

CHAPTER 1

How to Build a Kidney Stone Prevention Clinic

David S. Goldfarb

New York University School of Medicine, New York, NY, USA

“It’s the right thing to do” (Edward Goldfarb, DDS, 1968)

“It’s the right thing to do” (Michael Grasso, MD, 1996)

Introduction

Those identical, ethical mandates were told to me on two occasions: first, when as a preteen I objected to my father, a dentist, fluoridating the teeth of his young patients, suggesting that he was sacrificing his income (and my future college tuition) by the prevention of caries; second, when as a proto-lithologist, Michael Grasso and I discussed the founding of a kidney stone clinic and I asked Michael if he was worried that I would reduce the number of ureteroscopies and lithotripsies he would perform.

Kidney stones are common and preventable, but not commonly prevented. Instead, our experience has been that most patients, despite their interest, have not received any serious recommendations about how to avoid kidney stone recurrence. Stone formers seek advice regarding their disorder, whether that is about the choices for urological intervention or strategies and regimens for prevention. Bringing these two components of kidney stone practice together into a single setting is the goal of a kidney stone clinic.

Like any other disorder, expertise among practitioners develops with exposure and repetition. A kidney stone clinic offers these assets to its personnel while offering patients the confidence that develops when expertise is demonstrated. Simply titling one’s office or practice a “kidney stone clinic” may lead to some assurance that the disorder is seen repeatedly there, but developing a real integration of diverse skills and mastery will be even more convincing.

This book arises from the partnership that Michael Grasso and I began in 1996 when we first formed a kidney stone clinic. Michael brought his vast experience in endourology and urological intervention for kidney stones to our enterprise. My contribution, as a nephrologist and physiologist, was

Urinary Stones: Medical and Surgical Management, First Edition. Edited by Michael Grasso and David S. Goldfarb.

© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

4 Types of Urinary Stones and Their Medical Management

to specialize in the metabolic evaluation and prevention of stone disease. Thousands of patients later, we have exchanged enormous amounts of information and experience, so that our patients can be certain that together we can approach any problem related to nephrolithiasis.

The urological management of kidney stones is extensively described elsewhere in this book. In this chapter I will focus on the other components of a kidney stone clinic. There are some data regarding the performance of a kidney stone clinic but inevitably what I write here includes much opinion.

Personnel

The kidney stone clinic starts with a urologist interested in kidney stones. That urologist may be an endourologist with further postresidency training in the appropriate techniques but in many settings, such a subspecialist may not be available. No matter. Patients with stones are referred to urologists first, and infrequently to nephrologists or internists. In a smaller community where an endourologist is not available, a general urologist presumably has ample experience in the management of most stones, perhaps referring to an endourologist in only more complex cases. Referral may be appropriate for larger stones, stones associated with infection, cystine stones, and anatomically abnormal or solitary kidneys.

There are urologists who can constitute a kidney stone clinic by themselves, with no other personnel required. Such urologists are widely knowledgeable about urine chemistry and how to modify it and reduce stone recurrence risk with diet and medications. They are happy to discuss the relevant variables with their patients and answer questions about appropriate preventive regimens. There are also urologists who understandably are less interested in performing such duties. After all, urology residency training often does not emphasize such skills. Compensation for urologists has a procedure-based emphasis which necessitates a shorter office visit that may not lead interested patients to feel that their concerns have been adequately addressed.

In that case, the addition of a nephrologist or internist makes an important contribution to the prevention component of a kidney stone clinic. This person, interpreting results of diagnostic tests and prescribing dietary modification or medications, does not have to be a nephrologist. An internist can learn the syllabus quickly, as internists have been trained to pay attention to these sorts of preventive modalities. In recent years, we have had a general internist doing kidney stone prevention at Bellevue Hospital, a large public facility in New York City. Two general internists oriented towards preventive care, in consultation with me, learned the field, recognizing it as similar to addressing cardiovascular risk factors. The frequency of a clinic's occurrence can be variable and obviously would depend on the volume of appropriate cases. Even a monthly clinic would offer an important service.

I note, however, that a nephrologist or internist will not easily constitute a kidney stone clinic without the involvement or endorsement of a urologist. In my experience, it takes a long while before any volume of referrals can come from anyone other than the kidney stone clinic's urologist. First, kidney stones are often not given the serious attention they deserve; family practitioners and general internists may not recognize that any preventive regimen is appropriate until significant recurrences have occurred. Second, as stated previously, most patients are seen only by urologists, who, if not specializing in stone treatment, may give prevention little heed and are unwilling to refer their patients to specialists outside their own practice. Third, most patients are unaware that anyone specializes in kidney stone prevention and find a kidney stone clinic only after the frustration of recurrence. And fourth, while most nephrologists also have little to no training in stone prevention during their fellowships, they dabble in the field and are also reluctant to give to their patients another nephrologist's name. I therefore think that a kidney stone clinic must be based on the keystone of a high-volume endourologist.

The kidney stone clinic's nephrologist or internist cannot perform procedures, but can become expert in diagnosing and managing renal colic and knowing when referral to the urologist is appropriate. He or she can also be useful and offer a second opinion to patients deciding about treatment of symptomatic or asymptomatic stones, and in choosing between urological interventions. In addition, patients with kidney stones have a host of co-morbidities including diabetes, hypertension, gout, coronary artery disease and chronic kidney disease, all of which can be favorably influenced by the involvement of an internist. Urologists may be less at ease treating such patients, dealing with underlying electrolyte disturbances or those resulting from prescribed medications and changes in kidney function that result from obstruction and its reversal. While the prevalence of chronic kidney disease in the average endourology practice has not been quantified, a nephrologist can offer a different, medical perspective to such patients, addressing mineral and bone disorders, osteoporosis, hyperparathyroidism, kidney transplants, resistant hypertension and, rarely, management of and preparation for end-stage kidney disease.

It is highly desirable to have a dietician as part of the program [1]. Patients seek dietary advice, which often is confusing. Dietary prescriptions are preferable particularly for younger people who often are more reluctant than older adults to take medications like citrate supplements or thiazides. Older people often have co-morbidities such as diabetes and cardiovascular disease and feel they have "nothing left to eat" when vegetables like spinach, which they considered "healthy," turn out to be high in oxalate.

Dieticians are most likely to be accessible in a university or Department of Veterans Affairs setting because many health insurers in the United States will not pay adequately for visits with dieticians. In such cases, patients may be reluctant to pay for such advice themselves. There are many sources of online dietary education for kidney stone prevention online. There is also a useful book, co-authored by a nephrologist, a urologist and a dietician [2].

6 Types of Urinary Stones and Their Medical Management

In many urology practices, nurse practitioners play important roles in preparing patients for procedures and their aftermath and could easily help in interpreting results of 24-h urine collections and offering preventive regimens.

The final human component of the kidney stone clinic is the patient. One should not minimize the interest that patients have in understanding and preventing the disorder [3]. Medical practitioners are more likely than patients to consider kidney stones a transient condition that “passes” readily and has no consequences. In fact, as patients know, kidney stones are not just painful, but also costly and humiliating and lead to significant disruptions of quality of life [4]. As they affect a younger population than, for instance, end-stage kidney disease, each year 1% of American workers will miss some work time for this reason [5].

When surveyed, most patients with kidney stones express a desire for information regarding what to eat and drink [6]. Adherence to prescribed regimens varies, of course; we are all only human after all. It is true that patients’ interest in adhering to recommendations regarding fluid intake, dietary modification, or pharmacotherapy may vary from little, early in their course, to more intense, with progressive recurrence. Adherence may also be greater the more recent the episode of renal colic. At whatever stage they are encountered, patients deserve and desire advice regarding their condition.

Evaluation

24-hour urine collections

Ideally, 24-h urine collections are done by a laboratory specializing in assessment of kidney stone risk. The epitome of such a laboratory today is Litholink Corp. (Chicago, IL), the lab doing the most such analyses in the world today [7]. The patient is mailed a kit, does the collection, records the urine volume and returns a 50 mL aliquot via Fedex to the lab. Detailed instructions are included and lab personnel are available by phone to answer questions. This process is extremely user friendly and convenient, permitting the collection to be done at home without the patient making a visit to the hospital or lab. All analytes are measured on the same collection, with one part of the aliquot acidified in order to fully dissolve calcium salts, and another part alkalinized in order to ensure full dissolution of uric acid. In other words, the patient does not have to do two separate collections into acidified and alkalinized containers. The lab then reports the data in a cumulative fashion so that all prior data are presented in a useful fashion to the clinician. In addition, supersaturation of calcium oxalate, calcium phosphate and uric acid is calculated and recorded.

The importance of supersaturation is that it gives a single number to integrate the results of the various urinary analytes. It can be shown to patients to demonstrate the net effects of changes in urine calcium, oxalate, citrate excretion, urine volume, pH, and uric acid excretion. Patients today usually know the results of testing for cholesterol and low

density lipoprotein, prostate-specific antigen, and glycosylated hemoglobin. Supersaturation can have the same intuitive value: higher values are bad, lower values are good. Supersaturation values correlate with stone composition and although it is likely to be true, they have not been shown to correlate with recurrence rates [8]. Reduction of supersaturation has also been used to judge stone clinic efficacy. In one study, a group of kidney stone clinics was nearly as effective in lowering supersaturation as an academic, university-based stone clinic [7].

Writers have addressed whether first-time stone formers should do 24-h collections or whether this test should be reserved for recurrent stone formers [9]. The argument that first-time stone formers may be mostly uncomplicated with low rates of recurrence or lack motivation to adhere to prescribed regimens has merit. Sometimes first-time stone formers are older people who think they are likely to die before having a stone recurrence. On the other hand, some first-time stone formers have large and consequential stones or have co-morbidities, making stone prevention that much more important. I recommend leaving the choice to the patient, with many preferring the detailed and specific recommendations that derive from 24-h urine analysis, and others being satisfied with generic, non-individualized advice. Interpretation of 24-h urine data is detailed elsewhere in this volume.

There has long been discussion about the optimal number of 24-h urines to collect, with more collections (2–3) yielding more diagnoses of urinary risk factors than one [10]. However, there are no data demonstrating that making more diagnoses leads to better therapeutic outcomes. My practice is to do two collections before prescribing treatment and then one at intervals following patient adherence to the prescription(s) and any changes in the regimen.

Radiology

Appropriate intervals for radiological follow-up have not been established. One question that needs to be answered by physician and patient is what to do with evidence of asymptomatic, new stones or stone growth. Such findings might constitute an indication to review the adequacy of improved 24-h urine results. Some patients might want urological intervention for asymptomatic stones for a variety of reasons, while others prefer to leave well enough alone, depending on their experiences [11]. My usual practice is to repeat ultrasound of the kidneys at yearly intervals for a few years, and if metabolic activity appears quiescent, desist. The interval might decrease to 4 or 6 months for patients with particularly active disease, such as cystinuria or those suffering more frequent recurrences.

Bone mineral density

Patients with calcium stones and hypercalciuria often have decreased bone mineral density (BMD) [12]. For many, this may reflect disordered calcium metabolism and for others it is attributable as well to misguided restricted dietary calcium. A proportion of women stone formers find their way to the

8 Types of Urinary Stones and Their Medical Management

stone clinic because they have been found by their internists or gynecologists to have reduced BMD and are concerned about recommendations to increase dietary calcium or take calcium supplements. It is therefore frequently useful to order dual emission X-ray absorptiometry (DEXA) to measure and follow BMD and to develop expertise in assessing and treating osteoporosis. FRAX, software developed by the World Health Organization, assesses the likelihood of experiencing a fracture in the next 10 years and can aid in making decisions about when to initiate bisphosphonate therapy [13].

Treatment

Elsewhere in this volume specific recommendations for management of the various stone compositions are offered. The unfortunately limited number of randomized controlled trials that provide some of the evidence for successful stone prevention have recently been reviewed [14]. Some more general comments can be made here.

Although I endorse the performance of 24-h urine collections, and use them regularly, in fact, prescribing either dietary or pharmacological therapies based on the results has not been proven superior to making generic recommendations. Most lithologists believe that patients are interested, informed, and motivated by knowing their specific risk factors. For example, it seems illogical and counterproductive to counsel people with low sodium excretion to limit their sodium intake. It is important to note that stone preventive regimens can be prescribed for those who do not perform 24-h urine collections, either because of preference or because of limitations of insurance coverage and cost.

For people who do or do not perform 24-h urines, the most important requirement is an increase in urine volume, a manipulation proven by randomized controlled trials to be effective [15]. Many practitioners say “drink more” without being quantitative and detailed; many people think that they do drink “a lot” without having any idea what that means. A lengthy discussion about fluid intake and a handout detailing the prescribed regimen is essential. The optimal goal is a urine volume of at least 2.5L, requiring a fluid intake of 3L per day to account for the insensible losses of sweat and respiration. It is useful to model what 3L looks like and have varying serving sizes available. In the US, 3L is 96 ounces, or 8×12 oz (a can of soda), or 12×8 oz (a small coffee cup). On many occasions I have taken out a prescription pad and written “WATER, 3L per day” on it to emphasize that this is a serious protocol, with efficacy demonstrated by a randomized controlled diet.

Fluid intake should be spaced throughout the day and include a serving before bed, with hopes to disrupt sleep minimally. There should be recognition of the need for planning to avoid the urge to void when bathroom facilities are unavailable. An occupational history should focus on whether working conditions preclude fluid intake and voiding; for instance, teachers and anesthesiologists may have limitations imposed by work schedules. Athletes, beach goers, inhabitants of more tropical

climates, and outdoor workers may need to significantly increase input to account for increased extrarenal fluid losses. Measuring fluid intake in a more exacting way may be useful to help people understand what a daily, lifelong habit necessitates. I limit cola intake or other sweetened sodas to one can per day; “clear” diet sodas (e.g. 7-Up) are not limited. Coffee and alcohol are consistently associated with fewer kidney stones in epidemiological observational studies and are not proscribed [16]. If daily fluid intake and 24-h urine volume do not increase, dietary prescriptions and medications may be more important. Some patients are willing, and understand that measuring their urine volume themselves is easy, inexpensive, and worthwhile.

Dietary modifications may be appropriate for most stone formers. Ideally, dietary modifications are prescribed based on the results of 24-h urine collections. However, generic advice based on stone composition may be appropriate as well. The only successful study of diet for prevention of calcium stones showed that in men with hypercalciuria, limited intake of animal protein, salt and oxalate with higher intake of calcium was superior to a restricted calcium- and oxalate-containing diet [17]. The characteristics of the Dietary Approaches to Stop Hypertension (DASH) diet have been associated with fewer stones in observational studies, but it has not been tested in trials [18]. Uric acid and cystine stone formers should reduce animal protein intake to reduce uric acid excretion and increase pH; increasing fruits and vegetables will also increase urine pH [19].

Patients with calcium stones have often been told to restrict calcium intake by their friends and relatives and sometimes older practitioners. Observational studies have consistently shown that more, not less, dairy intake or calcium intake is associated with fewer stones [20]. This approach is supported by the single, small, randomized trial previously cited. However, the efficacy of that study’s protocol has not been tested in women, may require a level of sodium restriction that is difficult to achieve in most first world settings, and assumes that adults are willing and able to increase dairy intake when in fact many are not or cannot. Using calcium supplements in lieu of increased dairy intake may not be a useful alternative as they have been associated with more stones, though the absolute increase in risk is quite small [21]. If felt to be necessary, the preferred calcium salt is calcium citrate as it is associated with less increase in urinary supersaturation than calcium carbonate [22]. It should be administered after meals to serve as a binder of oxalate in the intestinal lumen and possibly to reduce oxaluria.

Pharmacological prevention

Medications are frequently prescribed for stone prevention. Potassium citrate is almost universally prescribed for calcium, uric acid and cystine stone formers [23]. It can be useful for those who fail to increase urine volume, even if urine citrate excretion is normal. One could make a case

that prescription of potassium citrate would be useful for prevention of all calcium stones and could be used in “unselected” cases, in other words, when 24-h urine data are not available. Such an approach is supported by observational studies and randomized controlled trials [24,25]. Sodium citrate is not preferred given the promotion of calciuria by the sodium load. I have often prescribed potassium citrate to use before athletic events, airplane flights, trips to the operating room, and at bedtime. Again, this is not an evidence-based approach but seems commonsensical.

Uric acid and cystine stones *in situ* can be dissolved if urine pH is maintained at values of 6.5 or 7.0 respectively around the clock. This approach usually requires administration of potassium citrate 10–30 mEq 2–3 times per day. Uric acid stones can be prevented by nocturnal treatment alone, once a day, but this approach would probably not suffice for cystine stones [26]. I have patients test urine pH using inexpensive test strips (see www.microessentials.com, item #067) rather than more expensive multitest strips. Patients test and record urine pH at least once a day at varying times and adjust doses appropriately. Prescription of allopurinol for uric acid stones is appropriate only if patients have gout or fail to adequately increase urine pH as may occur in people with chronic diarrhea or malabsorption syndromes [27].

Thiazides are probably underutilized for prevention of calcium stones, possibly because of the perception that they have metabolic side-effects. They have consistently been shown to prevent stones in randomized trials [28]. In addition, they are first-line agents for lowering blood pressure, especially systolic blood pressure. By lowering urine calcium excretion, thiazides are associated with increases in bone mineral density and reduction in fractures associated with osteoporosis, which often is found in people with hypercalciuria [29]. Administration with potassium citrate prevents hypokalemia, hyperglycemia, and hypocitraturia [30]. For prevention of calcium stones, prescription of allopurinol is currently reserved for people who do not have hypercalciuria, though the efficacy of urate-lowering therapy has not been tested in the presence of increased urine calcium excretion [31].

Management of struvite stones requires meticulous endoscopic removal of all stone fragments and usually low-dose suppressive antibiotics for at least 6 months [32]. Recalcitrant and recurrent stones and those less amenable to surgical removal may benefit from acetohydroxamic acid, though its side-effect profile does not make its use easy [33].

Conclusion

The kidney stone clinic is a concept that patients with recurrent kidney stones find attractive and sensible. A multidisciplinary approach to kidney stones leads to expertise and familiarity with urological and preventive regimens. The result is attention to the details of fluid, dietary and medical therapies that otherwise may be utilized in an haphazard and arbitrary fashion.

Understandably, the kidney stone field often seems dominated by a surgical approach: remove offending stones and move on. For a disorder that can successfully be prevented, more easily perhaps than hypertension and diabetes, incredibly little attention is given to the training of internists, nephrologists and urologists to actually implement preventive regimens for this highly prevalent disorder. There is a clear need for participation of today's trainees in a multidisciplinary kidney stone prevention program and a clear need for practitioners to offer appropriate time and expertise to our patients.

References

1. Penniston KL, Nakada SY. Diet and alternative therapies in the management of stone disease. *Urol Clin North Am* 2013; 40: 31–46.
2. Rodman JS, Sosa RE, Seidman C, et al. *No More Kidney Stones*. Hoboken, NJ: John Wiley, 2007.
3. Tiselius HG. Patients' attitudes on how to deal with the risk of future stone recurrences. *Urol Res* 2006; 34: 255–60.
4. Penniston KL, Nakada SY. Development of an instrument to assess the health related quality of life of kidney stone formers. *J Urol* 2013; 189: 921–30.
5. Saigal CS, Joyce G, Timilsina AR. Direct and indirect costs of nephrolithiasis in an employed population: opportunity for disease management? *Kidney Int* 2005; 68: 1808–14.
6. Grampas SA, Moore M, Chandhoke PS. 10-year experience with extracorporeal shockwave lithotripsy in the state of Colorado. *J Endourol* 2000; 14: 711–14.
7. Lingeman J, Mardis H, Kahnoski R, et al. Medical reduction of stone risk in a network of treatment centers compared to a research clinic. *J Urol* 1998; 160: 1629–34.
8. Parks JH, Coward M, Coe FL. Correspondence between stone composition and urine supersaturation in nephrolithiasis. *Kidney Int* 1997; 51: 894–900.
9. Uribarri J, Oh MS, Carroll HJ. The first kidney stone. *Ann Intern Med* 1989; 111: 1006–9.
10. Parks JH, Goldfisher E, Asplin JR, et al. A single 24-hour urine collection is inadequate for the medical evaluation of nephrolithiasis. *J Urol* 2002; 167: 1607–12.
11. Sarkissian C, Noble M, Li J, et al. Patient decision making for asymptomatic renal calculi: balancing benefit and risk. *Urology* 2013; 81: 236–40.
12. Heilberg IP, Weisinger JR. Bone disease in idiopathic hypercalciuria. *Curr Opin Nephrol Hypertens* 2006; 15: 394–402.
13. Unnanuntana A, Gladnick BP, Donnelly E, et al. The assessment of fracture risk. *J Bone Joint Surg Am* 2010; 92: 743–53.
14. Fink HA, Wilt TJ, Eidman KE, et al. Medical management to prevent recurrent nephrolithiasis in adults: a systematic review for an American College of Physicians Clinical Guideline. *Ann Intern Med* 2013; 158: 535–43.
15. Borghi L, Meschi T, Amato F, et al. Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a 5-year randomized prospective study. *J Urol* 1996; 155: 839–43.
16. Goldfarb DS, Fischer ME, Keich Y, et al. A twin study of genetic and dietary influences on nephrolithiasis: a report from the Vietnam Era Twin (VET) Registry. *Kidney Int* 2005; 67: 1053–61.

12 Types of Urinary Stones and Their Medical Management

17. Borghi L, Schianchi T, Meschi T, et al. Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. *N Engl J Med* 2002; 346: 77–84.
18. Taylor EN, Fung TT, Curhan GC. DASH-style diet associates with reduced risk for kidney stones. *J Am Soc Nephrol* 2009; 20: 2253–9.
19. Meschi T, Maggiore U, Fiaccadori E, et al. The effect of fruits and vegetables on urinary stone risk factors. *Kidney Int* 2004; 66: 2402–10.
20. Curhan GC, Willett WC, Rimm EB, et al. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 1993; 328: 833–8.
21. Jackson RD, LaCroix AZ, Gass M, et al. Calcium plus vitamin D supplementation and the risk of fractures. *N Engl J Med* 2006; 354: 669–83.
22. Levine BS, Rodman JS, Wienerman S, et al. Effect of calcium citrate supplementation on urinary calcium oxalate saturation in female stone formers: implications for prevention of osteoporosis. *Am J Clin Nutr* 1994; 60: 592–6.
23. Robinson MR, Leitao VA, Halebian GE, et al. Impact of long-term potassium citrate therapy on urinary profiles and recurrent stone formation. *J Urol* 2009; 181: 1145–50.
24. Preminger GM, Harvey JA, Pak CY. Comparative efficacy of “specific” potassium citrate therapy versus conservative management in nephrolithiasis of mild to moderate severity. *J Urol* 1985; 134: 658–61.
25. Ettinger B, Pak CY, Citron JT, et al. Potassium-magnesium citrate is an effective prophylaxis against recurrent calcium oxalate nephrolithiasis. *J Urol* 1997; 158: 2069–73.
26. Rodman JS. Intermittent versus continuous alkaline therapy for uric acid stones and ureteral stones of uncertain composition. *Urology* 2002; 60: 378–82.
27. Maalouf NM, Cameron MA, Moe OW, et al. Novel insights into the pathogenesis of uric acid nephrolithiasis. *Curr Opin Nephrol Hypertens* 2004; 13: 181–9.
28. Pearle MS, Roehrborn CG, Pak CY. Meta-analysis of randomized trials for medical prevention of calcium oxalate nephrolithiasis. *J Endourol* 1999; 13: 679–85.
29. Adams JS, Song CF, Kantorovich V. Rapid recovery of bone mass in hypercalciuric, osteoporotic men treated with hydrochlorothiazide. *Ann Intern Med* 1999; 130: 658–60.
30. Huen SC, Goldfarb DS. Adverse metabolic side effects of thiazides: implications for patients with calcium nephrolithiasis. *J Urol* 2007; 177: 1238–43.
31. Ettinger B, Tang A, Citron JT, et al. Randomized trial of allopurinol in the prevention of calcium oxalate calculi. *N Engl J Med* 1986; 315: 1386–9.
32. Preminger GM, Assimos DG, Lingeman JE, et al. Chapter 1: AUA guideline on management of staghorn calculi: diagnosis and treatment recommendations. *J Urol* 2005; 173: 1991–2000.
33. Griffith DP, Gleeson MJ, Lee H, et al. Randomized, double-blind trial of Lithostat (acetohydroxamic acid) in the palliative treatment of infection-induced urinary calculi. *Eur Urol* 1991; 20: 243–7.