#### From Urologic Nursing

# **Dietary and Holistic Treatment of Recurrent Calcium Oxalate Kidney Stones**

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# Abstract and Introduction

# Abstract

Urolithiasis is a condition that can cause significant morbidity among patients. Dietary manipulations traditionally advised include fluid, protein, oxalate, calcium, citrate, and sodium changes in the diet. Evidence-based practice guidelines suggest that there is not ample evidence to confidently recommend dietary changes, since inadequate studies have been done to quantify the risks of diet in stone formation. While fluid intake patterns have the weightiest evidence in the literature, not even fluid intake meets the guidelines for evidence-based practice. Health care providers should recognize that current patient education is largely based on intuition. It behooves us as clinicians to look critically at all our practices, review the available literature, and question what we believe we know. A summary of available literature is provided to guide the clinician in educating patients in reducing their risk of recurrent calcium oxalate stone disease.

#### Introduction

Delivering care to patients with recurrent kidney stones presents unique challenges for nurses and health care providers. Patients who develop symptomatic urolithiasis may present with characteristic flank or groin pain, nausea and vomiting, dysuria, and hematuria, regardless of the presence of hydronephrosis or hydroureter. Those who have developed one stone are at approximately 50% risk for developing another within 5 to 7 years (Parmar, 2004). For patients who are unfortunate enough to have recurrent stones, quality of life may be affected significantly. Members of this population often become distressed in their search for relief of symptoms and will look to health care providers for assistance. This article is designed to guide health care providers in educating patients to reduce their risk of recurrent calcium oxalate stones.

## **Evidence-Based Practice**

Nurses and other health care providers are increasingly turning to evidence-based practice (EBP) to critically evaluate the health information that may have been previously accepted as true. Our current practice may be based in fact, simple tradition, or intuition. EBP allows for critical evaluation of scientific studies. Available studies are critically appraised for validity, relevance, and applicability. This guides assimilation of the most accurate information, based on the best available evidence, and gives the clinician concrete evidence to guide practice, rather than relying on mere custom, intuition, or tradition.

#### Cochrane Database

Evidence-based practice relies heavily upon the randomized controlled trial (RCT) as the gold standard by which to judge information for validity, relevance, and applicability. Unfortunately, scant information collected regarding kidney stone formation and recurrence meets the RCT gold standard. The Cochrane Database of Systematic Reviews is one database that compiles information based on the best available data. Only one study is currently published in the Cochrane Database for kidney stone risk reduction, but it does not rise to the level of best recommendation as defined by the Cochrane Database. This study, on fluid intake, is the only recommendation listed in the Cochrane Database for the treatment of kidney stones. This further highlights the scarcity of available strong evidence upon which we base our practices.

#### The National Guideline Clearinghouse

In addition to the Cochrane Database, The National Guideline Clearinghouse also compiles recommendations for practice. Until earlier this year, the National Guideline Clearinghouse published guidelines recommending increased fluid intake for patients with stones. This guideline, however, was rescinded since it had not been updated from 1997. Until rescinded, increased fluids for treatment of kidney stones was the only recommendation suggested by the National Guideline Clearinghouse (2006).

The dearth of information available for use in development of recommendations for kidney stone management has not gone unnoticed (Gambaro, Reis-Santos, & Rao, 2004; Straub & Hautmann, 2005). Gambaro et al. (2004) note a stagnancy of research on the risks of stone formation, in part due to the popularity of extracorporeal shock wave lithotripsy (ESWL), which has grabbed the attention of researchers since its introduction in the 1980s. ESWL is a highly popular treatment for urolithiasis. Pak (1999) has been critical of the change in emphasis away from metabolic factors causing stones, now that ESWL has become a relatively easy treatment recommendation.

While having EBP recommendations for dietary kidney stone management is still optimal, clinicians must continue to provide care with the best knowledge at hand. In the meantime, there are individual studies to guide us in tentative recommendations to patients. Most studies are not as rigorously controlled, and therefore difficult to interpret for validity. Patients should be advised of the knowledge we have, but cautioned that our understanding is incomplete at best.

#### Dietary Patterns

Dietary patterns have been identified as possibly increasing stone risk. These patterns include fluid intake, ingestion of many minerals, such as calcium, oxalate, ascorbic acid, sodium, and magnesium, as well as protein and specific types of fluids. A discussion of the measurable evidence in individual studies follows.

## Fluid Intake

Scientists have suggested for decades that increased fluid intake could reduce the rate of stone formation, though the recommendation was based solely in intuition and tradition. Pak, Sakhaee, Crowther, and Brinkley (1980) were perhaps the first to scientifically measure the effect of fluid intake on the risk of stone formation. Their results indicate that if urine volume could be increased to 2.5 liters per day, the risk of stone formation was reduced.

Curhan, Willett, Rimm, and Stampfer (1993) also found that among 45,000 men studied, increased fluid intake was inversely proportional to the risk of symptomatic stone formation. Men with the highest fluid intake, over 2,530 ml per day, had a 0.71 relative risk of symptomatic stone formation compared with men who drank the lowest volume of fluids, less than 1,275 ml per day. Similar results were found for women. Among more than 91,000 women aged 34 to 59 years who were studied over 12 years, the relative risk for women who drank more than 2,592 ml per day was 0.61 compared with women who drank less than 1,412 ml per day (Curhan, Willett, Speizer, Spiegelman, & Stampfer, 1997).

Qiang and Ke (2004) reviewed available studies in a meta-analysis regarding fluid intake as one method to reduce stone formation. While many individual studies proposed that a reduced risk of stone formation occurred with increased fluids, only one study of 199 patients by Borghi et al. (1996) met the standard RCT criteria for inclusion as strong evidence upon which to base practice. Qiang and Ke (2004) concluded, in their opinion for Cochrane Database for Systematic Reviews, that this one study alone did not provide enough evidence to recommend increased fluid intake to reduce the incidence of primary or recurrent kidney stones. These researchers strongly emphasized the need for more RCTs to improve the information upon which to base recommendations.

## Calcium Intake

Calcium is present in more stones than any other element, with calcium oxalate the most common compound (Hall, 2002; Holmes, Goodman, & Assimos, 2001; Moyad, 2003). Tradition once held that a reduced calcium diet would benefit those with a history of urolithiasis by reducing the rate of calcium absorption and filtration into the urine. A large prospective study of the risk of symptomatic stone formation in more than 45,000 men ages 40 to 75 years of age was conducted by Curhan et al. (1993). They administered dietary pattern questionnaires and then tracked the incidence of symptomatic stones over the following 4 years. Contrary to expectations, there was a relative risk of only 0.66 for stone formation among men with the highest dietary calcium intake (1,050 mg per day or more), compared with men with the lowest dietary calcium intake (605 mg or less per day). Curhan and associates (1997) followed up this large study of men's dietary patterns with a similar study of women. In the Nurses' Health Study I of over 90,000 female nurses, ages 34 to 59 years, calcium intake was assessed via questionnaires, and cases of symptomatic stones were tracked for 12 years. The relative risk for women with the highest dietary calcium intake (more than 1,098 mg per day) was 0.65, compared with women with the lowest dietary calcium intake of less than 488 mg per day (Curhan et al., 1997).

Borghi et al. (2002) noted twice the rate of stone formation among the 60 stone-forming men who followed a low-calcium diet

compared with an equal number who followed a low-protein and low-sodium diet in this prospective randomized study. These studies have largely discredited the previous practice of reducing calcium intake among stone formers.

Calcium ingested in supplement form, however, may increase stone risk. Curhan et al. (1997) found that women may have a greater risk of stone formation (relative risk of 1.20) compared with those who do not use supplemental calcium. Of note, this risk was not found in men in two other studies. Curhan et al. (1993) studied men who took 500 mg calcium supplements daily and compared them to those who did not take calcium supplements. No added risk was found among the 45,000 men studied. In another study by Stitchantrakul, Sopassathit, Prapaipanich, and Domrongkitchaiporn (2004), 32 young healthy males with low dietary oxalate intake were studied. Researchers gave calcium supplements (amount not specified) to the men, then measured the impact of calcium supplementation upon factors thought to increase stone risk. They found that calcium supplements increased urinary citrate, decreased urinary oxalate, and increased urinary calcium levels. Researchers believed that the increased risk of hypercalciuria was offset by the protective effects of relative hypooxaluria and hypercitraturia provided by the calcium supplementation.

Concerning the traditional recommendations for calcium restrictions, Heilberg (2000) and McCarron and Heaney (2004) also called for adequate dairy intake, citing the improvements in stone formation risk, as well as effects on blood pressure, bone strength, and management of obesity.

#### Oxalate Intake

Many researchers have studied the role of dietary oxalate in the formation of calcium oxalate stones. No consensus, however, has emerged in dietary oxalate's impact on stone formation. This is likely because of the complexities of digestion and metabolism of minerals associated with the formation of oxalate, and its excretion from the body.

Oxalate is present in urine in much smaller quantities than calcium. It is believed that for this reason, changes in oxalate levels in the urine have a much greater impact on stone formation than changes in calcium concentration 23 times the impact for oxalate as for calcium (Morton, Iliescu, & Wilson, 2002).

Urinary excretion of oxalate in excess of 45 mg per day is regarded as hyperoxaluria. Hyperoxaluria may result from increased dietary intake, increased intestinal absorption of oxalate from the gut, or by increased endogenous production of oxalate by metabolic breakdown of ingested precursors (Siener, Ebert, Nicolay, & Hesse, 2003). Increased intestinal absorption can occur by mechanisms such as Crohn's disease, short bowel syndrome, or by destruction of *Oxalobacter formigenes*, a naturally present bacterium which breaks down oxalate in the gut (Martini & Wood, 2000; Parmar, 2004). Martini and Wood (2000) concluded that hyperoxaluria, due to excessive dietary intake of oxalate, may be unusual despite oxalate's presence in most foods. They contend that hyperoxaluria is a result of increased intestinal absorption in those who are prone to this abnormality, particularly malabsorption in the small bowel.

Siener et al. (2003) studied 186 stone formers, half with hyperoxaluria and half with normal urinary oxalate. The subjects provided 24-hour dietary diaries and underwent urine studies. There were no significant differences in dietary oxalate intake between the hyperoxaluric and normooxaluric subjects. The authors concluded that the higher rates of oxalate urinary excretion were associated with two phenomena: (a) hyperabsorption of oxalate from endogenous sources, rather than from dietary sources of oxalate; and (b) lower rates of calcium intake. This would lead to lower rates of complexing of calcium and oxalate in the gut, which would promote more oxalate filtration into the urine. Similar findings were reported by Chai, Liebman, Kynast-Gales, and Massey (2004). Likewise, Curhan et al. (1993) noted no added risk in ingestion of oxalate-rich foods on the formation of stones in their large epidemiologic study.

Contrary to these studies, Holmes et al. (2001) noted that little strong evidence was available to support the belief that stones are formed primarily by higher levels of absorption of oxalate rather than from dietary differences. In their study of 12 stone-forming persons, highly controlled diets were manipulated to provide variations in oxalate intake. They found that dietary oxalate contributed up to 50% of the variability in oxalate excretion. The highest urinary oxalate excretion was found when the calcium intake was most severely limited to 391 mg daily. The rate of actual stone formation among these persons was not investigated but rather the metabolic environment expected to facilitate stone formation.

Heilberg (2000) reviewed studies regarding calcium and oxalate intake in animals and humans. He found that oxalate stone formation was highly dependent on the balance of oxalate and calcium in the diet and blood. Exceedingly high oxalate intake

could be completely offset by a concomitant increase in calcium intake. This researcher concluded, however, that not enough information was available to recommend restrictions in oxalate or calcium. He recommended further studies to determine if there was a benefit to altering the intake of oxalate-rich foods, specifically rhubarb, spinach, chocolate, peanuts, pecans, almonds and instant tea.

## Citrate Intake

Citrates are compounds made from citric acid, or vitamin C, and are obtained exogenously through dietary ingestion of such foods as strawberries, lemons, oranges, cranberries, and grapefruits. Endogenous urinary citrate is derived via the breakdown of glucose through the Krebs cycle and excreted by renal tubular cells (Guyton & Hall, 2000; Parmar, 2004). Urinary citrate forms a soluble complex with calcium, and is believed to inhibit the formation of calcium stones (Seltzer, Low, McDonald, Shami, & Stoller, 1996). The normal range for citrate excretion is 300 to 700 mg per day. Excretion is reduced in periods of metabolic acidosis, such as with inflammatory bowel disease or renal tubular acidosis (Hall, 2002). Potassium citrate is often prescribed to increase urinary citrate for stone prevention.

## **Dietary Vitamin C in Beverages**

Whether dietary alterations of citrate can affect the rate of stone formation is unclear, as various studies contradict each other, and may vary by source of vitamin C. While most vitamin C is excreted as citrate, it can also be metabolized and excreted as oxalate (Mayne Pharma Ltd., 2004).

## Grapefruit Juice

Curhan, Willett, Speizer, and Stampfer (1998) found that grapefruit juice was directly associated with kidney stone formation in women, echoing similar findings in men (Curhan, Willett, Rimm, Spiegelman, & Stampfer, 1996). Grapefruit juice is a well-known inhibitor of the metabolism of numerous drugs via cytochrome P450 and its use is discouraged with many medications. However, it is not known if grapefruit's effect on stone formation may be due to some unknown metabolic alteration of metabolic processes with food breakdown similar to those associated with drug metabolism.

## Orange Juice

Orange juice ingestion is associated with no change in risk relative to water in the Nurses' Health Study (Curhan et al., 1998). However, other studies have shown orange juice to reduce stone risk. Wabner and Pak (1993) found that orange juice was equally as effective in reducing the lithogenic qualities of urine as was potassium citrate supplementation among 11 men in a prospective crossover study. Coe, Parks, and Webb (1992) found a favorable change in urinary citrate among six female participants who consumed calcium-fortified orange juice in an 11-week, crossover study. No change was appreciated in the six male participants. It is not known what part the calcium fortification may have played in the reduction of risk in this small study.

#### Lemonade

As another source of citrate, lemonade is often recommended to patients with stones. Seltzer et al. (1996) found that the intake of lemonade in 12 calcium stone formers could aid in reducing risk factors for stone formation. In this study, lemonade increased urinary citrate in 11 of 12 subjects with hypocitraturia (daily urinary citrate less than 320 mg) by a mean value of 204 mg per day. Lemonade was well tolerated and was believed to provide an inexpensive alternative to potassium citrate supplementation. The study did not seek, though, to determine the actual rates of stone formation. The Nurses' Health Study of 81,000 women showed no significant relationship between lemonade intake and stone risk, although lemonade and fruit punch use were studied together as one category (Curhan et al., 1998).

## **Cranberry Juice**

McHarg, Rodgers, and Charlton (2003) studied the effects of cranberry juice on the urinary qualities expected to impact the risk of stone formation. In a randomized crossover study, 20 South African men were given two different diets with and without cranberry juice, and urinary measurements were analyzed. Use of cranberry juice, which was high in both vitamin C and oxalate, resulted in improvements in urinary properties expected to reduce the risk of calcium oxalate stone formation, specifically increased urinary citrate, and reduced urinary oxalate and phosphate. Urinary calcium oxalate also decreased more with cranberry juice than without. McHarg et al. (2003) reported that while high in oxalate, cranberries' oxalate is not largely bioavailable, and thus, not readily absorbed. This may explain the reduction in urinary oxalate despite higher oxalate content.

Siener et al. (2003) studied dietary patterns in 186 stone-forming individuals with hyperoxaluria vs. normooxaluria. The sample was equally divided with 93 subjects with hyperoxaluria and 93 subjects with normooxaluria. Dietary contents were measured scientifically and recorded. Among those stone formers with hyperoxaluria, they noted higher dietary intake of ascorbic acid through fruits and vegetables. Larger ascorbic acid intake was believed to result in conversion to oxalate and hyperabsorption from the gut, when in the presence of reduced calcium intake. Researchers thought this was at least partly responsible for the presence of hyperoxaluria in this group of 93 stone formers.

Taylor, Stampfer, and Curhan (2004) found a greater incidence of stones among men with larger total vitamin C intake, regardless of origin. Among the 45,600 men studied over 14 years, men with the largest total vitamin C intake (over 1,000 mg daily) had a 41% greater risk of stone relative to those with the smallest intake of total vitamin C (less than 90 mg daily).

## Supplemental Vitamin C

Supplemental sources of vitamin C have been implicated in stone risk. Terris, Issa, and Tacker (2001) studied cranberry concentrate supplement use in a very small study of healthy adults. Five men and women provided urine studies before and after use of cranberry supplements for 7 days. Urinary oxalate levels increased in all subjects by an average of 43% after concentrate use. Other factors such as increases in urinary magnesium and potassium were noted which may reduce the risk of stone formation, mitigating the added risk of increased urinary oxalate.

Massey, Liebman, and Kynast-Gales (2005) found that ascorbic acid in supplement form caused increases in urinary oxalate among stone formers and non-stone formers alike, in their randomized crossover controlled study of 48 adults. Forty percent of the subjects had increases in urinary oxalate when given 1,000 mg ascorbic acid twice daily, compared to those without the supplementation. Oxalate stone-forming men and women had higher rates of oxalate absorption and endogenous oxalate synthesis than did non-stone formers when subjected to the same diet. In addition, these stone formers increased their own urinary oxalate levels when given ascorbic acid supplements, implying that vitamin C supplementation may be risky among known stone formers.

Opposing evidence has been presented. Taylor et al. (2004) noted no significant increased risk of stone formation with vitamin C supplementation in their study of men with kidney stones.

## Sodium Intake

The reabsorption of sodium and water in the kidney's proximal tubule provides a mechanism for passive reabsorption of calcium to the blood from the kidney's filtrate. Overingestion of sodium provides for less calcium reabsorption to the blood via passive reabsorption, leading to calcium excretion in larger quantities via the urine. A low-sodium diet is expected to conversely increase the reabsorption of sodium and calcium from the proximal tubule into the blood so that less remains in the urine, reducing stone risk. The recommendation for reduced dietary sodium is based on this understanding of the balance of sodium and calcium in the blood and urine. Kok, lestra, Doorenbos, and Papapoulos (1990) found that a high sodium diet induced increases in urinary calcium and reductions in urinary citrate, which are commonly recognized as risks for stone formation. This effect was more dramatic when diets were high in sodium and protein at the same time.

The role of sodium in actual stone formation, however, is less clear. Borghi et al. (2002) found reduced recurrence of stones in 120 men with a history of hypercalciuric stone formation if they maintained a low-protein, low-sodium diet, compared with a low-calcium diet. Curhan et al. (1993), however, found no relationship between sodium intake and stone formation in their study of 45,000 men. It would appear that recommendations for low-sodium diets are based mostly on the physiologic processes, yet is not yet solidly borne out by epidemiologic evidence.

## Magnesium Intake

Magnesium is thought to reduce stone risk by complexing with oxalate in the gut thereby reducing oxalate excretion into the urine. Sources of dietary magnesium include dairy products, meat, seafood, apples, apricots, avocados, bananas, whole grain cereals, nuts, dark green vegetables, and cocoa. Hirvonen, Pietinen, Virtanen, Albanes, and Virtamo (1999) studied 27,000 Finnish smoking men in a prospective epidemiologic study of the risks of stones. This was part of a larger study that looked at smoking men's risk of lung cancer if they supplemented their diets with alpha-tocopherol and beta-carotene. After 5 years of followup, 329 men developed kidney stones. They found that magnesium intake had a protective effect on stone formation. Those men with the highest magnesium intake (563 mg or more) had a relative risk of 0.52 for stone formation, compared to those with the lowest magnesium intake (382 mg or less). It is not known whether these results might be reproducible in other cultural groups, or what effect smoking may have had, if any, on these results.

Taylor et al. (2004) also found a reduced risk for stone formation among men aged 40 to 75 with increased dietary magnesium intake. Men with the highest dietary magnesium intake (over 450 mg/day) had a relative risk of stone formation of 0.71, compared with men who consumed the lowest amount of magnesium (less than 314 mg/day). In a study of the physiology of magnesium intake's effect on oxalate, Liebman and Costa (2000) found that a diet high in magnesium oxide reduced oxalate absorption and oxalate excretion, compared to a diet with low magnesium oxide among 24 healthy men and women. This may at least partially explain the phenomenon of variable stone risk.

#### Protein Intake

High-protein intake has long been proposed as a stone-forming dietary pattern. Those eating a high-protein, low-carbohydrate diet, so popular in recent years, may be at greater risk of stone formation than those with a more balanced nutritional intake.

Kok et al. (1990) studied eight healthy Dutch men who were given sodium and protein dietary modifications for 1 week followed by urine measurements of select elements. Results showed a diet high in protein (more than 2 g per kg body weight per day) produced increases in urinary calcium and uric acid, and decreases in urinary citrate, especially when the high-protein diet was accompanied by a high-sodium intake. The urine showed a significant decrease in the ability to inhibit the formation of calcium oxalate stones. The relative inability was dependent proportional to the degree of decrease in urinary citrate.

Curhan et al. (1993) studied the rate of stone formation in men relative to animal protein intake. They found that animal protein intake was directly associated with stone formation, with the highest protein intake (77 grams daily or more) showing a relative risk of 1.33 compared with the lowest protein intake (50 grams daily or less).

Giannini et al. (1999) took the protein intake question further by studying the effect of protein restriction on a small group of stone-forming adults. Researchers studied 18 men and women, all with histories of calcium stones and hypercalciuria. These 18 subjects restricted their protein intake to 0.8 g per kg of body weight per day for 15 days, after which serum levels and urinary excretion of significant elements were measured. Researchers noted a significant reduction in urinary uric acid, calcium, and oxalate after protein restriction, and increases in urinary citrate. Giannini et al. (1999, p. 270) noted "a reduction of the entire lithogenic potential of these patients" after the short 30 day trial. No measurements were made of the residual effects of a reduced-protein diet, nor of the effects of the reduction if it were undertaken for a longer period.

Hiatt et al. (1996) conducted a randomized controlled trial of 99 persons with histories of one former stone to determine if a low-protein diet might further reduce the risk of stone recurrence. Though not highly controlled over 4.5 years, their low-protein intake intervention group showed a significant increase in rates of recurrent stone formation compared to those who were instructed to only increase fluids (7.1 stones in 100-person years vs. 1.2 stones in 100-person years, respectively). Martini and Wood (2000) performed a meta-analysis of studies related to calcium and protein restrictions. They cautioned against stone-forming individuals undertaking low-protein diets, citing risk of elevation of parathyroid hormone, inducing bone loss. Martini and Wood (2000, p. 116) concluded that diets "restricting dietary protein to below RDA levels of 0.8 grams per kilogram per day are dangerous and should be avoided." As expected, these authors called for further studies to further delineate the connection, if any, between protein intake and stone formation.

#### **Other Beverages**

#### Coffee

Because of its oxalate content, coffee has been discussed as a potential stone-forming beverage. As a diuretic, coffee's increased risk may be mitigated because of caffeine's effect in urine dilution. Indeed, Curhan et al. (1998) found coffee was associated with a reduced risk of stones in women, whether caffeinated or decaffeinated. Caffeinated coffee had a 10% cumulative risk reduction for each 240 ml ingested, and decaffeinated coffee a 9% cumulative reduction in risk for each cup ingested per day. Tea was credited with an 8% cumulative reduction in stone risk per 240 ml ingested.

#### Wine and Beer

The most dramatic reduction in risk, however, was seen with wine consumption (Curhan et al., 1998). For each 240 ml intake of

wine per day, there was a 59% reduction in stone risk among women. Beer intake showed a 12% decrease in risk per 240 ml ingested. For no yet discernible reason, liquor's effects showed no change in risk.

Similar results on the risk of stones with beer intake were reported by Hirvonen et al. (1999). The risk of stones was reduced by 40% for each bottle (quantity not given) of beer ingested daily among smoking Finnish men. Other "spirits" (not specified as to type) had no significant effect on stone formation rates in this study.

#### Теа

While Curhan et al. (1998) found reduced stone formation among tea drinkers, some practitioners continue to suggest that teas, because of their high oxalate contents, be removed or limited in the diet of stone formers. In a separate study of various types of teas, black and herbal teas were studied to determine oxalate levels with brewing. Many herbal teas were found to have less oxalate than black tea, and were recommended by the researchers as possibly helpful to patients with recurrent stone risks (McKay, Seviour, Comerford, Vasdev, & Massey, 1995).

#### Cola

Limited research has been conducted concerning the risk of stones with cola intake. A small study of four men, one with a history of stones, underwent dietary manipulation to determine the risk of stone formation with cola ingestion (Weiss, Sluss, & Linke, 1992). Only three of the subjects were able to ingest a full 3 quarts of cola per day to complete the study. All subjects showed decreases in urinary citrate and magnesium, and increased urinary oxalate, which are believed to increase the risk of stone formation.

## Holistic Treatments

Holistic treatments embrace dietary and natural therapies to manage health. Phytotherapy, or herbal therapy, is central to holistic treatment. Phytotherapy is discussed below with regards to kidney stone disease management along with available scientific information to support it.

## Phytotherapy

Phytotherapy is included in many holistic recommendations for treatment of kidney stones, as well as numerous other human conditions. The European Scientific Cooperative on Phytotherapy (ESCOP), established in 1989, defines phytomedicines as "medicinal products containing as active ingredients only in plants, parts of plants or plant materials, or combinations thereof, whether in the crude or processed state...plant materials include juices, gums, fixed oils, essential oils, and any other directly derived crude plant product. They do not include chemically defined isolated constituents, either alone or in combination with plant materials" (European Society Cooperative on Phytotherapy, n.d.). ESCOP supports clinical studies on the safety and efficacy of phytotherapeutic agents through financial support of the European Union. At this time, holistic and phytotherapeutic management is based in the tradition of centuries, and seeks to validate its practices with quantifiable research, but much work remains to be done.

One phytotherapeutic agent, *Phyllanthus niruri*, has been studied in humans to begin to evaluate its effectiveness in prevention of stones. *Phyllanthis niruri* is an herb used in Brazilian folk medicine, with reported benefits to stone disease. Nishiura, Campos, Boim, Heilberg, and Schor (2004) studied the effects of this herb on the chemical promoters and inhibitors of stone formation in known stone-forming patients. Sixty-nine previous stone formers were randomized to take either 1,350 mg of aqueous extract of *P. niruri* divided in three doses or placebo for 3 months. Researchers found that among all subjects, there was no significant difference in urinary levels of measured metabolites calcium, uric acid, citrate, oxalate, and magnesium. However, when evaluating the results of those with hypercalciuria only, those who took *P. niruri* had a significant reduction in urinary calcium.

Micali et al. (2006) studied the effect of *P. niruri* on 150 people who had extracorporeal shock wave lithotripsy (ESWL). Seventy-eight patients received *P. niruri* for 3 months or more after ESWL, while 72 received none. Those with lower pole stones who took *P. niruri* had fewer stone recurrences over 6 months than those who did not use the herb. Stones in mid or upper-pole positions did not show significant recurrence rate changes compared with the control group.

In efforts to discover other examples of study of phytotherapy, a subject search on the search engine Alternative HealthWatch was performed in January 2006 with the words "kidney stone." Only peer-reviewed journals were used. The search retrieved 55

articles, none of which was a scientific study of phytotherapy's use in managing urolithiasis. A search in January 2006 of the last 6 years in the holistic journal *Phytotherapy Research* with the term "kidney stones" produced no experimental studies of herbal supplement on humans. Likewise, a title search in the holistic journal *Phytomedicine* in December 2006 found no human studies on kidney stone treatment with herbals over the last 6 years. Nor were any found in the journal *Alternative Medicine Review* for the last 7 years. Application of the principles of EBP indicates that there is currently no satisfactory body of evidence to satisfy EBP's guidelines regarding phytotherapy for kidney stones. While the above studies on *P. niruri* are exciting to see, they are quite preliminary at best. This author agrees with ESCOP that much work needs to be done with phytotherapeutic agents. Phytotherapy may prove beneficial if studies such as those discussed here continue to show possible benefits. For now, no such strong evidence exists.

#### **Obesity and Weight Gain**

Three large prospective epidemiologic studies looked at the link between body weight and the risk of stones. The Health Professionals Follow-up Study of 46,000 male physicians over 14 years, the Nurses' Health Study I of 93,000 older women, and Nurses' Health Study II of 101,000 younger women asked about weight and incidence of symptomatic kidney stones that followed over the course of years. Among the men in the Health Professionals Follow-up Study (who were aged 40-75 years) weighing over 220 lbs, the relative risk of stones was 1.44, compared to men who weighed less than 150 lbs. If the men gained more than 35 lbs since early adulthood, they had a relative risk of stones of 1.35 compared to men whose weight remained unchanged. Among men, a BMI of 30 or more translated to a risk of 1.33 vs. that of men with BMI of 21 to 22.9. Waist circumferences also showed significance. Men with waist measurements of more than 43 inches had 1.48 times the risk of stones than men with waist circumferences of less than 34 inches (Taylor, Stampfer, & Curhan, 2005).

Among the older women of the Nurses' Health Study I, aged 30 to 55, those weighing 220 lbs or more had a relative risk of stones of 1.89 compared with women weighing less than 150 lbs. Older women who gained more than 35 lbs since early adulthood had a relative risk for stone formation of 1.70 compared to those who did not gain weight. Among the older women, a BMI of 30 or more had a risk of stones of 1.9 of that of women with BMI of 21 to 22.9 (Taylor et al., 2005).

Similar trends were noted among the younger women of the Nurses' Health Study II, who were aged 25 to 42. Younger women weighing over 220 lbs had a risk of stones of 1.82 times the risk of women weighing less than 150 lbs. Those who gained 35 lbs or more risked stones 1.82 times that of women whose weight did not change over the course of their adult lives. Those with BMIs of 30 or more had 2.09 times the risk of stones than women with BMIs of 21 to 22.9. Finally, women with waist circumferences of more than 40 inches had 1.94 times the risk of stones than women with waist measurements of less than 31 inches. Among the three groups, the younger women had the greatest risk with greater degrees of obesity (Taylor et al., 2005).

## The Internet as a Source of Information

In December 2006, a search of kidney stone treatments on the World Wide Web via the Google search engine revealed a number of sites which offered to sell products to dissolve calcium oxalate stones. Among them were the following two sites: http://webagt.com/a/kidneystoneslink.htm; http://cgi.ebay.com/ws/eBayISAPI.dll?ViewItem&item=9519705774&refid=store. Other sites recommend herbal or phytotherapeutic solutions such as dandelion leaf as an alternative diuretic to hydrochlorothiazide (All Natural Net, n.d.). Gravel Root, Jo Pye Weed, and Queen of the Meadow are alternate names for an herb suggested for stones prevention as a pH altering substance, and for treating cystitis and dysuria (Purple Sage Botanicals, 2006). Such treatments are attractive to patients because usage does not require consultation from a physician or nurse, giving patients a sense of control over their own treatment decisions. Just as dietary changes can be made without prescription, a prescription is not required to obtain these herbal products.

Many commercial treatments offered online are difficult to evaluate, much less endorse. The lack of specific information about some of these products makes it difficult to discuss with patients who want input on their track records of success. In addition, many herbal remedies lack the standardization of content required of pharmaceutical agents regulated by the U.S. Food and Drug Administration. It is impossible to evaluate a therapy that does not give full disclosure of its contents. Clinicians must educate patients about purchasing treatments, sometimes at great expense, that are uninvestigated as agents for treatment of kidney stones. While some may be effective, they are clinically unproven.

# **Implications for Practice**

How do health care providers assimilate results from these multiple studies and apply them to our patients and practice? None of the information presented for dietary changes meets the strict criteria of EBP. However, there are varying levels of evidence which might guide clinicians in their recommendations to patients (see Table 1). There is good evidence to suggest that increasing fluids reduces the rate of stone formation. An easy guide is to suggest that urine should appear very light yellow to clear at all times. This technique makes it easy to quickly adjust oral intake, based on the appearance of urine, assuming the patient is not using drugs that change the color of urine, such as multivitamins with carotene, or pyridium. This recommendation is generally safe assuming the patient does not have kidney or heart failure precluding higher fluid intake.

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Nutrient	Weight of Evidence	Finding
Water	Good	Maintain intake of 2.5 liters/day, maintain light yellow urine at all tim es.
Dietary calcium	Good	Do not limit; maintain 1,000 m g/day by dietary sources.
Supplemental calcium	Fair	Take with food if used for bone strength.
Oxalate	Fair but insufficient data	May promote stones, but little evidence for limi- tation of dietary oxalate.
Dietary vitamin C	Fair	Grapefruit juice possibly harmful. Lemonade possibly helpful. Orange juice possibly helpful. Cranberry juice possibly helpful.
Supplemental vitamin C	Fair but contradictory	Possibly stone forming.
Sodium	Fair but contradictory	Possibly helpful to limit to 2.5 gm s/day.
Magnesium	Good	Likely beneficial.
Protein	Fair	High-protein diet may risk stone formation; conflicting information about reduced protein diet risk vs. benefit.
Coffee/Tea	Fair	Probably not stone forming; may be beneficial.
Wine	Fair	Probably not stone forming; may be beneficial.
Beer/Liquor	Fair	Possibly not stone forming.
Cola	Preliminary data	May increase stone risk.
P hyllanthus niruri	Preliminary data	May be beneficial to known stone formers.
Other phytotherapy/herbal products	No human studies to review	Cannot recommend or discourage
Source: Urol Nurs @ 2007 Society of Urologic Nurses and Associates		

Table 1. Recommendations to Guide Clinicians in Patient Education

There is also good, but not overwhelming evidence, that calcium intake should not be limited for the sake of stone risk. Dietary calcium may be safer than supplemental calcium. Those who use calcium supplements should consider administration with meals only, until more is learned about the risks of supplemental calcium for those with a history of stones.

There is some early evidence that high animal protein diets increase the risk of stones. Patients have one more reason to reconsider a decision to use a low-carbohydrate, high-protein diet for weight loss, because of the risk of kidney stones. Conflicting information exists on the benefit or harm of a reduced protein diet.

There is insufficient evidence to recommend a limited oxalate diet. Human oxalate levels may vary widely based on endogenous factors, and not dietary intake of oxalate, making dietary alterations impractical for the typical person. Patients with Crohn's disease or gastric bypass may benefit from reduction of dietary oxalate, but studies do not yet show this as beneficial.

There is some weak evidence that low-sodium diets may benefit stone formers. The science behind this recommendation, however, is very incomplete and needs further study.

The information on vitamin C intake is contradictory. Supplemental vitamin C use should be undertaken cautiously among stone formers. Lemonade may be a good fluid choice among patients known to have low levels of urinary citrate, rather than grapefruit juice. Future studies should attempt to evaluate the breakdown of ascorbate to oxalate vs. citrate, as the association each has to

stone formation is significant.

There is very little information upon which to base recommendations on the use of cola or other soft drinks. Given the empty caloric value of sugared soft drinks, their use in large quantities should continue to be discouraged. With their ubiquitous presence in our culture, however, they certainly deserve further study.

Patients with calcium stones can continue to use teas and coffees without particular concern, though the evidence is not clear that they are actually beneficial. Equally unclear are the possible benefits of alcoholic beverages, though wine and beer may carry some weight as stone inhibitors.

Maintenance of proper body weight may have benefits to reducing stone formation, though information is very limited. There are certainly enough reasons to maintain normal body weight, and risking stones may be another reason to avoid obesity.

Patients may find the use of herbal therapies appealing, particularly when traditional Western treatment fails. Clinicians need to inquire about herbal treatments used by patients in their assessments, especially when their stones recur. It is important for the clinician to communicate, through nonjudgmental language, that there is insufficient evidence to support the use of phytotherapeutic agents for kidney stones at this time as the field remains untested.

# **Future Implications**

There is ongoing need for urologic nurses and health care providers to research and investigate treatment modalities for kidney stones. As we embrace EBP to guide recommendations, this review of available literature on dietary management of calcium oxalate kidney stones show little is known with any degree of certainty. It behooves us as clinicians to look critically at all our practices, review the available literature, and question what we believe we know.

Kidney stones constitute a problematic health condition for many of our patients. Our profession requires us to update our knowledge as new information is revealed. Urologic nurses and associates can not only benefit from understanding the literature, but also from taking part in studies that seek to evaluate the patient's risk for kidney stones. In this way, we can develop powerful experience in urologic research. Mainstream Western medicine and alternative treatments should be considered as subjects for future study as well as seeking to incorporate the growing field of phytotherapy into our knowledge base.

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# References

- 1. All Natural Net. (n.d.). Dandelion Taraxacum officinale. Encyclopedia of herbs. Retrieved December 4, 2006, from http://www.allnatural.net/herbpages/dandelion.shtml
- 2. Borghi, L., Meschi, T., Amato, F., Briganti, A., Novarini, A., & Giannini, A. (1996). Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: A 5-year randomized prospective study. Journal of Urology, 155, 839-843.
- 3. Borghi, L., Schianchi, T., Meschi, T., Guerra, A., Allegri, F., Maggiore, U., et al. (2002). Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. New England Journal of Medicine, 346, 77-83.
- Chai, W., Liebman, M., Kynast-Gales, S., & Massey, L. (2004). Oxalate absorption and endogenous oxalate synthesis from ascorbate in calcium oxalate stone formers and non-stone formers (abstract). American Journal of Kidney Diseases: The official journal of the National Kidney Foundation, 44, 1060-1069.
- 5. Coe, F.L., Parks, J.H., & Webb, D.R. (1992). Stone-forming potential of milk or calcium-fortified orange juice in idiopathic hypercalciuric adults (abstract). Kidney International, 41, 139-142.
- 6. Curhan, G.C., Willett, W.C., Rimm, E.B., & Stampfer, M.J. (1993). A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. New England Journal of Medicine, 328, 833-838.
- 7. Curhan, G.C., Willett, W.C., Rimm, E. B., Spiegelman, D., & Stampfer, M.J. (1996). Prospective study of beverage use and the risk of kidney stones. American Journal of Epidemiology, 143, 240-247.
- 8. Curhan, G.C., Willett, W.C., Speizer, F.E., Spiegelman, D., & Stampfer, M.J. (1997). Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. Annals of Internal

Medicine, 126, 497-504.Curhan, G.C., Willett, W.C., Speizer, F.E., & Stampfer, M.J. (1998). Beverage use and risk for kidney stones in women. Annals of Internal Medicine, 128, 534-540.

- 9. European Society Cooperative on Phytotherapy. (n.d.). What is ESCOP? Retrieved December 22, 2006, from http://www.escop.com
- 10. Gambaro, G., Reis-Santos, J.M., & Rao, N. (2004). Nephrolithiasis: Why doesn't our "learning" progress? European Urology, 45, 547-556.
- 11. Giannini, S., Nobile, M., Sartori, L., Carbonare, L.D., Ciuffreda, M., & Corro, P., et al. (1999). Acute effects of moderate protein restriction in patients with idiopathic hypercalciuria and cal cium nephrolithiasis. American Journal of Clinical Nutrition, 69, 267-271.
- 12. Guyton, A.C., & Hall, J.E. (2000). Textbook of medical physiology (10th ed.). Philadelphia: Saunders.
- 13. Hall, P.M. (2002). Preventing kidney stones: Calcium restriction not warranted. Cleveland Clinic Journal of Medicine, 69, 885-888.
- 14. Heilberg, I.P. (2000). Update on dietary recommendation and medical treatment of renal stone disease. Nephrology, Dialysis, Transplantation, 15, 117-123.
- Hiatt, R.A., Ettinger, B., Caan, B., Quesenberry, C.P., Duncan, D., & Citron, J.T. (1996). Randomized controlled trial of a low animal protein, high fiber diet in the prevention of recurrent calcium oxalate kidney stones. American Journal of Epidemiology, 144, 25-33.
- 16. Hirvonen, T., Pietinen, P., Virtanen, M., Albanes, D., & Virtamo, J. (1999). Nutrient intake and use of beverages and the risk of kidney stones among male smokers. American Journal of Epidemiology, 150, 187-194.
- 17. Holmes, R.P., Goodman, H.O., & Assimos, D.G. (2001). Contribution of dietary oxalate to urinary oxalate excretion. Kidney International, 59, 270-276.
- Kok, D.J., lestra, J.A., Doorenbos, C.J., & Papapoulos, S.E. (1990). The effects of dietary excesses in animal protein and in sodium on the composition and the crystallization kinetics of calcium oxalate monohydrate in urines of healthy men (abstract). Journal of Clinical Endocrinology and Metabolism, 71, 861-867.
- 19. Liebman, M., & Costa, G. (2000). Effects of calcium and magnesium on urinary oxalate excretion after oxalate loads (abstract). Journal of Urology, 163, 1565-1569.
- 20. Martini, L.A., & Wood, R.J. (2000). Should dietary calcium and protein be restricted in patients with nephrolithiasis? Nutrition Reviews, 58, 111-117.
- 21. Massey, L.K., Liebman, M., & Kynast-Gales, S.A. (2005). Ascorbate increases human oxaluria and kidney stone risk. The Journal of Nutrition, 135, 1673-1677.
- 22. Mayne Pharma Ltd. (2004). Information for health professionals data sheet: Ascorbic acid injection. Retrieved January 21, 2006, from http://www.medsafe.govt.nz/profs/Datasheet/a/Ascorbicacidinj.htm
- 23. McCarron, D.A., & Heaney, R.P. (2004) Estimated healthcare savings associated with adequate dairy food intake. American Journal of Hypertension, 17, 88-97.
- 24. McHarg, T., Rodgers, A., & Charlton, K. (2003) Influence of cranberry juice on the urinary risk factors for calcium oxalate kidney stone formation. BJU International, 92, 765-768.
- 25. McKay, D.W., Seviour, J.P., Comerford, A., Vasdev, S., & Massey, L.K. (1995). Herbal tea: An alternative to regular tea for those who form calcium oxalate stones (abstract). Journal of the American Dietetic Association, 95, 360-361.
- Micali, S., Sighinolfi, M.C., Celia, A., DeStefani, S., Grande, M., Cicero, A.F. et al. (2006). Can Phyllanthus niruri affect the efficacy of extracorporeal shock wave lithotripsy for renal stones? A randomized, prospective, long-term study. The Journal of Urology, 176, 1020-1022.
- 27. Morton, A.R., Iliescu, E.A., & Wilson, J.W.L. (2002). Nephrology 1: Investigation and treatment of recurrent kidney stones. Canadian Medical Association Journal, 166, 213-218.
- 28. Moyad, M. (2003). Calcium oxalate kidney stones: Another reason to encourage moderate calcium intakes and other dietary changes. Urologic Nursing, 23, 310-313.
- 29. National Guideline Clearinghouse. (2006). Nephrolithiasis. Retrieved on December 4, 2006 from http://www.guideline.gov/summary/summary.aspx?doc\_id=7463&nbr=004409&string=kidney+AND+stones
- Nishiura, J.L., Campos, A.H., Boim, M.A., Heilberg, I.P., & Schor, N. (2004). Phyllanthus niruri normalizes elevated urinary calcium levels in calcium stone forming (CSF) patients. Urology Research, 32, 362-366.
- 31. Pak, C.Y.C. (1999). Medical prevention of renal stone disease. Nephron, 81(Suppl. 1), 60-65.
- 32. Pak, C.Y.C., Sakhaee, K., Crowther, C., & Brinkley, L. (1980). Evidence justifying a high fluid intake in treatment of nephrolithiasis. Annals of Internal Medicine, 93, 36-39.
- 33. Parmar, M.S. (2004). Kidney stones. British Medical Journal, 328, 1420-1424.

- 34. Purple Sage Botanicals. (2006). Gravel root. Retrieved December 4, 2006, from http://www.purplesage.org.uk/profiles/gravelroot.htm
- 35. Qiang, W., & Ke, Z. (2004). Water for preventing urinary calculi. The Cochrane Database of Systematic Reviews 3(CD004292.pub2). Retrieved November 23, 2005, from http://www.cochrane.org/cochrane/revabstr/AB004292.htm
- 36. Seltzer, M.A., Low, R.K., McDonald, M., Shami, G.S., & Stoller, M.L. (1996). Dietary manipulation with lemonade to treat hypocitraturic calcium nephrolithiasis. Journal of Urology, 156, 907-909.
- 37. Siener, R., Ebert, D., Nicolay, C., & Hesse, A. (2003). Dietary risk factors for hyperoxaluria in calcium oxalate stone formers. Kidney International, 63, 1037-1043.
- Stitchantrakul, W., Sopassathit, W., Prapaipanich, S., & Domrongkitchaiporn, S. (2004). Effects of calcium supplements on the risk of renal stone formation in a population with low oxalate intake (abstract). The Southeast Asian Journal of Tropical Medicine and Public Health, 35, 1028-1033.
- 39. Straub, M., & Hautmann, R.E. (2005). Developments in stone prevention (abstract). Current Opinion in Urology, 15, 119-126.
- 40. Taylor, E.N., Stampfer, M.J., & Curhan, G.C. (2004). Dietary factors and the risk of incident kidney stones in men: New insights after 14 years of follow-up. Journal of the American Society of Nephrology, 15, 3225-3232.
- 41. Taylor, E.N., Stampfer, M.J., & Curhan, G.C. (2005). Obesity, weight gain, and the risk of kidney stones. JAMA, 293, 455-462.
- 42. Terris, M.K., Issa, M.M., & Tacker, J.R. (2001). Dietary supplementation with cranberry concentrate tablets may increase the risk of nephrolithiasis. Urology, 57, 26-29.
- 43. Wabner, C.L., & Pak, C.Y. (1993) Effect of orange juice consumption on urinary stone risk factors (abstract). The Journal of Urology, 149, 1405-1408.
- 44. Weiss, G.H., Sluss, P.M., & Linke, C.A. (1992). Changes in urinary magnesium, citrate, and oxalate levels due to cola consumption. Urology, 32, 331-333.

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Disclosure: The author reported no actual or potential conflict of interest in relation to this continuing nursing education article.

Urol Nurs. 2007;27(2):113-122, 143. © 2007 Society of Urologic Nurses and Associates