Diet and Alternative Therapies in the Management of Stone Disease

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KEYWORDS

• Urolithiasis • Diet • Nutrition • Prevention • Therapy

KEY POINTS

- Nutrition therapy, widely used for secondary prevention of urolithiasis, is the application of nutritional assessment, diagnosis, intervention, and counseling to prevent or manage disease.
- Nutrition therapy for prevention of kidney stone recurrence is based primarily on the idea that the reduction of known lithogenic risk factors reduces or prevents calculus formation and growth.
- After assessment of the nutritional intake of the patient, urinary and other risk factors are evaluated with respect to their cause and whether or not nutrition intervention is likely to address them.

INTRODUCTION

Therapeutic nutrition recommendations for the secondary prevention of urolithiasis are widely used. General nutrition guidelines are useful in promoting public health and for developing nutrition plans that reduce the risk for or attenuate the effects of diseases that are affected by nutrition. Examples of such guidelines are the dietary reference intake values[1] (which include the recommended dietary allowance (RDA), adequate intake, and the tolerable upper intake level for individual nutrients) and the dietary guidelines for Americans.[2] However, general guidelines are insufficient in developing interventions to address specific disease conditions in individual patients. Nutrition therapy is the application of nutritional assessment, diagnosis, intervention, and counseling to prevent or manage disease.[3]

Food and nutrition are inherently complex. Plants grow in different soils and conditions throughout the world and therefore have variations with respect to their nutrient and molecular profiles. Animalia of all types eat different foods and are subject to different management techniques, rendering their nutrient profiles variable. People from different cultures and backgrounds may derive the same essential nutrients but from vastly different foods and preparation methods. Conversely, the intake of certain nutrients and biologically active nonnutrients is also known to vary between cultures, between individuals, and even within individuals over time. The intake of individual nutrients or food components rarely, if ever, occurs in isolation; a single food item may contain hundreds of biologically active compounds. In the context of an entire meal, thousands of nutrients and nonnutrients are consumed. Certain micronutrients and other food constituents interact in antagonistic, synergistic, or benign ways. Individuals vary with respect to their consumption, digestion, and absorption of foods and their components, even within an individual over the course of the life span. Moreover, a single food-derived compound may affect hundreds of molecular systems and even cause epigenomic changes.[4]

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General nutritional influences on stone disease are difficult to characterize. Although interest for nutrition interventions is high among patients, evidence-based data from well-designed research studies to support specific recommendations are lacking. A recent systematic review of published randomized trials on nutritional prevention of urolithiasis collectively identified 8 trials with reasonable but variable quality, all but one reporting reduced stone recurrence (**Table 1**).[13] Few studies have been designed to assess the effects of a whole diet intervention or of multiple, simultaneous nutrition interventions. Many more studies have evaluated the effects of single nutrients or individual food components, but most of these have assessed effects on stone risk factors, not stone formation. The use of stone risk factors as outcomes is attractive because it is accomplished in a shorter time frame than assessment of stone formation and growth and may be evaluated with a single diagnostic test, such as a 24-hour urine analysis. Although risk reduction alone has not been definitively tied to reduced recurrence, much of what we believe and practice about nutrition interventions to prevent recurrence comes from this assumption.

Table 1
Published randomized trials involving nutrition intervention for urolithiasis

Author, Year, Journal	Intervention	Duration
Borghi et al,[5] 1996, J Urol	Increased fluids vs no treatment	5 y
Sarica et al,[6] 2006, Urol Res	Increased fluids vs no treatment	2–3 y
Di Silverio et al,[7] 2000, Eur Urol	Mineral vs tap water	19 mo
Shuster et al,[8] 1992, J Clin Epidemiol	Decreased soft drinks vs no treatment	3 y
Dussol et al,[9] 2008, Nephron	Increased fiber vs decreased animal protein	4 y
Hiatt et al,[10] 1996, Am J Epidemiol	Whole diet approach (vs control diet)	2 y
Borghi et al,[11] 2002, N Engl J Med	Whole diet approach (vs self-select diet)	5 y
Kocvara et al,[12] 1999, BJU Int	Whole diet approach (tailored vs empiric diet)	3 y

NUTRITION THERAPY: THE APPROACH

Nutrition therapy for prevention of kidney stone recurrence is based primarily on the idea that the reduction of known lithogenic risk factors, such as urine supersaturation and the relative urinary excretion of lithogenic promoters versus inhibitors, reduces or prevents calculus formation and growth. In concert with pharmacologic therapy, or as monotherapy, nutrition therapy seems useful. Nutrition therapy includes the assessment of a patient's nutritional status and intake, the diagnosis of the nutritional risk factor(s), and the development and application of the nutrition intervention.[3]

Role of Registered Dietitian

A registered dietitian is helpful as a member of the health care team because the application of nutrition therapy requires detailed nutrition knowledge and expertise in delivering individualized patient education. Education that is not tailored appropriately to the individual patient's learning style, education background and nutrition knowledge, economic capacity, food preferences, and motivation to change is likely to be unsuccessful.[14] Moreover, unless it is integrated into their individual regimen, patients with diabetes, Crohn disease, and cardiovascular disease likely have received specific nutrition recommendations for those conditions and thus may not embrace nutrition therapy for stone prevention. These scenarios may confound the true impact of nutrition intervention on the course of urolithiasis and might lead to the false conclusion that "dietary changes don't work" or that "patients won't comply."

Empiric Versus Tailored

There are 2 approaches for applying nutrition therapy. The first is an empiric approach, applied to all patients. This approach might involve a general discussion of various nutritional strategies that address multiple risk factors and could be provided to a patient without knowing their specific urinary risk factors. If the stone composition of the patient is known, this approach could be modified by developing multiple versions of a stone prevention diet based on the patient's previous stone composition. The second is a tailored approach that is continually monitored and altered as needed based on the disappearance or emergence of a patient's specific risk factors. Both approaches could be termed whole diet approaches because both include recommendations about multiple foods and nutrients. One study that compared the empiric versus tailored

nutrition therapy approach reported reduced stone recurrence with the latter.[11] Two other studies in calcium stone formers found reduced stone recurrence with an empiric whole diet approach, but this was not directly compared with a tailored approach.[10,12]

In practice, because of time constraints or for simplicity, urologists and other urology providers may rely more on empiric approaches such as general handouts or standardized patient instructions. Shortcomings of this approach include:

- It potentially addresses risk factors that the patient does not show, and thus may impose unnecessary recommendations.
- It does not prioritize the recommendations, which could lead to patients' confusion about what is most important for them.
- Patient compliance with nutrition and other therapies may hinge on the number of recommendations provided, with greater compliance more achievable with a short list of modifications.
- Unless otherwise addressed, it may conflict with other nutrition information that the patient has received for a different comorbidity.
- Unless otherwise addressed, specific strategies to aid the patient in achieving the stated goals are lacking. These include, for example, behavioral modifications, recommendations for alternative food choices or different food preparation methods, changes in grocery shopping habits, education on estimating portion sizes, tips for adherence when eating out, strategies and resources for economically disadvantaged patients, and motivational techniques to encourage patients' movement along the stages of change toward action.[15]

Attention to these potential barriers to success of the nutrition intervention is strongly encouraged if an empiric approach is used.

Clearly, a tailored nutrition therapy approach is favorable and may avoid some of the pitfalls. In this approach, nutrition therapy is targeted to the patient's individual risk factors (**Fig. 1**), which may be different than another patient's, even if they both form the same type of calculi. Risk factors that are manifest are addressed foremost, and secondary focus is given, if appropriate, to nonexistent potential risk factors. A tailored or individual approach also allows for the integration of stone prevention strategies with nutritional therapy that the patient may have received for other conditions. By focusing on the most salient risk factors rather than discussing all potential

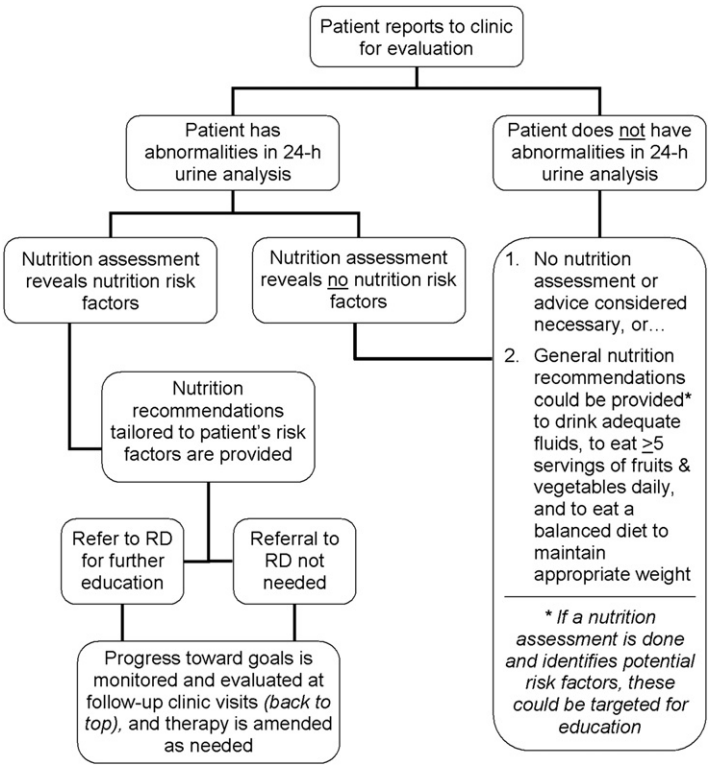

Fig. 1. Tailored nutrition therapy.

risk factors, there may be time to provide patients with pragmatic solutions to specific problems. These solutions might include how to read nutrition labels to monitor sodium intake, making appropriate food choices when eating out or during frequent travel, and titrating calcium supplementation for patients with hyperoxaluria, if needed, with a patient's usual food calcium intake.

Lithogenic risk factors should be assessed first for nutrition influences. If nutrition is determined to be contributory, then identifying the nutrition risk is necessary in order to apply the appropriate nutrition therapy. Some risk factors have an obvious cause and solution. Low urine output, for example, is usually safely assumed as originating from a fluid intake too low to produce the target urine volume. Although it may mean compensating for extraordinary dermal, fecal, or other losses, the cause and solution remain the same, the solution being to drink more fluids. Examples of conditions without obvious cause include hyperoxaluria and hypercalciuria, each of which may manifest but for multiple different reasons. If a patient's hyperoxaluria is caused primarily by a suboptimal calcium intake or one that is not timed with meals, then admonishing them to avoid spinach, rhubarb, beets, and chocolate without addressing their calcium intake is not likely to result in reduced urinary oxalate excretion. Similarly, if a patient's hypercalciuria is believed to be caused primarily by acidosis and excessive bone resorption, then the most stringent of sodium restrictions may have little effect and may, as a side effect, reduce the palatability of the patient's diet or their fluid intake.[16]

NUTRITION THERAPY: ASSESSMENT OF RISK

The cause of urolithiasis is multifactorial; nutritional factors are not always relevant. Risk factors associated with urolithiasis include nutritional, physiologic, medical, genetic, pharmacologic, and nonnutritional environmental. These risk factors may exist singly or in concert with one another. Nutritional factors and specific physiologic and medical conditions with nutritional implications are addressed later, after which follows a description of the nutritional implications of commonly assessed urinary risk factors. Calcium and uric acid stones are addressed, although aspects of the specific nutrition therapies presented may apply to patients who form cystine, struvite, or other stones.

Nutritional Risks in the Diet

Assessment of a patient's habitual diet and use of over-the-counter supplements is useful in determining where there may be excesses, deficiencies, or imbalances of nutrients and other food constituents that are not nutrients but that are relevant to kidney stones. Techniques used by a registered dietitian could include a 24-hour diet recall conducted one-on-one with the patient (either with or without the use of nutrient analysis software), a multiple-day diet record kept by the patient and returned to the dietitian for analysis, or a targeted assessment that evaluates the most relevant nutritional factors. In the nutrition assessment, the dietitian considers a combination of general age-specific and gender-specific nutrition guidelines as well as accepted therapeutic nutritional recommendations for certain medical conditions[17] (see next section). The nutrition diagnosis should focus on the nutrition-related cause for or contributor to the patient's risk for urolithiasis. In the case of hyperoxaluria, an example of the nutrition diagnosis is "Increased nutritional lithogenic risk related to suboptimal calcium intake not timed with meals, contributing to low oxalate binding potential in gastrointestinal tract and resulting in hyperoxaluria."

The following may be considered the major nutritional factors that contribute to increased lithogenic risk:

• Low fluid intake	• High urine supersaturation
• Excessive sodium salt intake	• Hypercalciuria, hypocitraturia
• High intake of refined carbohydrates	• Hypercalciuria
• Excessive caffeine or alcohol intake (especially by sensitive patient subpopulations)	• Hypercalciuria, hyperuricosuria (alcohol)
• Overall diet habitually high for potential renal acid load	• Hypercalciuria, hypocitraturia, acid urine
• Excessive supplementation (exceeding physiologic needs or the RDA) of calcium	• Hypercalciuria
• Low fruit/vegetable intake	• Hypocitraturia, acid urine
• Intake of high-oxalate foods, especially with low calcium intake	• Hyperoxaluria

• Suboptimal calcium intake	• Hyperoxaluria
• Excessive intake of some over-the-counter supplements such as vitamin C, and possibly some herbal or plant-derived concentrates (eg, cinnamon, cranberry, turmeric)	• Hyperoxaluria
• Excessive calorie intake resulting in overweight	• Acid urine, hypocitraturia

Aside from single foods or food groups, overall dietary patterns seem to be more or less risk-conferring than others.[18] For example, data confirm that the Atkins diet for weight loss[19] or the ketogenic diet for seizure disorders[20] can both increase risk for stone formation. Disordered eating patterns, by people with pica or other eating disorders, may also result in increased risk for urinary tract stones.[21] Vegetarian diets, despite typically being higher in oxalate, are associated with reduced risk,[22] as was a low-salt, adequate-calcium, moderate-protein diet (not unlike the dietary pattern known as the dietary approaches to stop hypertension [DASH] diet).[12] Recently, specific gastrointestinal microbiotic profiles have been identified, containing discrete combinations of bacterial species, and these seem to be regulated in large part by dietary patterns.[23] For example, people who consume high-fiber diets have a different microbiotic profile than those who do not.[24] Another study showed that people whose diets are rich in meats have a different bacterial enterotype than those whose diets are rich in carbohydrates.[25] As research progresses, it is possible that certain dietary patterns could results in changes in the gut microbiome that could be linked with antilithogenic effects, such as a more favorable concentration of oxalate-degrading bacteria.

Nutritional Risks Related to Specific Physiologic and Medical Factors

Diabetes confers known risks for urinary tract stones.[26] It is not clear whether good control of diabetes with prescribed diabetic nutrition interventions results in reduced stone risk. However, it seems intuitive that appropriate control of insulin and blood glucose through nutrition and pharmacologic therapy would be helpful, especially with the integration of specific nutrition strategies to reduce stone risk factors. Malabsorptive conditions, including Crohn disease, celiac sprue, short bowel, postgastric bypass or duodenal switch, and chronic diarrhea, confer well-known risks for urinary tract stones.[27] Multiple nutritional strategies to attenuate the malabsorptive effects of these conditions may be used that could have antilithogenic effects. Although not a nutritional problem per se, chronic or frequent antibiotic use could reduce gastrointestinal bacteria capable of degrading oxalate.[28] Every course of antibiotics tends to deplete beneficial bacteria, and in the months required to recover these, pathogenic bacteria may grow.[29] Nutritional and supplemental means, such as probiotic foods and supplements and foods rich in prebiotic components, are capable of altering and optimizing gut bacterial profiles; nutrition therapy may thus play an important role in addressing urolithiasis risk in the setting of antibiotic exposure.[23–25]

Nutritional Implications of Urinary Risk Factors

The analysis of a 24-hour urine versus a spot urine collection is necessary to account for diurnal and other rhythmical excretion patterns of various products of metabolism. Multiple analyses over time are most useful in establishing risk and in monitoring changes.[30] Parameters commonly measured and monitored to predict risk of lithogenesis are: calcium, oxalate, uric acid, urine pH, urine volume, phosphate, citrate, magnesium, and supersaturation indices for specific crystalloids. Where cystinuria is suspected or known, cystine is measured. Urinary phytate could be measured, because it is a potent inhibitor of calcium lithogenesis, but it is not currently assessed by major commercial laboratories.[31]

Many of the urinary parameters monitored for stone risk are related to nutritional intake but are not necessarily surrogates for intake. For example, calcium is under tight homeostatic control, and its excretion in urine is not always related to intake.[32] Sulfate, although commonly used as a surrogate for meat intake, may also reflect the intake of soy beans and foods made from soy (eg, tofu, tempeh), because soy is rich in methionine. Frequently, more than 1 parameter in the 24-hour urine collection must be viewed together and, in addition to the nutrition assessment, may provide a good picture of what is going on in the diet.

Other parameters frequently measured in urine may not be risk factors for renal stone formation

per se but may (1) contribute indirectly to lithogenesis by altering renal handling of other excretory products, (2) be used for calculation of urine supersaturation, or (3) provide information to corroborate or rule out underlying disorders or nutritional contributors. These parameters include sodium, potassium, sulfate, ammonium, chloride, urine urea nitrogen, and protein catabolic rate (calculated from the product of urine urea nitrogen and a factor accounting for the average nitrogen content of dietary proteins, divided by the patient's body weight). Although this latter group of urine parameters may be useful in estimating nutritional potentiates of stone formation and growth, many may be altered in the setting of underlying disorders, and none are perfect biomarkers for intake; nutritional assessment of the patient's diet is thus imperative.

NUTRITION THERAPY: IN PRACTICE

After assessment of the nutritional intake of the patient, urinary risk factors for urolithiasis are evaluated with respect to their cause and whether or not nutrition intervention is likely to address them. Frequently, multiple risk factors are present in a patient's 24-hour urine analysis. If nutrition therapy to address multiple risk factors is applied, the need to integrate them into a whole diet, addressing any contradictions between recommendations, is important. This strategy includes the need to integrate stone prevention strategies with nutrition strategies that the patient is following for any other health condition.

Hypercalciuria

Assess for nutrition contributors (**Fig. 2**). Sodium, acid load of diet, gastrointestinal and renal calcium handling, and omega-3 fatty acids are addressed.

Sodium

Sodium exerts a potent hypercalciuric influence because of expansion of extracellular volume and competition between sodium and calcium ions in the renal tubule.[33] If dietary sodium seems contributory to hypercalciuria, assess food source(s), focusing not only on notoriously high-sodium foods but also on foods that are not necessarily high in sodium but, when consumed in large quantity, confer a high sodium load (**Table 2**). Foods at the top of the list for sodium content include miso, table salt, canned sauerkraut and tomato sauce, cured ham, and baking soda, all of which provide more than 1000 mg sodium in a single serving.[34] However, these are not necessarily foods that patients might eat every day or in large quantity. On the other hand, foods that are far lower on the sodium content scale

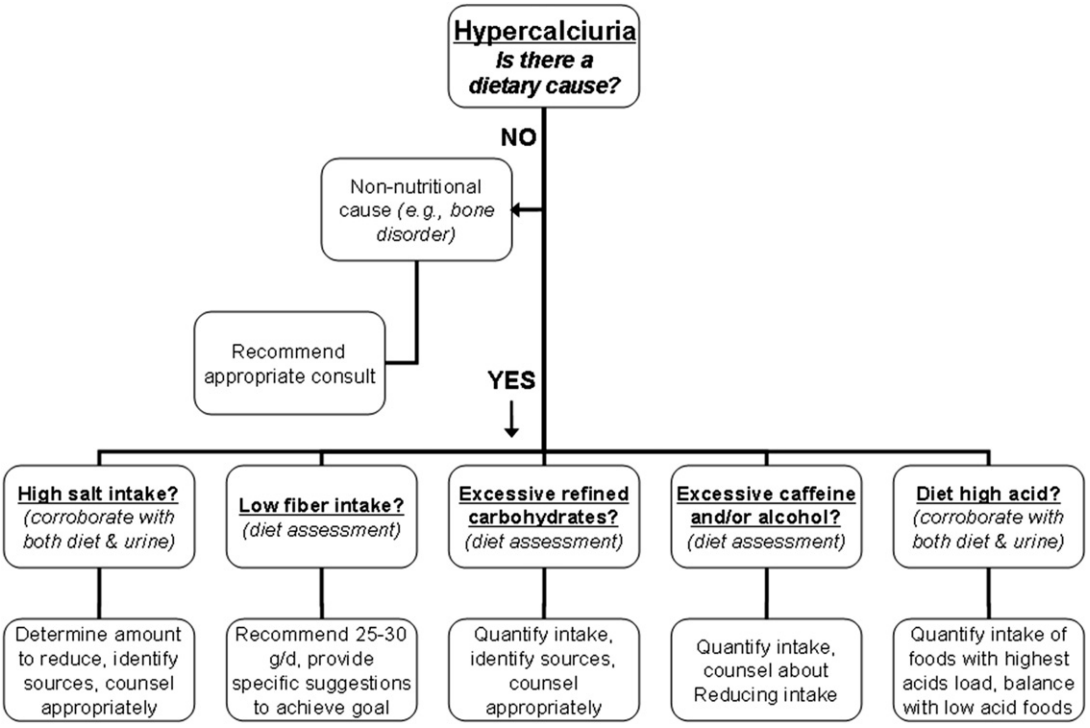

Fig. 2. Nutritional contributors to hypercalciuria.

Table 2
Nutritional sodium sources identified from multiple-day weighed-diet records of stone-forming patients at a stone clinic

Food Group	Contribution to Total Sodium Intake (%)	Cumulative Percentage Toward Total Sodium Intake
Luncheon meats and other processed meats	14	–
Breads and baked goods (bagels, buns, muffins, rolls, tortillas)	14	28
Added salt (NaCl) and spices containing salt	14	42
Canned soups/vegetables and pickled goods	9	51
Salad dressings, condiments, spreads, sauces	8	59
Salty snacks (chips, pretzels, popcorn, candy)	7	73
Homemade casseroles, soups, and other mixed dishes	7	80
Cheese and cheese products	7	66
Pizza and prepared sandwiches (including fast food)	6	86
Meal starters and helpers (eg, pasta and rice mixes)	5	91
Breakfast cereals	5	96
Milk, yogurt, frozen dairy	3	99
Miscellaneous	1	100

Data from Penniston KL, Wojciechowski KF, Nakada SY. The salt shaker provides less than 15% of total sodium intake in stone formers: food strategies to reduce sodium are needed. J Urol 2011;185:e861.

are sometimes items that are eaten daily in high quantity.[35] For example, 5 servings of bread, which is easily achievable with 2 pieces of toast in the morning, a sandwich at lunch, and a roll at dinner, could provide as much or more than 1000 mg sodium. These foods and their intake patterns must be identified when providing nutrition therapy if sodium intake is determined to be a nutritional risk factor.

Acid load of diet

Dietary acid load has a well-known effect on urinary calcium excretion, believed to be caused by reduced renal tubular calcium reabsorption, increased glomerular filtration rate, increased bone mineral mobilization to buffer the acid load, or increased intestinal calcium absorption.[36] To address the acid load of diet if it is a suspected contributor, intervention aims to balance the intake of high-acid foods with low-acid or alkaline foods. A scale has been developed to estimate the potential renal acid load (PRAL) of foods.[37] It accounts for the anion/cation ratio of a food and has been suggested as a reasonable model for estimating the effects of the diet on renal net acid excretion. Foods conferring an acid load caused by the amount of sulfur in their amino acid structure include:

- All foods of flesh origin, including those from land and water
- Cheese, all types
- Eggs, largely from the yolk
- Grains, nearly all types, especially when consumed in high quantity

Milk, yogurt, and fats are neutral on the PRAL scale. Foods conferring an alkaline load (negative numbers on the PRAL scale) include nearly all fruits and vegetables. The few fruits and vegetables that have a slight acid load, and these include cranberries and lentils, need not be restricted, because the magnitude of their acid load is so much lower than that of the high-acid foods so as to be negligible. Moreover, fruits and vegetables are usually recommended to be increased, and the unnecessary restriction of some is a frequent source of frustration and confusion for patients.

Gastrointestinal and renal calcium handling

Reducing the gastrointestinal absorption of calcium in an effort to reduce the renal filtered load could be considered in those who are not at risk for calcium deficiency. Fiber may reduce the amount of gastrointestinal calcium absorbed.[38] If fiber intake is not at recommended levels (25–30 g/d for most adults), and if calcium and bone status seems normal, then it is appropriate to recommend increased fiber intake from foods or in combination with over-the-counter fiber supplements. Because of a high binding affinity, oxalate is also capable of reducing gastrointestinal calcium absorption, and its intake has been correlated inversely with urinary calcium excretion.[39] A high intake of carbohydrates may contribute to hypercalciuria, although it may be a transient effect.[40,41] If nutritional assessment suggests that a high carbohydrate intake is contributory, especially of refined carbohydrates (eg, sweetened beverages and juices, candy, refined grains, and foods made from them), intake should be reduced by suggesting whole-grain alternatives, whole fruits instead of juices, and nonsweetened beverages and foods. Caffeine and alcohol may contribute to urinary calcium excretion, but the need to limit or restrict these compounds should be individually assessed based on the amount typically consumed and on patient preferences.[42,43]

Omega-3 fatty acids

Some reports suggest efficacy of omega-3 fatty acids in reducing urinary calcium excretion,[44–46] and these may be supplemented using commercially available, over-the-counter formulations. However, the dosages required to achieve reduced urinary calcium excretion are unclear.

Hyperoxaluria

Assess for nutrition contributors (**Fig. 3**). Calcium intake, food oxalate, and over-the-counter supplements are addressed.

Calcium intake

If the nutrition assessment reveals a low calcium intake, or one that is not timed with meals, there could be a lack of oxalate-binding potential in the gastrointestinal tract.[47] For most patients, it might be sufficient to recommend consuming something containing around 300 mg of calcium at each meal daily. Assuming 3 meals daily, this figure would provide 900 mg of calcium from calcium-rich foods or beverages alone. Considering that other foods in a generally balanced diet collectively provide, on average, around 300 to 400 mg calcium, there is no need to supplement in this scenario. Special strategies for calcium intake that meets both physiologic needs and enhances binding potential for oxalate must be devised for: (1) patients who are

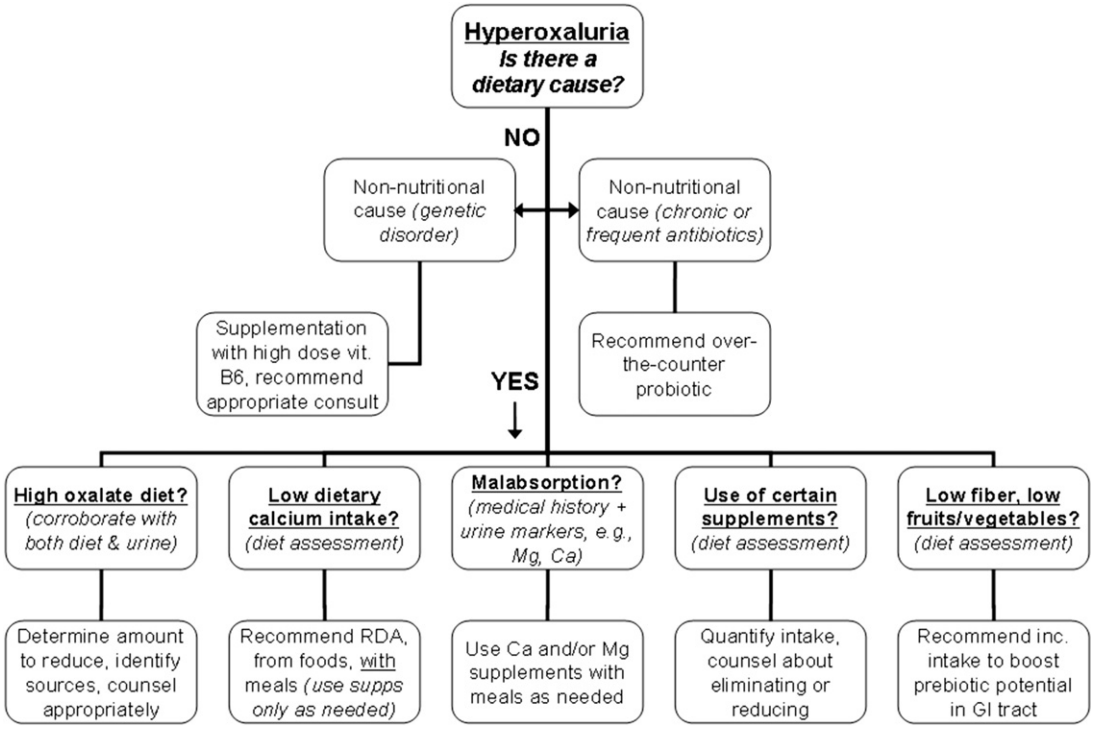

Fig. 3. Nutritional contributors to hyperoxaluria.

lactose intolerant or otherwise do not use dairy foods, which are among those highest in calcium per serving, (2) those who do not eat regular meals daily, (3) those who snack or graze frequently throughout the day instead of eating discrete meals, and (4) those who have altered gut physiology or any other condition resulting in malabsorption, because the extraordinary fecal calcium in these individuals is bound to fatty acids, resulting in less calcium available to bind to oxalate. A combination of foods and supplements, frequently large doses but always timed with meals, is usually required in these cases. Magnesium is also known to bind oxalate in the gut and thereby reduce its absorption[48] and could also be incorporated into nutrition therapy.

Food oxalate

The restriction of food-derived oxalate is controversial. For the most part, foods that contain oxalate are healthy foods and, moreover, are frequently those conferring general health benefits and specific nutrients that are often underconsumed, including fiber, potassium, magnesium, and antioxidants. Elimination or restriction of such foods may do more harm than good, especially if other strategies could be used, such as appropriate calcium (and magnesium) intake timed with meals and snacks. A reduction of dietary oxalate also requires a simultaneous reduction in dietary calcium in order to maintain an appropriately low calcium/oxalate ratio in urine, and some have questioned the value of the low-oxalate strategy for this reason.

The relative bioavailability of oxalate in foods is another topic of interest, because foods high in oxalate might not necessarily be those from which oxalate is readily absorbed.[49] Although more research is needed on the different forms of dietary oxalate, it is assumed that the less water soluble the oxalate, the lower its bioavailability. Thus, restricting high-oxalate foods based on their oxalate concentration without accounting for bioavailability could result in unnecessary restriction. Research to confirm and identify foods with high oxalate bioavailability is needed. Oxalate is a prebiotic for oxalate-degrading bacteria.[50] Although there may be no need for oxalate-degrading bacteria in the gut in a setting of a low oxalate intake, bacteria capable of degrading oxalate may also provide other biological benefits and serve as part of the microbiome required for optimum health status. (**Table 3** provides definitions for and examples of food probiotics and prebiotics.)

Therefore, if dietary oxalate seems contributory to hyperoxaluria, focus not only on foods that are known to be high in oxalate but also on foods that are not necessarily high-oxalate but, when consumed in large quantity, confer a high oxalate load (**Table 4**). Several of the oft-cited high-oxalate foods are not necessarily those that are consumed daily or in high amounts. Rather than focusing on the few pieces of rhubarb pie a patient might have in a year, a better strategy is to identify foods with appreciable oxalate that are eaten habitually and in high amounts. Depending on the individual, these foods might include chocolate, nuts and seeds, spinach, potatoes, and potato chips. In addition, because whole grains are frequently ample for oxalate but not necessarily identified as high in oxalate, and because grains are frequently eaten multiple times in a day, these can be a source for oxalate (see **Table 4**).[51] Discretion in recommending reduced oxalate intake must be used and individual plans developed for patients who rely on nuts and seeds as a protein source or as a low-carbohydrate snack and for those who are vegetarian and who enjoy ample fruits, vegetables, and whole grains. Recommendations to avoid all oxalate in these situations might reduce the nutritional quality and diversity of the diet, not to mention risking diminished compliance.

Over-the-counter supplements

Over-the-counter supplements have been implicated in increased urinary oxalate excretion, and these include cinnamon, turmeric,[52] and cranberry.[53] Others are associated with reduced oxalate excretion, and these include omega-3 fatty acids[46,54] and pyridoxine (vitamin B_6).[44] The dosages required to achieve reduced urinary oxalate excretion with omega-3 fatty acids are unclear and its success in practice is not well characterized. Similarly, although supraphysiologic supplementation with pyridoxine is used in patients with primary hyperoxaluria to address enzyme deficiencies, its effectiveness and practice in patients with idiopathic or enteric hyperoxaluria are not well characterized.

Hyperuricosuria

Assess for nutrition contributors. Purine intake, alcohol and fructose, and acid load of diet are addressed.

Purine intake

Some foods that are rich in nucleoproteins known as purines may contribute to hyperuricosuria, because uric acid is an end-product of purine metabolism.[55] The average daily intake of purines seems to range between 500 and 1500 mg.[56] Virtually all foods have some purines, but those

Table 3
Definitions for and examples of probiotics and prebiotics

Definition	Mechanism	Examples	Food Sources
Probiotics			
Live, nonpathogenic microorganisms in the gastrointestinal tract that confer a health benefit on the host when administered in adequate amounts	Effects are strain specific (not species or genus specific) and include immune modulation, production of antimicrobial compounds, and maintenance of gut integrity and function	Certain variants of: Lactobacilli Bifidobacteria Streptococci Bacilli Yeasts	Cultured yogurts and fermented dairy products, aged cheeses, some nondairy products (eg, soy milk), fermented foods, over-the-counter supplements, chewing gum, lozenges, infant formulas
Prebiotics			
Nondigestible food component or ingredient that beneficially affects the host through effects on the microbiome	Must reach the large intestine intact, where overall effect is to selectively stimulate growth or activity of 1 or a limited number of bacteria or to directly stimulate immunity, protect against pathogens, and facilitate host metabolism and mineral absorption	Certain nondigestible carbohydrates, including: Inulin Various oligosaccharides Pyrodextrins Fructan Lactulose Lactitol	Fruits (especially bananas, berries, kiwi), vegetables (especially onions, garlic, leeks, artichokes), whole grains (especially oats, barley), and whole-grain foods, honey, over-the-counter supplements, powders, commercial extraction of chicory root, fortified foods

Data from Saulnier DM, Spinler JK, Gibson GR, et al. Mechanisms of probiosis and prebiosis: considerations for enhanced functional foods. Curr Opin Biotechnol 2009;20:135–41; and Figueroa-Gonzalez I, Quijano G, Ramirez G, et al. Probiotics and prebiotics–perspectives and challenges. J Sci Food Agric 2011;91:1341–8.

most concentrated (providing up to 1000 mg per serving of 85–113 g [3–4 ounces]) include anchovies, sardines, organ meats (eg, brain, liver, kidney), and glandular tissue, commonly referred to as sweetbreads. Appreciable amounts of purines, up to 100 mg per serving of 85 g to 113 g (3–4 ounces), are provided by shellfish, game meats, water fowl, mutton, beef, pork, poultry, and fish.[57] As with other nutrition recommendations, the patient who does not typically eat purine-rich foods does not benefit from advice to limit or eliminate them from their diet. If nutrition assessment documents a high intake of purine-rich foods, education about lowering dietary purines is appropriate. Avoiding the foods highest in purine concentration and reducing recurrent intake of those with lower concentrations would be recommended. Foods of plant and dairy origins contain purines, but the impact of these on uric acid synthesis is different. A recent study in men with gout concluded that vegetable-derived purines did not increase risk and dairy foods lowered risk.[58] Thus, patients are unlikely to benefit from avoiding plant and dairy foods that contain purines because they might compromise their vegetable intake, calcium intake, and the diversity of their overall diet.

Another potential concern is the tendency to refer only to red meat as the major culprit with respect to uric acid synthesis. Recently, fish and chicken were reported to increase both serum and urine uric acid to the same degree as or higher than red meat.[59] Recommending reduced red meat intake may cause the patient with hyperuricosuria to substitute with more chicken and fish, when a reduction of all of these foods may be necessary to achieve favorable results. The amount of reduction should be individually titrated based on the current amount of these foods the patient eats. Reduction could occur with reduced portion sizes, reduced frequency of intake throughout the week, or both. Patients usually

Table 4
Nutritional oxalate sources identified from multiple-day weighed-diet records of stone-forming patients at a stone clinic

Food Group	Contribution to Total Oxalate Intake (%)	Cumulative Percentage Toward Total Oxalate Intake
Nuts, seeds, nut butters	26	–
Spinach	12	38
Breads, flours, baked goods	12	50
Cereals	7	57
Potatoes (includes sweet potatoes), French fries	7	64
Leafy vegetables, nonspinach	6	70
Mixed dishes, casseroles, meats	6	76
Nonleafy vegetables	5	81
Chips, crackers	5	86
Chocolate	5	91
Soymilk, kefir, cheese	4	95
Tea, spices	2	97
Fruit	2	99
Pasta, rice	1	100

Data from Penniston KL, Wojciechowski KF, Nakada SY. Dietary oxalate: what's important and what isn't for patients with calcium oxalate stones? J Urol 2011;185:e824–5.

require assistance conceiving of alternate means for obtaining protein, especially if their protein intake is compromised by compliance with the recommendation.

Alcohol and fructose

Alcohol is a contributor to uric acid biosynthesis, because it enhances purine degradation and increases xanthine oxidase expression, which is the enzyme that catalyzes the final step in uric acid production.[60] Fructose, a monosaccharide found naturally in sucrose (table sugar) and fruits and also used ubiquitously in food manufacture and production as a sweetener, has also been suggested to increase serum uric acid and potentially urinary uric acid excretion.[61,62] The nutrition assessment should quantify the intake of both alcohol and fructose in the patient with hyperuricosuria and discuss ways to reduce intake if it is believed to be contributing to stone risk.

Acid load of diet

Although not a contributor to uric acid biosynthesis and the urinary excretion of uric acid, the acid load of the diet can reduce urine pH such that urinary uric acid is less soluble. Refer to elsewhere in the text for addressing and correcting acid load of diet if the nutrition assessment identifies it as a risk factor.

Hypocitraturia

Assess for nutrition contributors (**Fig. 4**). The acid load of the diet, dietary citrate, chronic or frequent diarrhea, and sodium are addressed.

Acid load of diet

If the diet is assessed as high for acid load, which exerts a hypocitraturic effect because of enhanced renal citrate reabsorption,[63] reducing the acid load with smaller amounts of cheese, meats, and other flesh foods would be advised.[37] Specific strategies to achieve this goal could be tailored to patients' needs. For example, for the patient unable or unwilling to give up meat or some other flesh food at both lunch and dinner, a specific recommendation for smaller portions at each of these meals could have the same effect as eating those foods at only 1 meal of the day. If a patient's calorie load is not a concern, simply balancing their present intake of high-acid foods with an appropriate quantity of low-acid or alkaline foods (ie, most fruits and vegetables) could be suggested.

Dietary citrate

Although citric acid does not fit the definition for a nutrient and thus does not have a recommended intake or RDA, increased intake from foods and beverages may enhance urinary citrate excretion.[64–67] This goal could be achieved with specific

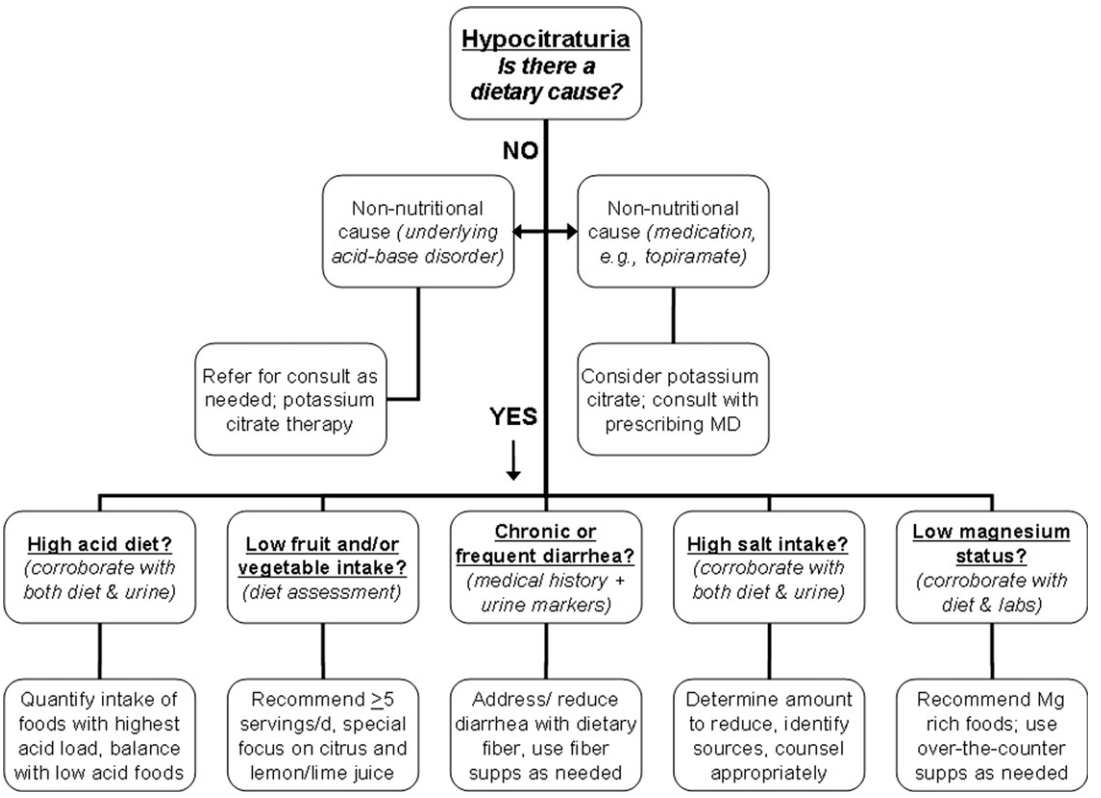

Fig. 4. Nutritional contributors to hypocitraturia.

recommendations about using lemon or lime juice, which are particularly concentrated with citric acid, diluted in water or another beverage to prevent degeneration of tooth enamel. Recommendations to use commercially available, ready-to-consume lemonade preparations, especially if they are not sugar-free, are rarely if ever indicated, because they contain a minimal amount of lemon juice and provide ample carbohydrates and food calories. Recommendations for increased citrus fruit intake might be incorporated and would provide beneficial nutrients as well, such as fiber, potassium, antioxidants, and prebiotics.

Recently, low-sugar, low-calorie beverage drinks flavored with citrate and other organic acids were suggested as agents capable of enhancing urinary citrate.[68] Depending on the urinary citrate level targeted as therapeutic for an individual patient, specific volumes of these beverages could be recommended and may also have a side benefit of increasing overall fluid intake. However, the ability of diet-derived citrate to fully correct severe hypocitraturia is questionable, but this may depend on the magnitude of the patient's hypocitraturia and on other nutritional and physiologic factors.

Chronic or frequent diarrhea

If frequent diarrhea is believed to be contributory to hypocitraturia, because of excessive bicarbonate losses in stool resulting in enhanced renal citrate reabsorption, nutrition strategies to correct diarrhea can be used.[69] Increased dietary fiber, with a specific focus on insoluble versus soluble as determined by the specific situation, could be recommended and specific strategies provided to achieve the goal. Over-the-counter fiber supplements, of which there are multiple varieties, may be beneficial in addressing and stemming diarrhea, and this could result in correction of hypocitraturia.[70] A growing body of literature supports probiotic supplementation for correcting diarrhea, and multiple probiotic formulations are commercially available and could be tried.[71,72]

Sodium

If a high sodium salt intake is considered contributory to hypocitraturia, refer to the section on sodium under hypercalciuria earlier in the text.[73]

Low Fluid Intake

Fluids of any kind help promote urine output and may be the single most useful way to reduce

recurrence risk.[5] Low-sugar, low-calorie beverages are most desired, but it is acceptable to count other beverages toward one's fluid intake; a diversity of different fluids, most of which are noncaloric, should be encouraged.

Fluid intake may be considered low when urine output does not meet the target volume. It may help to explain to a patient that they may require more fluids than another patient to produce a target amount of urine given variable extrarenal fluid losses between individuals depending on such factors as how much a person sweats or how much they lose in stool. It may also be helpful to identify the day of the week that the person carried out the 24-hour urine collection on which the assessment of low urine volume is made. Some people have ample fluid intakes during the workweek, when they are eating and drinking in more or less a similar pattern, and may even be conscious of drinking a certain volume of fluids, but on a weekend or nonwork day, schedules and dietary patterns are frequently different. Knowledge of how a patient drinks throughout the week, accounting for workday versus nonworkday differences, helps to address specific days when fluid intake is suboptimal.

Some patients benefit from more specific advice than to simply increase fluid intake. In these situations, a fluid intake schedule can be devised. By breaking the day into 3 equal sections (eg, of 5 hours each depending on the patient's lifestyle), with advice to drink about 1200 mL of fluids in each section, a person could consume approximately 4 L (120 ounces) of fluids. It may be helpful to ask the patient to use a fluid container with visible volume measurements to make meeting the specific goal easier. Carrying a fluid container was identified as an important cue to action in a recent analysis of factors influencing fluid intake in stone formers.[74] As necessary, fluid recommendations should compensate for excessive dermal or fecal losses, and patients may need to be educated as appropriate to their lifestyle and comorbid conditions.

Those at particular risk for low fluid intake for other reasons may require special attention. These at-risk groups include those with occupations requiring self-censorship of fluid intake because of lack of access for long periods to restrooms[75] (eg, truck drivers, elementary school teachers, airplane pilots) and those who live or work in hot conditions. Recently, armed services personnel stationed and working in a desert environment had low urine output despite intakes of fluids exceeding 17 L per day.[76] Individuals with urinary incontinence may limit their fluid intake in an effort to avoid publicly embarrassing situations. In these situations, fluid goals and fluid intake schedules should be amended on a patient-by-patient basis. In the case of urinary incontinence, special attention in developing a plan may be required with respect to patients' emotional concerns and quality of life. There are a growing number of community-based or hospital-based urinary incontinence support groups, and providing information about these to the patient may be helpful. Collaboration with a health psychologist who could work with the patient to identify ways to achieve fluid goals might also be useful in this situation.

Hyperphosphaturia

As with calcium, urinary phosphorus excretion is not always related to nutritional intake because it is subject to homeostatic regulation involving parathyroid hormone, vitamin D, bone status, calcium status, and renal reabsorptive mechanisms.[77] Phosphorus is widely distributed in foods of both plant and animal origin. Patients with chronic kidney disease and whose circulating phosphorus concentrations are increased are managed multifactorially to reduce serum phosphorus, and this may include dietary restriction. However, the reduction of dietary phosphorus in stone formers to reduce risk for calcium phosphate stone formation is not widely practiced. In these patients, the control of urinary citrate, calcium, urine pH, and volume are of most importance.

Overweight/obesity are associated independently with increased risk for lithogenesis.[78] Because both are conditions of malnutrition, with or without concomitant genetic or metabolic contributors, nutrition therapy should address weight loss. Nutrition interventions can be highly successful in motivated individuals, and patients should be referred as needed to nutritionists with expertise and experience in weight-loss counseling.[79]

SUMMARY

A tailored nutritional approach, targeted to patients' lithogenic risk factors, is recommended. There are some risk factors, observed in the 24-hour urine analysis, for example, which may not have a nutritional input and may not therefore be amenable to nutrition intervention. In part because of the complexity of studying nutrition and disease, evidence from appropriately designed studies may be lacking; yet nutrition therapy for kidney stone prevention is widely practiced. This article synthesizes best practice scenarios, most of which are evidence-based, for successful nutrition therapy against stone recurrence. An important concept stressed throughout is the need to

determine the cause of the observed risk factor(s) and to apply nutrition therapy accordingly.

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