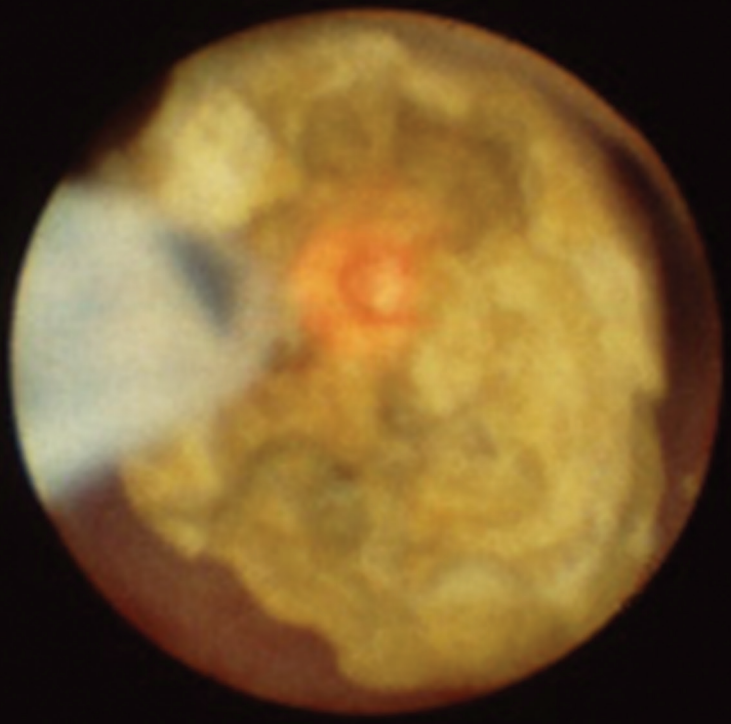

Urinary Stones

MEDICAL AND SURGICAL MANAGEMENT

Edited by
Michael Grasso
David S. Goldfarb

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Medical and Surgical Management

EDITED BY

Michael Grasso, MD

Professor and Vice Chairman
Department of Urology
New York Medical College
Valhalla, NY, USA

David S. Goldfarb, MD, FASN

Clinical Chief, Nephrology Division
NYU Langone Medical Center;
Professor of Medicine and Physiology
New York University School of Medicine
New York, NY, USA

WILEY Blackwell

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Part 2: Surgical Management of Urinary Stones

List of Contributors

Sachin Abrol, MS
Resident in Urology
Muljibhai Patel Urological Hospital
Nadiad, Gujarat, India

Ahmed Alasker, MD, FRCS(C)
Endourology, Robotic and Laparoscopy Fellow
Albert Einstein College of Medicine
Montefiore Medical Center
Bronx, NY, USA

Bobby Alexander, MD
Fellow
Division of Endourology
Lenox Hill Hospital
New York, NY, USA

John R. Asplin, MD, FASN
Medical Director, Litholink Corporation;
Clinical Associate
Department of Medicine
University of Chicago
Chicago, IL, USA

Demetrius H. Bagley, MD, FACS
The Nathan Lewis Hatfield Professor of Urology
Professor of Radiology
Department of Urology
Thomas Jefferson University
Philadelphia, PA, USA

Michael S. Borofsky, MD
Chief Resident in Urology
New York University Langone Medical Center
New York, NY, USA

Kai-wen Chuan, MD
Chief Resident
The Arthur Smith Institute for Urology
North Shore-Long Island Jewish Health System
New Hyde Park, NY, USA

Michael J. Conlin, MD
Associate Professor
Portland VA Medical Center;
Department of Urology
Oregon Health & Science University/Portland VA Medical Center
Portland, OR, USA

Angela M. Cottrell, FRCS (Urol), MBBS, BSc, Dip Clin Ed
Specialist Registrar, Urology
Derriford Hospital
Plymouth Hospitals NHS Trust
Plymouth, UK

Michel Daudon, PhD
Chief of the Stone Laboratory
Department of Clinical Physiology
APHP, Tenon Hospital
Paris, France

Michael Degen, MD
Fellow
Division of Endourology and Minimally Invasive Urology
Westchester Medical Center;
Department of Urology
New York Medical College
Valhalla, NY, USA

Mahesh R. Desai, MS, FRCS
Medical Director
Muljibhai Patel Urological Hospital
Nadiad, Gujarat, India

Sameer M. Deshmukh, MD
Resident in Urology
Department of Urologic Sciences
Stone Centre at Vancouver General Hospital
Vancouver, BC, Canada

Andrew J. Dickinson, MD, FRCSUrol, FRCSEd
Consultant Urologist
Derriford Hospital
Plymouth Hospitals NHS Trust
Plymouth, UK

Christopher M. Dixon, MD
Associate
Division of Endourology
Lenox Hill Hospital
New York, NY, USA

Brian D. Duty, MD
Assistant Professor
Department of Urology
Oregon Health & Science University/Portland
VA Medical Center
Portland, OR, USA

Vidar O. Edvardsson, MD
Director of Pediatric Nephrology
Children's Medical Center
Landspitali – The National University Hospital of Iceland;
Faculty of Medicine, School of Health Sciences
University of Iceland
Reykjavik, Iceland

Brian H. Eisner, MD
Co-Director of Kidney Stone Program
Department of Urology
Massachusetts General Hospital
Harvard Medical School
Boston, MA, USA

Majid Eshghi, MD, FACS
Division of Endourology and Minimally Invasive Urology
Westchester Medical Center;
Department of Urology
New York Medical College
Valhalla, NY, USA

Andrew I. Fishman, MD
Assistant Professor of Urology
Department of Urology
New York Medical College
Valhalla, NY, USA

Israel Franco, MD
Director of Pediatric Urology
Maria Fareri Children's Hospital
Professor of Urology
New York Medical College
Valhalla, NY, USA

Sean Fullerton, MD
Assistant Professor
Department of Urology
New York Medical College
Valhalla, NY, USA

Arvind P. Ganpule, MS, DNB
Vice-Chairman
Department of Urology
Muljibhai Patel Urological Hospital
Nadiad, Gujarat, India

Reza Ghavamian, MD
Professor of Clinical Urology
Chairman of Urology
Albert Einstein College of Medicine
Montefiore Medical Center
Bronx, NY, USA

Jordan Gitlin, MD
Attending Pediatric Urologist
Cohen Children's Medical
Center of New York;
The Arthur Smith Institute for Urology
North Shore-Long Island Jewish Health System
New Hyde Park, NY, USA

David S. Goldfarb, MD, FASN
Clinical Chief, Nephrology Division
NYU Langone Medical Center;
Professor of Medicine and Physiology
New York University School of Medicine
New York, NY, USA

Michael Grasso, MD
Professor and Vice Chairman
Department of Urology
New York Medical College
Valhalla, NY, USA

Kelly A. Healy, MD
Assistant Professor
Department of Urology
Thomas Jefferson University
Philadelphia, PA, USA

Nicole Hindman, MD
Assistant Professor of Radiology
Department of Radiology
New York University Lagone Medical Center
New York, NY, USA

David Hoenig, MD
Associate Professor of Clinical Urology
Albert Einstein College of Medicine
Montefiore Medical Center
Bronx, NY, USA

Paul Jungers, MD
Emeritus Professor of Nephrology
Paris V University;
APHP, Department of Nephrology
Necker Hospital
Paris, France

Francis X. Keeley Jr, MD, FRCS(Urol)
Consultant Urologist
Bristol Urological Institute
Bristol, UK

Nir Kleinmann, MD
Attending Urologist
Department of Urology
Sheba Medical Center
Tel Hashomer, Israel

Abhishek Laddha, MS
Resident in Urology
Muljibhai Patel Urological Hospital
Nadiad, Gujarat, India

Dirk Lange, BSc, PhD
Assistant Professor
Department of Urologic Sciences
University of British Columbia
Vancouver, BC, Canada

Julien Letendre, MD, FRCSC
Fellow of Endourology
Department of Urology
Tenon Hospital, Assistance Publique – Hôpitaux de Paris
Pierre et Marie Curie University
Paris, France

John C. Lieske, MD
Professor of Medicine
Division of Nephrology and Hypertension
Mayo Clinic
Rochester, MN, USA

James E. Lingeman, MD
Professor
Department of Urology
Indiana University School of Medicine
Indianapolis, IN, USA

Naim M. Maalouf, MD
Assistant Professor of Medicine
Department of Internal Medicine and
Charles and Jane Pak Center for Mineral Metabolism and Clinical Research
University of Texas Southwestern Medical Center
Dallas, TX, USA

Sunil Mathur, MD, FRCS (Urol)
Consultant Urologist
Great Western Hospital
Swindon, UK

Lesli Nicolay, MD
Assistant Professor
Division of Pediatric Urology
Loma Linda University Medical Center
Loma Linda, CA, USA

Runolfur Palsson, MD
Chief, Division of Nephrology
Landspitali – The National University Hospital of Iceland;
Associate Professor of Medicine
Faculty of Medicine, School of Health Sciences
University of Iceland
Reykjavik, Iceland

Jessica E. Paonessa, MD
Endourology Fellow
Department of Urology
Indiana University School of Medicine
Indianapolis, IN, USA

Sherry S. Ross, MD
Director of Pediatric Urology Stone Clinic
Department of Surgery
Division of Urology
Section of Pediatric Urology
Duke University Medical Center
Durham, NC, USA

Ojas Shah, MD
Associate Professor, Director of Endourology and Stone Disease
New York University Langone Medical Center
New York, NY, USA

Shonni J. Silverberg, MD
Professor of Medicine
Columbia University
College of Physicians and Surgeons
New York, NY, USA

Olivier Traxer, MD, PhD
Professor of Urology
Department of Urology
Tenon Hospital, Assistance Publique – Hôpitaux de Paris
Pierre et Marie Curie University
Paris, France

Robert J. Unwin, PhD, FRCP, FSB, CBiol
Professor of Nephrology and Physiology
Head of Centre and Research Department of Internal Medicine UCL
UCL Centre for Nephrology
University College London Medical School
London, UK

Marcella Donovan Walker, MD, MS
Assistant Professor of Medicine
Columbia University
College of Physicians and Surgeons
New York, NY, USA

Stephen B. Walsh, PhD, MRCP
Clinical Senior Lecturer in Experimental Medicine/Honorary Consultant Nephrologist
UCL Centre for Nephrology
University College London Medical School
London, UK

Oliver M. Wrong, DM, FRCP
Former Emeritus Professor of Medicine
UCL Centre for Nephrology
University College London Medical School
London, UK

Preface

The natural history of urinary calculi reflects a spectrum of clinical presentations, some with a benign course but many others with the potential for severe and often catastrophic outcomes. Urinary calculi frequently are the sequelae of major underlying metabolic disorders, which if left untreated are regularly associated with recurrent stone events with the ultimate potential for renal parenchymal loss. It is the co-ordination of both surgical intervention to remove obstructing concretions and improve drainage, and the simultaneous application of novel medical therapies employed to alter the underlying hypermetabolic disorder that ultimately changes the natural history of this morbid ailment.

As Editors of this book we represent varied perspectives on stone management, with 18 years of daily collaboration treating the most complex hypermetabolic stone formers. We created the first multimodality stone center in New York and continue to regularly care for patients together. This collaborative spirit of endourology and nephrology has led to a broad spectrum of innovative therapies, many of which will be presented in this text. Our chapter authors reflect international thought leaders in urinary stone management, each offering unique insight into patient evaluation and specific therapies.

We, the editors and authors, are fundamentally committed to improving patient care by developing and employing new treatments, and by encouraging and nurturing the next generation of providers through fellowship training and scholarly efforts. We have always believed and taught that nephrologists need to more fully understand the surgical management of stone disease in order to counsel their patients, and urologists who understand metabolic stone disorders will offer their patients a higher and more attractive level of service.

This text is designed to be a resource for the practitioner when confronted with a challenging clinical presentation. There is an orderly division of chapters: patient assessment, imaging, surgical interventions, and medical therapies. The underlying theme, however, is collaboration of implementation – mixing and matching therapies as required by the presented clinical variables. For example, a patient who presents with urinary tract obstruction and with urosepsis during systemic chemotherapy for acute leukemia requires input from many areas to craft a comprehensive treatment plan. The emergency renal drainage algorithm in the surgical section is promptly applied. Varied interventions as necessary are

employed next to clear the stone burden, with subsequent additional medical therapies to treat the underlying hyperuricosuria and minimize future episodes.

It is our intention to offer a user-friendly resource to the clinician. Various treatments are presented with regard to indications, technical nuances, complications, continuity of care, and preventive measures. It is our hope that through efforts like this text, comprehensive collaborative treatment centers will grow, employing many of the tenets described herein.

Michael Grasso
David S. Goldfarb

PART 1

Types of Urinary Stones and Their Medical Management

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

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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].

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-mordibities, 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

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 2.5 L, requiring a fluid intake of 3 L per day to account for the insensible losses of sweat and respiration. It is useful to model what 3 L looks like and have varying serving sizes available. In the US, 3 L 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, 3 L 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.microessentialslab.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.

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CHAPTER 2

Metabolic Evaluation: Interpretation of 24-Hour Urine Chemistries

John R. Asplin
Litholink Corporation *and* University of Chicago, Chicago, Il, USA

Introduction

The goals of metabolic evaluation are to provide a guide for treatment to reduce the risk of stone formation and to identify systemic disease presenting as kidney stone disease. As recommended by the NIH Consensus Conference, a limited work-up is appropriate for a patient with their first stone [1]. The limited work-up includes serum for electrolytes, calcium, and creatinine. Urine culture and/or urinalysis are needed to rule out urinary tract infection. If the stone is available, its composition should be determined. Radiological evaluation should be performed in all subjects presenting with their initial stone event, as a patient can only be considered a single stone former if no other stones are identified by imaging. Many patients have a non-contrast computed tomography (CT) scan when they present with their first attack of renal colic. If the symptomatic stone event resolved without radiological evaluation, a KUB X-ray or an ultrasound can be used to estimate stone burden. Ultrasound is often the preferred technique for children and pregnant women.

At the time of the initial stone event, if multiple stones are present on X-ray the patient should be considered a recurrent stone former and a full metabolic evaluation undertaken. The evaluation includes serum chemistries and 24-hurine collection(s) to identify the patient's specific risk factors for stone disease. In the case of children with stone disease, an extended evaluation should always be performed at initial presentation. Children are more likely to have inherited diseases such as cystinuria and primary hyperoxaluria as the cause of their stones [2]. The details of the laboratory evaluation of the stone patient are the focus of this chapter.

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

Serum chemistries

Measurement of serum chemistries is an important part of the metabolic evaluation of the stone former. Serum creatinine provides an estimate of kidney function. Electrolytes are used to screen for renal tubular acidosis, looking for the presence of acidosis or hypokalemia. Serum calcium should be used to screen for hyperparathyroidism and other mineral disorders. Even minimal elevations of serum calcium should be evaluated with repeat testing accompanied by parathyroid hormone measurement. Serum measurements need to be repeated during active drug therapy for stone prevention to monitor for hypokalemia and hyponatremia from thiazides and hyperkalemia from potassium alkali.

Stone analysis

Stone analysis should be performed on whatever stones are passed or removed surgically at initial presentation. If a patient has not had stone analysis but has saved stones from past episodes of renal colic, those stones can be sent for analysis. Optimally, stone analysis should be performed by infra-red (IR) analysis or X-ray diffraction. Optical microscopy is often employed as an adjunct to IR or X-ray [3].

Knowledge of kidney stone composition guides prophylactic therapy in concert with urine chemistries. Less common stones such as ammonium acid urate and xanthine are usually diagnosed by stone analysis. The stone analysis is the only way to diagnose stones composed of medications or their metabolites [4]. Once prophylactic therapy has been initiated, stones that form subsequently should be analyzed. Patients can form different types of stones and in fact, may transform from one stone type to another during medical therapy [5]. If stone analysis does not match the stone type that would be expected from urine chemistries, consider the possibility that the stone may have formed years earlier and became symptomatic only recently. In such a situation a search for changes in diet, environment or other transient medical problems might reveal the cause of stones.

24-hour urine chemistries

Standard medical practice calls for 24-h urine collection(s) to identify the risk factors leading to stones. Table 2.1 provides a list of urine tests to be performed on the 24-h sample. The tests in the left-hand column are the minimum set of tests for a stone evaluation. Inclusion of the tests in the right-hand column allows better understanding of diet and physiology related to stone formation. In addition, as to what to measure, the clinician needs to decide the conditions for the collection. Most