrition Focused Physical Exam*, 3<sup>rd</sup> ed. 2022

Nutrient	Test *serum/plasma **whole blood	Normal Value	Deficiency	Toxicity
Selenium	Glutathione peroxidase** Selenium*	63-160 µg/L	< 10.5 U/mL <40 µg/L	>400 µg/L
Iodine	Median urinary excretion of iodine T <sub>3</sub> (triiodothyronine) serum	100-199 µg/L	< 20 µg/L 20-49 yr: >204 ng/dL 50-90 yr >181 ng/dL	≥300 µg/L
Chromium	Chromium serum	<0.05-0.5 µg/L		
	Chromium erythrocyte	20-34 µg/L		
	Chromium urine	0.1-2 µg/L		

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## Monitoring Micronutrient Levels

- Check micronutrient levels for suspected potential deficiencies/toxicities every 3-12 months or according to dialysis unit policies/procedures or MD orders
- Correlate suspected deficiencies and toxicities with ...
  - Physical signs and symptoms
  - Dietary nutrient intake
  - Other sources of nutrients
  - Potential nutrient losses
  - Medications
  - Co-morbidities



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### Justifying Nutrient Monitoring and Supplementation

We need to determine a correlation among biochemical indices, functional activity, physical manifestations and nutrient intake in order to identify the most clinically and cost effective treatment strategies

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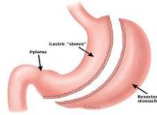
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### Which nutrients?

Following a gastrectomy, a patient complains of fatigue and poor memory. What potential nutrient deficiencies should be checked?

- A. Vitamin A, folic acid
- B. Vitamin C, pyridoxine
- C. Riboflavin, copper
- D. B<sub>12</sub>, iron



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### Which nutrients?

A patient with history of alcoholism presents with muscle pain, seborrheic dermatitis, alopecia, & pallor. Which of the following nutrients are most likely deficient?

- A. Biotin, pyridoxine
- B. Niacin, vitamin C
- C. Vitamin D, chromium
- D. B<sub>12</sub>, selenium



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### Which nutrients?

A PN patient is hyperglycemic (refractory to insulin therapy) and pancytopenic with hyperbilirubinemia. What nutrients could be contributing to these symptoms?

- A. Vitamin D, chromium
- B. Selenium, zinc
- C. Chromium, copper
- D. Thiamin, manganese



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### Which nutrients?

A mother is concerned that her teenage daughter is actually a vampire. The girl is pale, avoids sunlight, sleeps all day and has a blood red tongue. Before sharpening the wooden stake, what potential nutrient deficiencies should be investigated?

- A. Selenium, iron
- B. Iron, riboflavin
- C. Pyridoxine, thiamin
- D. Copper, vitamin A



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### Summary

- Assess patients for possible nutrient toxicities and deficiencies
- Provide complete nutrition daily
- Provide supplemental nutrients as indicated
  - Supplement 7-10 days then return to standard dose
  - Do not provide excessive doses
- Continuously re-assess for adequacy



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Answers: 1B, 2A, 3C, 4D, 5D, 6A, 7C, 8B

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Please send any additional feedback or comments to [clinicaleducation@pentechealth.com](mailto:clinicaleducation@pentechealth.com).

Since this is a CPE accredited program, feedback may be provided directly to Commission on Dietetic Registration CDR at [QualityCPE@eatright.org](mailto:QualityCPE@eatright.org).

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