Role of diet in prevention of recurrent nephrolithiasis
Roy DK

Summary
Nephrolithiasis is a major cause of morbidity involving urinary tract. While primary prevention of nephrolithisis is not of sufficient priority, prevention of recurrent stone formation demands greater attention. Diet plays an important role in the pathogenesis of kidney stones. Higher fluid intake leads to increased urinary volume and in turn to a decreased concentration of lithogenic factors presumably decreasing the rate of stone formation. At present the practice is to advice patient fluid intake sufficient to maintain his urine output around 2-3 liter per day. General recommendations on dietary modifications may be beneficial and cost effective at population level. Physician should no longer prescribe a low calcium diet to prevent recurrent calcium nephrolithiasis. The new trend is normalization of the dietary habits and not restriction of a single nutrient constituent.

Introduction
Nephrolithiasis is a major cause of morbidity involving urinary tract. The lifetime prevalence of symptomatic nephrolithiasis is approximately 10% in men and 5% in women. The total number of physician office visit for stone disease in USA nearly doubled from 9,50,000 visits in 1992 to 1,825,000 in 2000. In Germany the incidence rate rose during the last decade from 0.54 to 1.47 %. The reasons for this increase in prevalence and incidence rates are manifold: life style changes, dietary factors, obesity, improved medical facilities etc. Easy availability of better diagnostic tools like ultrasound in routine practice allows the diagnosis of asymptomatic nephrolithiasis. While primary prevention of nephrolithisis is not of sufficient priority, prevention of recurrent stone formation demands greater attention. Now a days excellent options for interventional stone therapy such as Extra corporeal shockwave lithotripsy (ESWL), Ureterorenoscopy (URS), and Percutaneous nephrolithotomy (PCNL) warrant comfortable stone management. It is therefore not surprising that stone removal has become a more attractive option then elaborate measures to prevent recurrent stone formation, which is more cost effective.

Diet plays an important role in the pathogenesis of kidney stones. The kidneys along with minerals like sodium, calcium and magnesium excrete uric acid, phosphate and oxalate from ingested food and from metabolism. These crystalloids remain in solution due to the presence of normal colloids. If the crystals are precipitated and bound by an organic matrix, a stone is formed. People eat food, which are complex mixture of different nutrients, the content and bioavailability of different component nutrients are known to vary. Many physiologic studies have examined changes in urine composition after dietary interventions and predictions about stone formations are then made based on the urinary changes.

About 80% of kidney stones contain calcium, and majority of calcium stones consists primarily of calcium oxalate. For less common types of stone like (Uric acid, Struvite, Cystine) there is little information concerning the influence of dietary factors in actual stone formation. Consumption of common foods containing animal protein like meat, chicken, sea food may lead to increased uric acid production due to the purine content of the animal flesh. On the

Dr. Dilip Kumar Roy, MBBS, FCPS (Med), MD (Neph)
Associate Professor, Department of Nephrology
National Institute of Kidney Diseases and Urology
Sher-E-Bangla Nagar, Dhaka, Bangladesh
other hand animal protein contains more sulfur containing amino acids and their metabolism leads to increased uric acid production with subsequent lowering of urinary pH. Both increased uric acid excretion and low urine pH increase the risk of uric acid crystal formation. So, restriction of dietary animal protein may be of help to prevent recurrence of uric acid stones. Most of our knowledge about dietary factors is related to calcium oxalate, the most common type of urinary tract stone. In these article dietary factors related to the formation and prevention of calcium stone will be discussed. From an etiologic perspective it is reasonable to focus on different nutrients individually rather than on the diet as a whole.

**Calcium**

The normal range of urinary calcium in adults taking an ordinary diet is 100-300 mg/day for men and 100-250 mg/day for women. Around 50% of patients who pass calcium stones in general tend to show increased urinary calcium excretion. Because of that, dietary calcium was believed to increase the risk of calcium oxalate nephrolithiasis. As a consequence, for long time "stone formers" were advised to restrict their dietary calcium to prevent stone recurrence. But there is no published data that demonstrated a decrease in the rate of stone formation by dietary calcium restriction. Three prospective observational studies involving more than 2,00,000 individuals found that a higher dietary calcium intake was associated with a reduced risk of incident stone formation. These findings of dietary calcium were independent of other dietary factors or fluid intake. Normal or high dietary intake of calcium significantly reduces the risk of calcium oxalate stone formation. Significant reduction of the intestinal oxalate absorption apparently mediates the beneficial effect of a normal or high dietary calcium intake, lowering the fraction of freely available oxalate in the urine and thereby decreasing the urinary crystallization risk for calcium oxalate. A highlight in basic research was published by the BONN group, where they demonstrated an inverse correlation between intestinal oxalate absorption and the daily calcium intake. There is also evidence that urinary calcium excretion depends more on dietary acid load than on calcium intake itself. Skeletal calcium reabsorption and hypercalcemia results from buffering of nutritional acid load by bones. Modern diets are rich in animal protein, which increases the acid load. Under these circumstances severe bone loss will occur if the calcium intake is additionally restricted. The substitution of meat protein by dairy products derived protein will provide a higher intake of phosphate, which co-precipitates with calcium in the intestinal lumen. Nevertheless, it has been shown that the benefit of high calcium supply do not apply to calcium supplements, which usually are not taken with meals hence loosing their oxalate chelating properties. Observational data suggested that calcium supplement use might increase the risk of incident stone formation in older women by around 20%. Calcium supplement use is a rare cause of incident stone formation. But for individual who has already had a stone the risk of supplemental calcium is likely to be substantially higher.

**Oxalate**

Calcium oxalate is a major component of about 75% of all urinary stones. Urinary oxalate is thought to be derived from three sources: 40-50% derived from hepatic synthesis, 40-50% from the breakdown of ascorbic acid in the body and the remaining 10-20% from the diet. Oxalate is a ubiquitous component of plants and thus may be an unavoidable component of the human diet. Seeds including cereal grains, some leaves such as spinach and some roots like beets are particularly enriched in oxalate, where it may represent up to 30% of the dry weight. A partial list of foods and their oxalate content is shown in table 1.
### Table-1: Partial list of oxalate content of foods

<table>
<thead>
<tr>
<th>Food</th>
<th>Mg of Oxalate Serving size in parenthese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinach, Cooked</td>
<td>608 (1/2 cup)</td>
</tr>
<tr>
<td>Rhubarb, frozen</td>
<td>570 (1/2 cup)</td>
</tr>
<tr>
<td>Spinach, Chopped raw</td>
<td>361 (1 cup)</td>
</tr>
<tr>
<td>Green beams, Steamed</td>
<td>40 (1/2 cup)</td>
</tr>
<tr>
<td>Bran flakes</td>
<td>40 (1/2 cup)</td>
</tr>
<tr>
<td>Peanuts</td>
<td>27 (1 oz)</td>
</tr>
<tr>
<td>Potato, microwave</td>
<td>25 (1 medium)</td>
</tr>
<tr>
<td>Celery</td>
<td>25 (1 stalk)</td>
</tr>
<tr>
<td>Tea, brewed</td>
<td>18 (1 cup)</td>
</tr>
<tr>
<td>Chocolate</td>
<td>16 (1 oz bar)</td>
</tr>
<tr>
<td>Peanut butter</td>
<td>15 (1 Tbsp)</td>
</tr>
<tr>
<td>White bread</td>
<td>5 (1 slice)</td>
</tr>
</tbody>
</table>

These are the values from Channing laboratory nutrient database.

It is clearly not possible to eliminate oxalate from the human diet, and a diet with oxalate content lower than 80 mg/day may not be practically possible and could be deficient in other essential nutrients. It should be remembered that the actual oxalate content of a food might not actually determine the risk since the bioavailability of oxalate may vary substantially. It is possible to decrease the oxalate content of vegetables by using phosphate fertilizer. A number of nutrients may influence the excretion of oxalate, for example, an increased consumption of ascorbic acid or a decreased intake of calcium and magnesium. A deficiency of oxalate degradation by *oxalobacter formigenes* in the intestine may contribute additionally to an increased absorption and urinary excretion of oxalate. The relative contribution of endogenous and exogenous oxalate source to urinary oxalate excretion remains a matter of debate. A study examining the impact of diet on urinary oxalate excretion found that high urinary oxalate predominantly results from increased endogenous production.

Siener R et al confirmed an inverse association between dietary calcium intake and the risk of hyperoxaluria. Magnesium has been suggested to be nearly as effective as calcium in decreasing intestinal oxalate absorption and urinary excretion. Dietary fiber and phytic acid have been suggested to increase the risk of oxalate stone formation by increasing oxaluria through binding of intestinal calcium, resulting in an increased absorption and increased urinary excretion of oxalate. Additionally, oxalate content of fiber rich food is also high. Most individuals, however, may have an imbalance in the calcium and oxalate content of individual meal and snacks, and thus may have a response closer to that observed with the restricted calcium diet. Although dietary oxalate intake was not identified as a risk for hyperoxaluria, reduction of food stuffs rich in oxalate might be essential in patients with enteric hyperoxaluria.

A sufficient dietary calcium intake, therefore, is required to compensate for the higher oxalate and lower calcium content of vegetable foods. An increased consumption of lean dairy products may be considered to meet the current dietary recommendations of calcium (1000 to 2000 mg/day). Exchange of dairy products instead of plant foods such as fruits, vegetables, and cereals may reduce dietary oxalate intake and thus recurrent stone formation.

**Sodium**

A high sodium intake leads to increased urinary calcium excretion independent of calcium intake, apparently due to inhibition of sodium and calcium reabsorption in the proximal tubule and along the loop of henle. Every 100 mmol increase in dietary sodium increases urinary calcium excretion by 25 mg. A high sodium chloride is expected to lower urinary citrate excretion as well. Many investigators have documented the adverse effects of high sodium intake and the resultant higher calcium excretion. An Italian randomized trial observed a reduced risk of stone recurrences in the group assigned to...
the high calcium, reduced animal protein and reduced sodium diet\textsuperscript{20}.

**Potassium**
An epidemiological study has reported that the lower the potassium intake, below 74mmol /day, the higher the relative risk of stone formation.\textsuperscript{8} Lemann J Jr et al\textsuperscript{31} reported that higher intake of dietary potassium may reduce the risk of stone formation by reducing urinary citrate excretion. Two other observational studies also found that the risk of stone formation decreased substantially with increasing dietary potassium.\textsuperscript{8,10} Randomized trials with potassium citrate supplementation also demonstrated protective effect\textsuperscript{32,33}.

**Protein**
Protein has universal effects on most parameters involved in stone formation. High protein intake of animal origin contributes to hyperuricosuria due to purine overload, to hyperoxaluria due to higher oxalate synthesis, to hypocitraturia due to higher tubular reabsorption of citrate\textsuperscript{34,35}. Modern diets are rich in animal protein which increases acid load. The nutritional acid load is mainly buffered by the bones leading to skeletal calcium mobilization and thus elevated filtered load of calcium. Giannini S et al\textsuperscript{36} reported that an acute moderate protein restriction reduces urinary oxalate, phosphate, hydroxyproline, calcium and uric acid and increases citrate excretion. Observational data suggested a slight increase in the risk of incident stone formation with higher animal protein intake in men.\textsuperscript{8}

**Vitamin C**
Vitamin C (ascorbic acid) in large doses has been implicated as a risk factor for calcium oxalate stone formation. In vivo ascorbate is metabolized to oxalate, which is then excreted in the urine. But the effect of large doses of Vitamin C in increasing urinary oxalate excretion is controversial\textsuperscript{37,38}. In prospective observational studies no association with risk of stone formation was observed for vitamin C intake, even among those with intake more than 1500mg/day\textsuperscript{39,40}. However, several short term feeding studies observed increased oxalate excretion and calcium supersaturation with high dose (2gm/day) of vitamin C\textsuperscript{41}. A large cross sectional study found a slightly increased risk of stone disease in men and women taking vitamin C supplements\textsuperscript{42}.

**Fluid intake**
An increase in fluid intake is routinely recommended for patients who have had a kidney stone to decrease the likelihood of recurrence. Higher fluid intake leads to increased urinary volume and in turn to a decreased concentration of lithogenic factors presumably decreasing the rate of stone formation. This approach is supported by many\textsuperscript{43-46} but not all\textsuperscript{47}. A very well conducted randomized, prospective study\textsuperscript{48} involving first stone episode patients has shown lower risk of recurrence (12\%) in those with a higher intake of water compared to those without (27\%), in absence of any drug therapy, or any dietary change over a period of 5 year follow up. At present the practice is to advice patient fluid intake sufficient to maintain urine output around 2-3 liter per day. As the calcium content of the drinking water increases urinary calcium excretion increases, but oxalate excretion falls\textsuperscript{49,50}. Water with large amount of bicarbonate may increase citrate excretion\textsuperscript{49} and magnesium content of water may favorably alter citrate and magnesium excretion\textsuperscript{51}. But to what extent the hardness and mineral composition of water affect stone risk remains undecided\textsuperscript{49,52,53}. There is still no definite evidence to support the notion that hard water rich in calcium and magnesium is more lithogenic then soft water.

Beverages differ in the amount of potentially important constituents, such as caffeine, oxalate, and alcohol that they contain. Therefore they may influence stone formation differently. Case control\textsuperscript{54} and cross sectional\textsuperscript{52} studies have suggested decreased risk for caffeinated and decaffeinated coffee, tea, bear and wine.
while increased risk for grape juice consumption. Curhan GC et al\textsuperscript{55} in a epidemiological study based on food frequency questionnaires showed that caffeinated and decaffeinated coffee was associated with a reduction of risk of 8-10\%, while wine decreased the risk by 59\%. In this study grape fruit juice ingestion was associated with a 44\% increased risk of stone formation. Because coffee and particularly tea were believed to be high in oxalate and thus the inverse association is unexpected. A study\textsuperscript{56} reported that black tea contains substantial amount of oxalate but very little is bioavailable. The protective effect of coffee, tea is possibly through urinary dilution by inhibition of anti diuretic hormone (ADH) in the distal tubule by caffeine. The mechanism for the increased risk observed for grape fruit juice is unknown. A metabolic study examining changes in the urine composition predicted that grapefruit juice should reduce the risk of stone formation by increasing urinary citrate\textsuperscript{57}. This is supported by the fact that other citrus juices such as orange and lemon apparently prevent\textsuperscript{58,59} and at least do not stimulate stone formation because of their high citrate content. A small short-term study suggested that home made lemonade is an effective approach to increase urinary citrate in individuals with hypocitraturia\textsuperscript{58}, but whether this will reduce the likelihood of stone recurrence is not proved yet. Relative risk for consumption of specific beverages and risk of incident stone formation is shown in table -2.

<table>
<thead>
<tr>
<th>Beverages</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee</td>
<td>0.90</td>
</tr>
<tr>
<td>Tea</td>
<td>0.89</td>
</tr>
<tr>
<td>Beer</td>
<td>0.80</td>
</tr>
<tr>
<td>Wine</td>
<td>0.60</td>
</tr>
<tr>
<td>Grapefruit juices</td>
<td>1.40</td>
</tr>
</tbody>
</table>

Table-2: Multivariate relative risks (per 240 ml) for consumption of specific beverages and risk of incident kidney stones\textsuperscript{54,55}

All these results must be interpreted cautiously until longterm randomized trials of dietary intervention are performed. Depending on the present knowledge the anti stone forming dietary recommendations are listed in table -3.

- Diet must be prescribed depending on the specific metabolic disturbances
- To ensure compliance, individual dietary habits should be taken into consideration.
- Avoid calcium restriction.
- Calcium and oxalate intake must be in balance.
- Advise moderate restriction of animal protein and NaCl intake.
- Encourage potassium intake.
- Fluid intake should be sufficient to produce at least 2.5-3.0 liters of urine per day.

Table-3: Dietary recommendations for prevention of recurrent nephrolithiasis.

**Conclusion**

The influence of diet on renal stone disease seems to be very complex as multiple interactions takes place between different nutrients and thus variably influence urinary parameters. But as dietary factors clearly play an important role in the etiology and recurrence of different types of stones in the urinary tract, general recommendations on dietary modifications may be beneficial and cost effective at population level. Patients may be informed that kidney stones can be prevented and dietary modification has an important role on this. Physician should no longer prescribe a low calcium diet to prevent recurrent calcium nephrolithiasis. The new trend is normalization of the dietary habits and not restriction of a single nutrient constituent. This type of diet will be of greatest value when it started early in the course of the disease.

**References**


Review Article


