Phosphate Additive Avoidance in Chronic Kidney Disease
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Eating patterns are an important modifiable behavior in the management of patients with diabetes. Indeed, dietary modification is recommended as a first-line treatment for prediabetes (1) and is an integral component of ongoing diabetes care (2). Because patients with diabetes are at increased risk of chronic diseases such as chronic kidney disease (CKD) and cardiovascular disease (CVD), medical nutrition therapy for diabetes extends beyond glycemic control to include other cardiometabolic risk factors (e.g., weight, hypertension, and lipids) (2). These associations are important because dietary counseling with a registered dietitian for these conditions may be unavailable to patients until their condition becomes compromised. In fact, according to the U.S. Centers for Medicare & Medicaid Services Medical Evidence Report (June 2005 to May 2007, n = 156,400), 97% of CKD patients starting hemodialysis either were not under the care of a renal dietitian (88%) or had less than 12 months of renal dietitian care (9%) (3).

Dietary phosphorus restriction is recommended for patients with CKD but is not included in dietary guidelines for diabetes because hyperphosphatemia generally presents in the later stages of CKD (4,5). However, there is growing evidence that, even in earlier stages of CKD and in the absence of hyperphosphatemia, excess dietary phosphorus intake contributes to osteodystrophy and CVD. Although the majority of dietary phosphorus occurs naturally in foods and some can be leached out by wet cooking methods such as boiling, food additives in processed foods are a major source of dietary phosphorus; restricting their intake may be a suitable approach for limiting phosphorus exposure in earlier stages of CKD.

In this review, we discuss the evidence favoring dietary phosphorus restriction in earlier stages of CKD, with specific emphasis on phosphorus-based food additives. The intended purpose is to provide background information on an important and growing area of research in the

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Renal Phosphorus Handling in Health and CKD

Under normal conditions, dietary phosphorus intake exceeds physiological requirements, and the kidneys help to maintain phosphorus balance by eliminating excess phosphorus in urine. Plasma phosphorus is readily filtered by the glomeruli into the lumen of the renal tubules so that the concentration of phosphorus in the tubular filtrate is ~90% that in plasma (6). The majority of filtered phosphorus is reabsorbed in the proximal tubule under the regulation of several interconnected regulatory molecules (7), which control the proportion of filtered phosphorus that is excreted in urine (also known as the fractional excretion of phosphorus).

During CKD, the number and mass of functioning nephrons in the kidneys declines, causing a corresponding decrease in the amount of plasma, and therefore phosphorus, that is filtered. This is represented by a decrease in the estimated glomerular filtration rate (eGFR). To maintain normal excretion of excess phosphorus, the amount of phosphorus that is reabsorbed in the renal tubules decreases (i.e., the fractional excretion of phosphorus increases) (8). The fractional excretion of phosphorus can be upregulated dramatically such that only a small fraction (~10%) of filtered phosphorus is reabsorbed, and serum phosphorus concentrations can be maintained in a normal range until kidney function is severely reduced (eGFR <30 mL/min/1.73 m²) (4,5,8). Concomitant changes in calcium metabolism occur (explained below), leading to a decline in serum calcium concentrations, which also leads to compensatory responses. The changes in regulatory factor concentrations that produce the decrease in phosphorus reabsorption and the decrease in serum calcium concentrations may have secondary consequences for CKD patients. The scenario in which serum phosphorus and calcium concentrations are maintained in the normal range at the expense of altered counterregulatory factors activity is known as the “trade-off hypothesis” (9).

Four key regulatory factors that generate the increase in fractional excretion of phosphorus in CKD are 1,25(OH)2-vitamin D (calcitriol), parathyroid hormone (PTH), fibroblast growth factor-23 (FGF-23), and its cofactor, klotho. The processes by which these regulatory factors work together to maintain phosphorus and calcium homeostasis and balance as CKD progresses are complex and incompletely understood. However, recent observational data, combined with mechanistic data, provide new insights into the pathways involved.

In cross-sectional analyses of CKD populations, higher FGF-23 concentrations are detected in those with mildly reduced kidney function (as early as stage 2 [eGFR 60–89 mL/min/1.73 m²]), often before any changes in calcitriol and PTH concentrations are evident (4,5). FGF-23 is a bone-derived regulatory factor that acts to increase the fractional excretion of phosphorus in the kidneys (7). Conversely, its cofactor klotho is decreased and may initiate the early increase in FGF-23 concentrations (10,11). As CKD progresses, calcitriol concentrations decrease (5). Although low calcitriol concentrations in CKD were traditionally attributed to a loss of the kidney’s capacity to produce 1-α-hydroxylase, the enzyme responsible for activating vitamin D, FGF-23 is a potent inhibitor of 1-α hydroxylase activity and may account for the decrease in calcitriol early on in CKD (12). The decrease in calcitriol both directly (by diminished inhibitory action on the parathyroid gland) and indirectly (by reducing intestinal calcium absorption) contributes to hyperparathyroidism, commonly seen in those with moderately reduced kidney function (eGFR <60 mL/min/1.73 m²) (5). Similar to FGF-23, PTH inhibits tubular phosphorus transporters to further increase the fractional excretion of phosphorus (7). In addition, PTH helps to maintain normal serum calcium concentrations by mobilizing calcium from bone, reabsorbing calcium in the kidneys, and increasing calcium absorption in the intestines (by increasing 1-α hydroxylase activity/ calcitriol synthesis in the kidneys) (13). Importantly, other factors influence renal phosphorus handling, and these regulatory factors are linked through several feedback loops. Consequently, the actual adaptation process is difficult to study in vivo and more complex than described here.

Potential Consequences of Excess Dietary Phosphorus

The observed changes in calcitriol, PTH, FGF-23, and klotho are all features of an altered metabolic state in CKD, which leads to osteodystrophy, vascular calcification, and cardiac abnormalities, referred to as CKD-mineral and bone disorder (CKD-MBD) (14). In prospective studies of CKD patients, abnormal concentrations of these regulatory factors, in particular FGF-23, have been linked to CKD progression and CVD and fracture risk (4,15–20). Furthermore, calcitriol, PTH, and FGF-23 have been shown to directly affect bone turnover (21,22), vascular calcification (23,24), and left ventricular hypertrophy (25), suggesting that they may have a mediating role in the pathogenesis of CKD-MBD and that this process may begin in early CKD with the observed changes in these regulatory factors (26).

Importantly, animal models of CKD demonstrate that restricting dietary phosphorus intake can prevent the regulatory factor changes seen in CKD-MBD and slow the progression of CKD (27–31). Because phosphorus is found in most foods, it is unlikely that the low phosphorus intakes in these studies could be achieved in humans without using
synthetic diets or compromising nutrition status. However, it may be possible to sufficiently reduce dietary phosphorus intake to delay or diminish the regulatory factor changes. Indeed, modifying dietary phosphorus intake has been found to alter FGF-23 concentrations in people with and without CKD (32–35) and to reduce secondary hyperparathyroidism in CKD patients (36,37). Addressing hyperparathyroidism earlier through dietary restriction may prevent the progression of glandular hyperplasia to nodular hyperplasia, which is more difficult to suppress (38). Avoiding more severe elevations in PTH is expected to improve bone mineral density and reduce fracture rates, while precluding the eventual need for parathyroidectomy. Despite the apparent biological link between dietary phosphorus and CKD-MBD, prospective studies of reported dietary phosphorus intake and 24-hour urine phosphorus content with CVD mortality have generated inconsistent findings (39–41).

**Limiting Dietary Phosphorus Intake**

As previously mentioned, dietary phosphorus restriction is an integral component of hyperphosphatemia treatment in patients with moderately to severely reduced kidney function (14) and therefore has been extensively studied and tested in practice. Renal dietitians in particular devote substantial time and effort to determining the phosphorus content of foods and beverages (especially commercial products), and counseling CKD patients on how they can best limit phosphorus in their diet. A low-phosphorus diet (<800–1,000 mg/day) may include any and all of the following: 1) limiting foods naturally high in phosphorus, 2) leaching phosphorus from foods using wet cooking methods (e.g., boiling meat), and most recently 3) avoiding phosphorus-based food additives (42).

Although restricting high-phosphorus foods is commonly practiced in advanced CKD, this approach has several important limitations. First and foremost, many high-phosphorus foods are healthy choices for people with adiposity-based chronic diseases such as type 2 diabetes. Indeed, low-fat dairy products, nuts, seeds, legumes, and whole grains (all high-phosphorus foods) are key components of the DASH (Dietary Approaches to Stop Hypertension) diet (43) and of the American Diabetes Association’s nutrition recommendations for individuals with diabetes (2).

Dietary guidelines for diabetes do not encourage a one-size-fits-all eating pattern, but instead advise that patients consume a variety of nutrient-dense foods (2). Many of the factors that reduce the nutrient density of foods (e.g., refining or adding sugars and fats) also reduce phosphorus density (Table 1). Consequently, patients who choose nutrient-dense foods as part of a diabetic diet may have a high phosphorus intake. Although not supported by the guidelines (2), individuals with diabetes who are aware of their diagnosis tend to report lower carbohydrate intakes than those who are unaware (44), perhaps because they are attempting to reduce postprandial glycemic excursions. This may result in a higher phosphorus intake because carbohydrates are replaced, in part, with protein (44), which is positively correlated with phosphorus intake because carbohydrates are replaced, in part, with protein (44), which is positively correlated with phosphorus intake.

Another important issue with restricting high-phosphorus foods is that the crude phosphorus content of foods may not reflect the bioavailable (and therefore bioactive) fraction of dietary phosphorus. Notably, the majority of phosphorus compounds in plant foods are indigestible phytates, contributing to a lower overall phosphorus bioavailability than with animal-derived phosphorus (32,45,46). The issue of phosphorus bioavailability is still being explored, but it is likely that dietary recommendations for a low-phosphorus diet will change in the future to reflect bioavailability, as is already being suggested for whole grains (47). It may be possible for people with diabetes to reduce their dietary phosphorus intake by avoiding certain high-phosphorus foods that are already restricted on a diabetic diet, such as high-fat dairy products (e.g., ice cream and cheese). However, even if dietary phosphorus were demonstrated to promote CKD-MBD in early CKD without hyperphosphatemia, it is doubtful that limiting intake of healthy foods that are high in phosphorus would have a net beneficial effect in patients with diabetes and mildly reduced kidney function.

Leaching is another approach that has been explored for managing hyperphosphatemia in CKD patients (48,49). During leaching, foods undergo prolonged cooking with water (i.e., boiling for 30 minutes), causing minerals to diffuse out of foods and dissolve into the water, which is then discarded. In addition to reducing the phosphorus content of foods by up to half or more (48–50), cooking foods with water instead of fats avoids the added calories from fats and helps prevent high-temperature reactions that create potentially harmful compounds (e.g., heterocyclic amines, advanced glycation end-products, and trans fatty acids). However, leaching is time consuming and may be impractical for many high-phosphorus foods (e.g., dairy foods and peanut butter), or make them less palatable. Moreover, other water-soluble nutrients that may be beneficial for patients (e.g., potassium) are also removed by leaching (48).

Avoiding processed foods that contain phosphorus-based food additives may be the most appropriate means of reducing phosphorus intake in diabetes patients with mildly reduced kidney function. Phosphorus additives have many functional properties (51) and are used in almost every major processed food category (e.g.,
frozen foods, dry food mixes, packaged meats, bread and baked goods, and soups) (52). A 2013 study analyzing the amount of phosphorus in 56 pairs of similar food products (one with and one without phosphorus additives) (52) found that products containing phosphorus additives contained ~60% more phosphorus (178 ±202 vs. 111 ±112 mg/100 g). However, the absolute and relative differences in phosphorus content varied substantially between and even within food product categories. For example, the difference in phosphorus among cheese products (n = 4 pairs) was +347 mg/100 g (+85%), with an SD of 158 mg/100 g (52). It is difficult to obtain a clear estimate of usual intake of phosphorus from food additives, but analyses of menus selecting foods containing phosphorus additives suggest that they may contribute up to ~600–700 mg/day of inorganic phosphorus (52,53), which is thought to be highly bioavailable (51). Such additives may, with further study, constitute an important target for efforts to restrict dietary phosphorus intake. Importantly, there are usually phosphorus additive–free alternatives, albeit at a slightly higher cost (52).

Most phosphorus additives are easily identified in ingredients lists by the root “phos” (e.g., phosphoric acid, phosphates, diphosphates, and polyphosphates), although some are either indistinguishable (e.g., modified food starch) (54) or unlisted, as in the case of certain enhanced meats (55,56). Consequently, if patients are willing and able to read the ingredients lists of food products, they can often eliminate the majority of phosphorus additives from their diet. Avoiding processed foods may be difficult for most patients but has the additional benefit of helping to limit other potentially harmful compounds commonly found in these products (e.g., added sugars and sodium).

For now, the public health impact of phosphorus additives is largely unknown, in part because food manufacturers are not required to report

### TABLE 1. Phosphorus Content of Foods According to Food Group

| Food                          | Serving Size | Phosphorus (mg) | Per Serving | Per 100 kcal |
|-------------------------------|--------------|-----------------|-------------|--------------|
| **Protein foods**             |              |                 |             |              |
| Chicken breast, roasted, skin removed | 3 oz         | 194             | 139         |              |
| Chicken breast, roasted       | 3 oz         | 182             | 109         |              |
| Chicken breast, fried with batter | 3 oz         | 157             | 71          |              |
| Ground beef, 93% lean         | 3 oz         | 167             | 103         |              |
| Ground beef, 70% lean         | 3 oz         | 141             | 69          |              |
| Eggs                          | 2 large      | 197             | 138         |              |
| Black beans                   | 1 cup        | 241             | 106         |              |
| Peanut butter, creamy         | 2 Tbsp       | 107             | 56          |              |
| Sesame seeds                  | 1 oz         | 181             | 113         |              |
| **Dairy products**            |              |                 |             |              |
| Milk, skim                    | 1 cup        | 247             | 298         |              |
| Milk, whole                   | 1 cup        | 205             | 138         |              |
| Yogurt, low-fat, plain        | 1 cup        | 353             | 229         |              |
| Yogurt, low-fat, vanilla      | 1 cup        | 331             | 159         |              |
| Cheddar cheese                | 1.5 oz       | 193             | 112         |              |
| Vanilla ice cream             | 1 cup        | 139             | 51          |              |
| **Grains**                    |              |                 |             |              |
| Bread, white                  | 1 slice      | 24              | 36          |              |
| Bread, whole wheat            | 1 slice      | 68              | 84          |              |
| Rice, brown                   | 1 cup        | 208             | 84          |              |
| Rice, white                   | 1 cup        | 68              | 33          |              |
| Cereal, Kellogg’s Corn Flakes | 1 cup        | 29              | 29          |              |
| Cereal, Kellogg’s All-Bran    | 1 cup        | 356             | 445         |              |
| Bran muffin                   | 1 medium     | 425             | 139         |              |
| Croissant                     | 1 medium     | 60              | 26          |              |
| **Fruits**                    |              |                 |             |              |
| Apples                        | 1 cup        | 12              | 21          |              |
| Applesauce, sweetened         | 1 cup        | 18              | 9           |              |
| Peaches                       | 1 cup        | 31              | 52          |              |
| Peaches, canned in juice      | 1 cup        | 42              | 38          |              |
| Peaches, canned in heavy syrup| 1 cup        | 29              | 15          |              |
| **Vegetables**                |              |                 |             |              |
| Carrots                       | 1 cup        | 45              | 87          |              |
| Broccoli                      | 1 cup        | 60              | 194         |              |
| Tomatoes                      | 1 cup        | 43              | 134         |              |
| Tomatoes, canned              | 1 cup        | 77              | 100         |              |
| Tomatoes, canned, stewed      | 1 cup        | 51              | 77          |              |
| Potatoes                      | 1 medium     | 123             | 73          |              |
| Potatoes, mashed              | 1 cup        | 101             | 43          |              |
| Potatoes, French fries, McDonald’s | 1 medium   | 149             | 39          |              |
the amount of phosphorus additives used or the total phosphorus content of their products (because the evidence linking excess phosphorus to health outcomes has been deemed inadequate). Without this information, conventional nutrition assessment methods are unable to estimate phosphorus additive intake, preventing epidemiological studies, which would be needed to evaluate the public health impact of these additives. However, there is evidence that clinically relevant reductions in phosphorus intake can be achieved by eliminating phosphorus additives. In a landmark study (57), Sullivan et al. found that educating hemodialysis patients with hyperphosphatemia to avoid phosphorus additives reduced serum phosphorus concentrations compared to usual care. Similar studies are underway, including a 6-month, technology-supported, behavioral intervention targeting weight loss, physical activity, sodium restriction, and avoidance of phosphorus additives in overweight patients with type 2 diabetes and stages 1–4 CKD by members of our group (clinicaltrials.gov identifier NCT02276742).

Conclusion
In this review, we have discussed the potential health consequences of excess dietary phosphorus intake in patients with early CKD, an emerging area of research interest. In particular, there is growing concern that the compensatory changes in regulatory factors, which maintain phosphorus balance in patients with high dietary phosphorus intake and diminished glomerular filtration by increasing the fractional excretion of phosphorus in the kidneys, may contribute to CKD progression, as well as to skeletal and vascular disorders (i.e., CKD-MBD). More research is needed to determine whether reducing dietary phosphorus intake is beneficial in CKD patients without hyperphosphatemia. However, even if excess phosphorus were demonstrated to be harmful in this population, the conventional low-phosphorus diet may be inappropriate for diabetes patients with early CKD because it restricts the intake of many foods recommended for these patients.

Phosphorus additives in processed foods are major sources of highly bioavailable dietary phosphorus, which may become a novel target for diabetes patients in the future, particularly those with reduced kidney function. Current regulations require that the presence of food additives be indicated in the ingredients list of food products, but the amount of phosphorus is not required to be included in the nutrition facts panel. Given that phosphorus additives are widely used in processed foods and excess phosphorus intake may cause harm in individuals with kidney disease, mandatory labeling of phosphorus on food products may be an important public health intervention.

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Duality of Interest
No potential conflicts of interest relevant to this article were reported.

References
1. Garber AJ, Handelsman Y, Einhorn M, et al. Diagnosis and management of prediabetes in the continuum of hyperglycemia: when do the risks of diabetes begin? A consensus statement from the American College of Endocrinology and the American Association of Clinical Endocrinologists. Endocr Pract 2008;14:933–946
2. American Diabetes Association. Lifestyle management. Sec. 4. In Standards of Medical Care in Diabetes—2017. Diabetes Care 2017;40(Suppl. 1):S33–S43
3. Slinin Y, Guo H, Gilbertson DT, et al. Prehemodialysis care by dietitians and first-year mortality after initiation of hemodialysis. Am J Kidney Dis 2011;58:583–590
4. Fliser D, Kollerits B, Neyer U, et al., for the MMKD Study Group. Fibroblast growth factor 23 (FGF23) predicts progression of chronic kidney disease: the Mild to Moderate Kidney Disease (MMKD) study. J Am Soc Nephrol 2007;18:2601–2608
5. Isakova T, Wahl P, Vargas GS, et al., on behalf of the Chronic Renal Insufficiency Cohort (CRIC) Study Group. Fibroblast growth factor 23 is elevated before parathyroid hormone and phosphate in chronic kidney disease. Kidney Int 2011;79:1370–1378
6. Mizgala CL, Quamme GA. Renal handling of phosphate. Physiol Rev 1985;65:431–466
7. Prasad N, Bhaduria D. Renal phosphate handling: physiology. Indian J Endocrinol Metab 2013;17:620–627
8. Slatopolsky E. The intact nephron hypothesis: the concept and its implications for phosphate management in CKD-related mineral and bone disorder. Kidney Int 2011;79(Suppl. 121):S3–S8
9. Gutierrez OM. Fibroblast growth factor 23 and disordered vitamin D metabolism in chronic kidney disease: updating the “trade-off” hypothesis. Clin J Am Soc Nephrol 2010;5:1710–1716
10. Hu MC, Shi M, Zhang J, et al. Klotho deficiency causes vascular calcification in chronic kidney disease. J Am Soc Nephrol 2011;22:134–136
11. Asai O, Nakatani K, Tanaka T, et al. Decreased renal α-Klotho expression in early diabetic nephropathy in humans and mice and its possible role in urinary calcium excretion. Kidney Int 2012;81:539–547
12. Gutierrez OM, Isakova T, Rhee E, et al. Fibroblast growth factor-23 mitigates hyperphosphatemia but accentuates calcitriol deficiency in chronic kidney disease. J Am Soc Nephrol 2005;16:2205–2215
13. Mundy GR, Guise TA. Hormonal control of calcium homeostasis. Clin Chem 1999;45:1347–1352
14. Kidney Disease: Improving Global Outcomes (KDIGO) CKD–MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease–mineral and bone disorder (CKD–MBD). Kidney Int 2009;76(Suppl. 113):S1–S130
15. Mirza MA, Karlsson MK, Mellstrom D, et al. Serum fibroblast growth factor-23 (FGF-23) and fracture risk in elderly men. J Bone Miner Res 2011;26:857–864
16. Titan SM, Zatz R, Graciolli FG, et al. FGF-23 as a predictor of renal outcome in diabetic nephropathy. Clin J Am Soc Nephrol 2007;18:2601–2608
17. FGF-23 and cardiovascular disease in the general population: the Multi-Ethnic Study...
of Atherosclerosis. Circ Heart Fail 2014;7:409–417.

3. J Ren Nutr 2005;15:e1–e4

29. Ibel LS, Alfrey AC, Haut L, Huffer WE. Preservation of function in experimental renal insufficiency in the dog. J Clin Invest 1971;50:492–499

28. Slatopolsky E, Caglar S, Gradowska L, Cantabrury J, Reis E, Bricker NS. On the prevention of secondary hyperparathyroidism in experimental chronic renal disease using “proportional reduction” of dietary phosphorus intake. Kidney Int 1972;2:147–151

27. Slatopolsky E, Caglar S, Pennell JP, et al. On the pathogenesis of hyperparathyroidism in chronic experimental renal insufficiency in the dog. J Clin Invest 1970;51:402–409

26. Martin KJ, Gonzalez EA. Prevention and control of phosphate retention/hyperphosphatemia in CKD-MBD: what is normal, when to start, and how to treat? Clin J Am Soc Nephrol 2011;6:440–446

25. Foul C, Amaral AP, Oskouei B, et al. FGF23 induces left ventricular hypertrophy. J Clin Invest 2011;121:4393–4408

24. Mary A, Renauld L, Boudot C, et al. Calcitriol prevents in vitro vascular smooth muscle cell mineralization by regulating calcium-sensing receptor expression. Endocrinology 2015;156:1965–1974

23. Schmidt N, Brandsch C, Schuthkows A, Hirsch F, Stangl GI. Dietary vitamin D inadequacy accelerates calcification and osteoblast-like cell formation in the vascular system of LDL receptor knockout and wild-type mice. J Nutr 2014;144:638–646

22. Silva BC, Bilezikian JP. Parathyroid hormone: anabolic and catabolic actions on the skeleton. Curr Opin Pharmacol 2015;22:41–50

21. Goltzman D. Inferences from genetically modified mouse models on the skeletal actions of vitamin D. J Steroid Biochem Mol Biol 2015;148:219–224

19. Lutsey PL, Alonso A, Selvin E, et al. Fibroblast growth factor-23 and incident coronary heart disease, heart failure, and cardiovascular mortality: the Atherosclerosis Risk in Communities study. J Am Heart Assoc 2014;3:e00936

18. Sciolla JJ, Xie H, Rahaman M, et al. The Chronic Renal Insufficiency Cohort (CRIC) Study Investigators. Fibroblast growth factor-23 and cardiovascular events in CKD. J Am Soc Nephrol 2014;25:349–360

17. Goltzman D. Inferences from genetically modified mouse models on the skeletal actions of vitamin D. J Steroid Biochem Mol Biol 2015;148:219–224

16. Denda M, Finch J, Slatopolsky E. Phosphorus accelerates the development of parathyroid hyperplasia and secondary hyperparathyroidism in rats with renal failure. Am J Kidney Dis 1996;29:596–602

15. Moe SM, Zidehfarai MP, Chambers MA, et al. Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease. Clin J Am Soc Nephrol 2011;6:257–264

14. Sigrist M, Tang M, Beaulieu M, et al. Responsiveness of FGF-23 and mineral metabolism to altered dietary phosphate intake in chronic kidney disease (CKD): results of a randomized trial. Nephrol Dial Transplant 2013;28:161–169

13. Gutierrez OM, Luzuriaga-McPherson A, Lin Y, Gilbert LC, Ha S, Beck GR Jr. Impact of phosphorus-based food additives on bone mineral density. J Clin Endocrinol Metab 2015;100:4264–4271

12. Trautvetter U, Jahreis G, Kiehntopf M, Glei M. Consequences of a high phosphorus intake on mineral metabolism and bone remodeling in dependence of calcium intake in healthy subjects – a randomized placebo-controlled human intervention study. Nutr J 2016;15:7

11. Llach F, Massry SG, Koffler A. Secondary hyperparathyroidism in early renal failure: role of phosphate retention. Kidney Int 1977;12:459–463

10. Slatopolsky E, Dusso A, Brown AJ. The role of phosphorus in the development of secondary hyperparathyroidism and parathyroid cell proliferation in chronic renal failure. Am J Med Sci 1999;317:370–376

9. Drueke TB. Hyperparathyroidism in chronic kidney disease. In Endotext [Internet]. De Groot LJ, Beck-Peccoz P, Chrousos G, et al., Eds. South Dartmouth, Md., Text.com, Inc., 2015. Available from http://libguides.gwumc.edu/c.php?g=27773&p=170272. Accessed 27 February 2017

8. Palomino HL, Rifkin DE, Anderson C, Criqui MH, Wholesley MA, Isx JH. 24-hour urine phosphorus excretion and mortality in patients with chronic kidney disease. Clin J Am Soc Nephrol 2013;8:1202–1210

7. Chang AR, Lazo M, Appel LJ, Gutierrez OM, Grams ME. High dietary phosphorus intake is associated with all-cause mortality: results from NHANES III. Am J Clin Nutr 2014;99:320–327

6. Selamet U, Tighiouart H, Sarnak MJ, Levy RJ, Vassilatos L, Alper ES, Wright JT. The association of dietary phosphorus intake with risk of end-stage renal disease and mortality in chronic kidney disease stages 3-5: the Modification of Diet in Renal Disease study. Kidney Int 2016;89:176–184

5. St-Jules DE, Woolf K, Pompeii ML, Kalantar-Zadeh K, Sevick MA. Reexamining the phosphorus-protein dilemma: does phosphorus restriction compromise protein status? J Ren Nutr 2010;20:136–140

4. Sacks FM, Obarzanek E, Windhauser MM, et al., for the DASH investigators. Rationale and design of the Dietary Approaches to Stop Hypertension trial (DASH): a multicenter controlled-feeding study of dietary patterns to lower blood pressure. Ann Epidemiol 1995;5:108–118

3. Bardenheier BH, Cogswell ME, Gregg EW, Williams DE, Zhang Z, Geiss LS. Does knowing one’s elevated glycemic status make a difference in macronutrient intake? Diabetes Care 2014;37:3143–3149

2. Karp HJ, Vaihia KP, Karkkainen MUM, Niemisto MJ, Lamberg-Allardt CJE. Acute effects of different phosphorus sources on calcium and bone metabolism in young women: a whole-foods approach. Calcif Tissue Int 2007;80:251–258

1. Gallant KMH. Studying dietary phosphorus intake: the challenge of when a gram is not a gram. Am J Clin Nutr 2015;102:237–238

2. Williams C, Ronco C, Kotanko P. Whole grains in the renal diet – is it time to reevaluate their role? Blood Purif 2013;36:210–214

3. Jones WL. Demineralization of a wide variety of foods for the renal patient. J Ren Nutr 2001;11:90–96

4. Cupisti A, Comar F, Benini O, et al. Effect of boiling on dietary phosphate and nitrogen intake. J Ren Nutr 2006;16:36–40

5. Meiners CR, Derise NL, Lau HC, Crews MG, Ritchey SJ, Murphy EW. The content of nine mineral elements in raw and cooked maturelegumes. J Agric Food Chem 1976;24:1126–1130

6. Kalantar-Zadeh K, Gutekunst L, Mehrrota R, et al. Understanding sources of dietary phosphorus in the treatment of patients with chronic kidney disease. Clin J Am Soc Nephrol 2010;5:519–530

7. Leon JB, Sullivan CM, Sehgal AR. The prevalence of phosphorus containing food additives in top selling foods in grocery stores. J Ren Nutr 2013;23:265–270

8. Carrigan A, Klinger A, Choquette SS, et al. Contribution of food additives to sodium and phosphorus content of diets rich in processed foods. J Ren Nutr 2014;24:13–19

9. Calvo MS, Moslehig AH, Tucker KL. Assessing the health impact of phosphorus in the food supply: Issues and considerations. Adv Nutr 2014;5:104–113

10. Murphy-Gutekunst L, Uribarri J. Hidden phosphorus-enhanced meats: Part 3. J Ren Nutr 2005;15:61–64

11. Sherman RA, Mehta O. Phosphorus and potassium content of enhanced meat and poultry products: implications for patients who receive dialysis. Clin J Am Soc Nephrol 2009;4:1370–1373

12. Sullivan C, Sayre SS, Leon JB, et al. Effect of food additives on hyperphosphatemia among patients with end-stage renal disease: a randomized controlled trial. JAMA 2009;301:629–635