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Vitamin and Mineral Recommendations for Older People with Chronic Kidney Disease

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Introduction

The number of people aged 65 and older in the US is currently more than 36 million and will increase to 86 million by 2050 (1). At age 65, life expectancy is an additional 18.2 years (1). The prevalence of chronic diseases, including chronic kidney disease (CKD), is high, and chronic diseases are responsible for almost half of all disabilities among older adults (2). Four out of five older Americans experience limitations as a result of chronic disease (2).

It is important for health professionals to consider that 80% of people newly diagnosed with CKD are 65 or older (3). Both age and CKD can influence nutrient requirements. Generally, the Dietary Reference Intakes (DRI) should be used as the basis for nutrient recommendations (Recommended Dietary Allowances (RDA) and Adequate Intakes (AI))(4)(Table 1). The Dietary Guidelines for Americans should also be used because they recently increased the amount of vitamin D recommended for older adults (5) (Table 1). The DRIs recommend that compared to people aged 50 or younger, those 51 and older need less iron (women only), more calcium and vitamin D, and should consume vitamin B12 in the crystalline form. The DRIs also provide Tolerable Upper Intake Levels (UL) that can help health professionals and their patients avoid excess amounts of some vitamins and minerals (Table 1). The most authoritative source of nutrient recommendations specifically for CKD are the guidelines established by the National Kidney Foundation (NKF) Kidney Disease Outcome Quality Initiative (K/DOQI) (6), which in some cases differ markedly from the DRIs (e.g., for iron). There are several other sources of vitamin and mineral recommendations that are cited in the CKD literature (7,8). The purpose of this article is to: 1) identify authoritative vitamin and mineral recommendations for older people with CKD and 2) provide practical advice regarding inconsistencies in recommendations and supplement formulations.

Iron

Iron is often depleted in CKD and anemia is common (7,9,10). The RDA for iron is 8 mg/day for older adults (Table 1). However, for those with CKD, especially those receiving dialysis or erythropoietin therapy, iron needs far exceed the RDA and the UL (6). Most references support K/DOQI recommendations of 200 mg/day and suggest oral supplementation (7,10), but a daily dose of 200 mg of elemental iron may not maintain iron stores and intravenous administration is often necessary (9,10). Problems such as poor bioavailability and lack of patient compliance accompany the use of oral supplements. Multivitamins do not provide sufficient

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oral iron for the CKD patient (Table 1). IV iron sources include iron dextran, gluconate, and sucrose and side effects of IV iron tend to be mild and transient for most people. Patients receiving IV iron should be monitored for iron overload at least every 3 months by evaluating serum ferritin levels (6,10).

Calcium

The AI for calcium in older people is 1,200 mg/day (Table 1). The maximum amount of calcium recommended for CKD is generally lower than the UL of 2,500 mg/day (Table 1). For example, K/DOQI recommends that the total elemental calcium (including dietary calcium and calcium-based phosphate binders) should not exceed 2,000 mg/day (6). Others recommend that when calcium-based binders are used, the total elemental calcium should not exceed 1,500 mg/day (8). These recommendations reflect the concern about calcium homeostasis in those with CKD and the need for close dietary management of calcium intake as an effective strategy for maintaining calcium levels within normal limits and preventing calcification of body tissue and vasculature (11,12). Although calcium intake may be restricted in CKD, an adequate intake is needed for maintenance of bone health. Hypercalcemia is common in those receiving calcium-based phosphate binders; therefore, a reduced dosage or alternative non-calcium containing binder may be recommended. Multivitamin/mineral supplements for the general population of older adults can be a source of calcium (Table 1), so their use should be considered in calculating total calcium intake in CKD.

Vitamin D

Vitamin D is best known for its roles in calcium homeostasis and bone health, and poor vitamin D status is associated with high PTH. Because diminished skin synthesis of vitamin D occurs with aging (13), the Dietary Guidelines for Americans recommends that older people consume 1,000 IU of vitamin D daily from foods and supplements (5). 25-hydroxyvitamin D is a biomarker for the nutritional status of vitamin D and reflects the contributions of sunlight, diet, and dietary supplements (13). The Dietary Guidelines (5) and K/DOQI (6) have similar recommendations for optimal serum 25-hydroxyvitamin D concentrations of 75 nmol/L to 80 nmol/L.

Unless otherwise contraindicated by the physician and the stage of CKD, it may be reasonable to consider that older people with CKD should consume the new recommendation for vitamin D of 1,000 IU/day. Supplements would be needed, because there are few rich dietary sources (e.g., one cup of milk has 100 IU vitamin D, 13). Multivitamin/mineral supplements for the general population typically have 400 IU vitamin D, but those for CKD do not contain vitamin D (Table 1).

K/DOQI (6) provides guidelines for treating vitamin D deficiency and insufficiency (Table 2). For those with severe deficiency, supplementation would average about 7,000 IU/day. Although this is well above the UL of 2000 IU/day, it reflects the body's high need for vitamin D to correct deficiency (14). K/DOQI (6) also provide guidelines for reducing PTH, with active oral vitamin D sterols (calcitriol, alfacalcidol, paracalcitol or doxercalciferol) when serum levels of 25 (OH)D are greater than 30 ng/ml (75 nmol/L) and plasma levels of intact PTH are above the target range for the CKD stage.

Vitamin A

It seems reasonable to recommend that older people with CKD consume the RDA for vitamin A from foods (7,15,16), such as vitamin A-rich vegetables, and avoid exceeding the UL of 3,000 µg of pre-formed retinol/day (Table 1). Others note the need for vitamin A for wound healing and recommend that intake not exceed 1000 µg/day from all sources (17). It is difficult to compare the amount of vitamin A in foods and supplements with the DRIs, because the DRI units are µg/day, while dietary supplements use units of "IU" (additional information can be found at reference 18). Also, some supplements may have only pre-formed retinol, while others may have the less bioavailable beta-carotene. One CKD supplement was reported to contain vitamin A and provided 3000 IU (19), which is similar to most multivitamin/mineral supplements for the general older adult population (Table 1). With a decline in kidney function, vitamin A has the potential to accumulate in serum. However, both high and low serum vitamin A concentrations have been found in those with CKD (15) and the increase in serum vitamin A often seen in CKD parallels the increase in retinol-binding

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Table 1

Vitamin and Mineral Recommendations for Older People with CKD

	Males[a] 51-70 y >70 y	Females[a] 51-70 y >70 y	UL[a]	MVM CKD[c]	MVM Older Adults[d]
Vitamin A, retinol (µg/d)	900	700	3000	0 or 3000 IU	2500-3500 IU
Vitamin C (mg/d)	90	75	2000	40-100	60-120
Vitamin D (µg/d)[b]	25	25	50	-	400 IU
Vitamin E (mg/d)	15	15	1000	30-100 IU	33-45 IU
Vitamin K (µg/d)	120	90	NE	-	10-20
Thiamin (mg/d)	1.2	1.1	NE	1.5-3.0	1.5-4.5
Riboflavin (mg/d)	1.3	1.1	NE	1.5-2.0	1.7-3.4
Niacin (mg/d)	16	14	35	20	20
Vitamin B_6 (mg/d)	1.7	1.5	100	10-50	3-6
Folate (µg/d)	400	400	1000	800-5000	400
Vitamin B_{12}, crystalline (µg/d)	2.4	2.4	NE	6-2000	25
Panthothenic (mg/d)	5	5	NE	5-10	10-15
Biotin (µg/d)	30	30	NE	150-300	30
Choline (mg/d)	550	425	3.5g	-	-
Calcium (mg/d)	1200	1200	2500	-	120-200
Chromium (µg/d)	30	20	NE	-	150-180
Copper (µg/d)	900	900	10000	-	2 mg
Fluoride (mg/d)	4	3	10	-	-
Iodine (µg/d)	150	150	1100	-	150
Iron (mg/d)	8	8	45	-	-
Magnesium (mg/d)	420	320	350	-	100
Manganese (mg/d)	2.3	1.8	11	-	2-4
Molybdenum (µg/d)	45	45	2000	-	75-90
Phosphorus (mg/d)	700	700	4000 (19-70 yrs) 3000 (>70 yrs)	-	0-48
Selenium (µg/d)	55	55	400	0-70	20-105
Zinc (mg/d)	11	8	40	12.5-50	15-22.5

Abbreviations: MVM is multivitamin/mineral supplement; NE is Not Established; UL is Tolerable Upper Intake Level

[a]From Food and Nutrition Board, Institute of Medicine, National Academies. *Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals, Vitamins, Elements*. National Academy of Sciences. Washington DC, National Academy Press, 2004. (41)

[b]From USDHHS & USDA, 2005. *2005 Dietary Guidelines for Americans*; ref #); the recommendation for vitamin D is for "older adults", but age is not defined; 40 IU - 1 µg. (5)

[c]From Feiertag PN. Dietary supplement use in patients with chronic kidney disease. *Ren Nutr Forum*. 2006;25:11-20. (19)

[d]From Centrum® Silver® and One-A-Day® 50+ daily multivitamin supplements.

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Table 2

Recommended Supplementation for Vitamin D Deficiency/Insufficiency in Patients with CKD Stage 3 and 4

Serum 25(OH)D	Definition	Ergocalciferol Dose (Vitamin D2)	Average Daily Dose	Duration (months)	Comment
< 5 ng/ml, <12.5 nmol/L	Severe vitamin D deficiency	50,000 IU/wk orally x 12 wks: then monthly 500,000 IU as single I.M. dose	7143 IU/day	6 months	Measure 25(OH)D levels after 6 months Assure patient adherence: measure at 6 months
5-15 ng/ml 12.5-37.5 nmol/L	Mild vitamin D deficiency	50,000 IU/wk x 4 wks then 50,000 IU/month orally	7143 IU/day	6 months	Measure 25(OH)D levels after 6 months
16-30 ng/ml 40-75 nmol/L	Vitamin D insufficiency	50,000 IU/monthly orally	1667 IU/day	6 months	

K/DOQI (6). 25(OH)D is 25-hydroxy vitamin D. 1 IU of vitamin D = 0.25 µg.

protein (20). It has been noted that elevated levels of vitamin A can contribute to anemia and abnormalities of lipid and calcium metabolism (21).

Vitamin E

Vitamin E is an antioxidant vitamin and vitamin E supplements may enhance the immune system of older people (22,23), but the benefits for cardiovascular health are disappointing (7). Studies reviewed by K/DOQI suggest that oral supplements of vitamin E reduced oxidative stress for some with CKD. For example, the Secondary Prevention with Antioxidants of Cardiovascular Disease (SPACE) trial showed a significant benefit from vitamin E (800 IU/day) supplementation in hemodialysis patients with pre-existing CVD. In contrast, another study found that supplements did not reduce oxidative stress in those undergoing hemodialysis (400 mg, 888 IU/day, 24).

Similar to vitamin A, the units for vitamin E can be confusing because there are different chemical forms in foods (tocopherols and tocotrienols), different stereoisomers ("d" and "l") in supplements, and "IU" is defined differently by the DRI and on supplement labels (for more information see reference 25). The DRI defines one IU as 1 mg d-alpha-tocopherol; thus, for a supplement of dl-alpha-tocopherol label as 400 IU, only about half of this would be in the "d" form. It may be reasonable to consider that people with CKD consume at least the RDA (15 mg/day as alpha-tocopherol) and avoid exceeding the UL of 1,000 mg/day (Table 1). This UL is for supplements only, because of concern that very high intakes of vitamin E (> 1,000 mg/day) can become antagonistic to vitamin K, putting individuals at risk for hemorrhage, particularly those using oral anticoagulants (7,25).

Recommendations for CKD include 15 IU of vitamin E daily for older adults undergoing hemodialysis (8) and meeting the vitamin E requirement through diet (16), but the US diet generally provides only half of the RDA (25). Supplements for CKD and for the general population of older adults contain similar amounts of vitamin E (Table 1), but do not contain the amount that has been shown to enhance immune function in older people (about 200 IU, 22).

Vitamin K

Vitamin K is required for synthesis of proteins needed for blood coagulation and bone metabolism (18). There is concern that the current AI for vitamin K may be too low (26), but because vitamin K might interfere with certain mediations (e.g, anticoagulants), vitamin K is added in only low amounts to general multivitamin/mineral supplements and apparently is not added to supplements for CKD (Table 1). Intake may be low in people advised to limit green leafy vegetables because of anticoagulation therapy (27). Supplements for vitamin K are not typically recommended for people with CKD and it has been suggested that needs

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are usually met with diet (16). No UL has been established for vitamin K and single supplements are normally not taken by the general population (18). More research is needed about vitamin K and CKD, especially regarding the role of vitamin K in bone metabolism.

Folate

Folate is involved in the prevention of megaloblastic anemia and the regulation of homocysteine levels. The RDA for older adults is 400 µg/day and the UL is 1,000 µg/day and pertains to supplements only (28). For CKD, folate supplements in the range of 1,000 to 5,000 µg/day have been recommended (7,29), which may be of concern because these levels exceed the UL of 1,000 µg/day (Table 1). The rationale for the UL for folate includes potential masking of vitamin B12 deficiency.

The rationale for high supplemental intakes of folate in CKD is for homocysteine lowering, with homocysteine being a risk factor for cardiovascular disease. Menon et al. (30) showed a reduction in elevated homocysteine levels for half of the participants that were supplemented with 1,000 µg of folic acid in combination with 10 mg of vitamin B6 and 6 µg of vitamin B12/day. Wrone et al. (31) showed that dosages of 5,000 µg, 10,000 µg, and 15,000 µg/day reduced homocysteine levels, but the study failed to support doses over 1,000 µg/day for reduction of CVD or other outcomes. Other studies indicate that folic acid supplementation is not effective for lowering homocysteine levels in those undergoing dialysis (32) and there is limited support for supplementation for all stages of CKD (30).

Vitamin B12

Vitamin B12 is needed for the nervous system and red cell synthesis (28). Vitamin B12 presents unique concerns for the older adult population, often attributable to malabsorption problems associated with atrophic gastritis or Helicobacter pylori infection (28,33,34). Between 5% and 40% of the older adult population may have vitamin B12 deficiency, depending on the population and the criteria used for assessment of deficiency (35).

The RDA for vitamin B12 is 2.4 µg/day for older adults and should be in the crystalline form found in dietary supplements or fortified foods for enhanced absorption (5,28). For CKD, others recommend consuming 100% of the RDA (7), 3 µg/day (8), and 6 µg/day for those with CKD receiving renal replacement therapy (36,37). Also, Menon et al. (30) noted that supplementation with 6 µg of vitamin B12, along with supplements of folic acid and vitamin B6, were effective in reducing homocysteine. Vitamin B12 absorption in CKD was much lower than that of healthy controls, perhaps suggesting that requirements are higher in CKD than the non-CKD population (36,38). Obeid et al. (38) has proposed that elevations in homocysteine seen in CKD may be related to "vitamin B12 resistance," because of impaired cellular uptake of vitamin B12. There is a large range of vitamin B12 in multivitamin/mineral supplements for CKD and for older adults, but most provide at least 6 µg (Table 1).

Vitamin B6

Vitamin B6 is involved in hemoglobin synthesis and hence is important in the prevention of anemia, especially for those with CKD. The RDA for vitamin B6 is just under 2 mg/day for older men and women (Table 1). Others recommend that those with CKD receiving renal replacement therapy should obtain 100% of the RDA (7) compared to the older segment of CKD patients receiving renal replacement therapy that should consume 2 mg of vitamin B6 (8).

Vitamin B6 deficiency may occur in CKD, and approximately 10 mg daily is recommended for treatment of deficiency (30,37,39). This does not exceed the UL of 100 mg/day. This UL is based on concern that excessive vitamin B6 can lead to peripheral neuropathy (28). Therefore, attention should also be given for the prevention of toxicity (39). Vitamin B6 in multivitamin/mineral supplements is many fold higher in formulations for those with CKD compared to the general older adult population (Table 1), but is less than the UL. However, animal studies show that renal insufficiency increases vitamin B6 toxicity (39), so the high level found in CKD supplements is potentially of concern.

Comparison of Multivitamin/mineral Supplements

Those with CKD may be advised not to take any over-the-counter dietary supplements (40). However, several formulations specifically for people with CKD provide only a few of the vitamins and minerals known to be essential,

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provide some nutrients at high levels (e.g., folate and vitamin B6), and do not contain any vitamin D which is of particular concern for older adults (Table 1). Perhaps improvements could be made in multivitamin/mineral supplements that might provide additional nutritional support for the CKD patient.

Recommendations for the Renal Dietitian

1. Assist patients in meeting their vitamin and mineral needs for their prescribed nutrition plan.
2. Encourage patients to consult their dietitian and physician before taking dietary supplements.
3. Recognize that the current formulations of multivitamin/mineral supplements for CKD vary considerably, typically contain fewer nutrients compared to general multivitamin/mineral, and contain some nutrients in excess of the UL.
4. Understand that current formulations multivitamin/mineral supplements for the general older adult population may contain some vitamins and minerals contraindicated in some patients with CKD.

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References

1. Centers for Disease Control and Prevention. (2006) United States Trend Tables - Older Population Age 65 Years and Over. Available at http://www.cdc.gov/nchs/products/pubs/pubd/hus/older.htm. Accessed January 2007.
2. Administration on Aging. (2003) Evidence-Based Disease Prevention Program Fact Sheet. Available at http://www.aoa.dhhs.gov/press/fact/pdf/fs_Evidenced-Based.pdf. Accessed January 2007.
3. Office of Disease Prevention and Health Promotion, Department of Health and Human Services. Healthy People 2010, Chronic Kidney Disease. Available at www.healthypeople.gov/document/HTML/Volume1/04CKD.htm. Accessed January 2007.
4. National Policy and Resource Center on Nutrition and Aging, Institute of Medicine. Dietary Reference Intakes for Older Adults. Available at http://nutritionandaging.fiu.edu/DRI_and_DGs/DRI_and_RDAs.asp. Accessed January 2007.
5. United States Department of Health and Human Services and United States Department of Agriculture. Dietary Guidelines for Americans 2005. Available at http://www.healthierus.gov/dietaryguidelines/. Accessed January 2007.
6. National Kidney Foundation Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines. Available at: http://www.kidney.org/professionals/kdoqi/guidelines.cfm. Accessed January 2007.
7. Masud Tahsin. Trace elements and vitamins in renal disease. In: Mitch WE, *Klahr S Handbook of Nutrition and the Kidney*. 4th ed. Philadelphia, PA:Lippincott-Raven Publishers;2002:233-252.
8. Niedert KC, Dorner B. *Nutrition Care of the Older Adult.* 2nd ed. United States:American Dietetic Association; 2004:57-62.
9. Charytan C, Qunibi W, Bailie G. Comparison of intravenous iron sucrose to oral iron in the treatment of anemic patients with chronic kidney disease. *Nephron Clin Pract.* 2005;100:c55-c62.
10. Hudson JQ, Comstock T. Considerations for optimal iron use for anemia due to chronic kidney disease. *Clin Ther.* 2001;23:1637-1671.
11. Hudson J. Secondary hyperparathyroidism in chronic kidney disease: focus on clinical consequences and vitamin D therapies. *Ann Pharmacother.* 2006;40:1584-1593.
12. Bailie G, Massry S. Clinical practice guidelines for bone metabolism and disease: an overview. *Pharmacother* 2005;25:1688-1707.
13. Johnson MA, Kemlin M. Vitamin D, aging, and the 2005 Dietary Guidelines for Americans. *Nutr Rev* 2006;64:410-21.
14. Holick M. Vitamin D for health and in chronic kidney disease. *Semin Dial.* 2005;18:266-275.
15. Cabral PC, Diniz A, Grande de Arruda I. Vitamin A and zinc status in patients on maintenance haemodialysis. *Asian Pac J Neph.* 2005;10:459-463.
16. National Institutes of Health, Medline Plus. Diet for people with chronic kidney disease. Available at www.nlm.nih.gov/medlineplus/ency/article/002442.htm. Accessed January 2007.

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17. Cotton A. Nutrition support for wound healing in the dialysis patient. Fall 2003. Available at http://www.kidney.org/professionals/journals/pdf/RL_Fa03_CoverStory.pdf#search=%22Renal%20Support%20AND%20ann%20cotton%22. Accessed January 2007.
18. Food and Nutrition Board, Institute of Medicine. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.* Washington, DC:National Academies Press; 2000.
19. Feiertag PN. Dietary supplement use in patients with chronic kidney disease. *Ren Nutr Forum.* 2006;25:11-20.
20. Bonnefont-Rousselot D, Jaudon MC, Issad B, Cacoub P, Congy F, Jardel C, Delattre J, Jacobs C. Antioxidant status of elderly chronic renal patients treated by continuous ambulatory peritoneal dialysis. *Nephrol Dial Transplant*, 1997;12:1399-1405.
21. Klahr Saulo. Effects of renal insufficiency on nutrient metabolism and endocrine function. In: Mitch WE, Klahr S. *Handbook of Nutrition and the Kidney*. 4th ed. Philadelphia, PA:Lippincott-Raven Publishers;2002:24-41.
22. Meydani SN, Meydani M, Blumberg JB, Leka LS, Siber G, Loszewski R, Thompson C, Pedrosa MC, Diamond RD, Stollar BD. Vitamin E supplementation and in vivo immune response in healthy elderly subjects:a randomized controlled trial. *JAMA*.1997;277:1380-1386.
23. Meydani SN, Leka LS, Fine BC, Dalla GE, Keutsch GT, Singh MF, Hamer DH. Vitamin E and respiratory tract infections in elderly nursing home residents:a randomized controlled trial. *JAMA*. 2004;292:828-836.
24. Hodkova M, Dusilova-Sulkova S, Kalousova M, Soukupova J, Zima T, Mikova D, Malbohan I, Bartunkova J. Influence of oral vitamin E therapy on micro-inflammation and cardiovascular disease markers in chronic hemodialysis patients. *Ren Fail.* 2006;28:395-399.
25. Institute of Medicine. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC:National Academies Press; 2000:186-283.
26. Booth SL, Martini L, Peterson J, Saltzman E, Dallal G, Wood R. Dietary phylloquinone depletion and repletion in older women. *J Nutr.* 2003;133:2565-2569.
27. Johnson MA. Influence of vitamin K on anticoagulant therapy depends on vitamin K status and the source and chemical forms of vitamin K. *Nutr Rev*. 2005;63:91-100.
28. Institute of Medicine. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline*. Washington, DC:National Academies Press; 1998.
29. Jenkins Karen. Anaemia management in nephrology. In: *Advanced Renal Care*. Malden, MA:Blackwell Publishing Ltd; 2004:27-49.
30. Menon V, Wang X, Greene T, Beck G, Kusek J, Selhub J, Levey A, Sarnak M. Homocysteine in chronic kidney disease: effect of low protein diet and repletion with B vitamins. *Kidney Int*. 2005;67:1539-1546.
31. Wrone EM, Hornberger J, Zehnder J, McCann L, Coplon N, Fortmann S. Randomized trial of folic acid for prevention of cardiovascular events in end-stage renal disease. *J Am Soc Nephrol*. 2004;15:420-426.
32. Shemin D, Bostom A, Selhub J. Treatment of hyperhomocysteinemia in end-stage renal disease. *Am J Kidney Dis.* 2001;38:S91-S94.
33. Hermann W, Obeid R, Schorr H, Geisel J. The usefulness of holotranscobalamin in predicting vitamin B12 status in different clinical settings. *Curr Drug Metab*. 2005;6:47-55.
34. Park S, Johnson M. What is an adequate dose of oral vitamin B12 in older people with poor vitamin B12 status? *Nutr Rev.* 2006;64:373-378.
35. Baik HW, Russell RM. Vitamin B12 deficiency in the elderly. *Annu Rev Nutr.* 1999;19:357-377.
36. Friedman AN. Pharmacologic B-vitamin therapy for hyperhomocysteinemia in dialysis patients: has the time come? *Nutr Clin Care.* 2002;5:20-24.
37. Umeakunne Kayellen. Approaches to successful nutrition intervention in renal disease. In: Mitch WE, *Klahr S Handbook of Nutrition and the Kidney*. 4th ed. Philadelphia, PA:Lippincott-Raven Publishers; 2002:292-325.
38. Obeid R, Kuhlmann M, Kirsch C, Herrmann W. Cellular uptake of vitamin B12 in patients with chronic renal failure. *Nephron Clin Pract.* 2005;99:c42-c48.
39. Levine S, Saltzman A. Pyridoxine (vitamin B6) toxicity: enhancement by uremia in rats. *Food Chem Toxicol.* 2002;40:1449-1451.
40. United States Department of Health and Human Services National Institutes of Health and National Institute of Diabetes and Digestive and Kidney Diseases. Kidney failure-Eat right to feel right on hemodialysis, 2001.
41. Food and Nutrition Board, Institute of Medicine, National Academies. Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals, Vitamins, Elements. National Academy of Sciences. Washington DC, *National Academy Press*, 2004.