

Guidelines for the Medical Management of Urolithiasis

a report by

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Cost-effectiveness of Metabolic Evaluation

There is much controversy regarding the selection of patients for diagnostic evaluation of nephrolithiasis. Although studies suggest that 'single-stone formers' have a similar incidence and severity of metabolic disorders as those patients with recurrent stone disease, some patients will not develop additional stones despite the absence of further treatment. In addition, many single-stone formers that are treated conservatively with avoidance of dietary excess and increased fluid intake, have demonstrated a low incidence of recurrent stone disease.

Critics of medical therapy charge that it is not always cost-effective. Studies have suggested that medical therapy may only be cost-effective in certain patient populations, specifically those patients with recurrent nephrolithiasis. An international cost survey from 10 countries compared the cost of medical prophylaxis with the management of acute stone episodes. The study determined that the stone frequency at which costs of these management options became equivalent range from 0.3 to four stone episodes per year. The results therefore suggested that medical management of a first stone episode was not cost-effective and that metabolic evaluation and medical management should only be instituted in those patients with recurrent nephrolithiasis.

Nevertheless, the accepted stone recurrence rate for all patients is approximately 50% over 10 years. This is not a trivial recurrence rate from a patient's perspective – considering the morbidity, cost of treatment to the individual, and cost of lost work time, notwithstanding the severe pain associated with renal colic. Medical treatment has been demonstrated to prevent stone recurrence. A retrospective review of 301 patients determined that stone recurrence rates were 34% with patients treated with drugs versus 61% with patients on conservative therapy. Additionally, the advancement in stone disease metabolic evaluation provides over 97% chance of a specific diagnosis. The relatively low cost of a comprehensive medical evaluation might justify its wider use, especially if it averts the expense associated with additional surgery or the treatment of

complications associated with stone disease. In the absence of definitive literature guidance regarding cost-effectiveness, it is reasonable and appealing to pursue a specific diagnosis and provide medical therapy for those patients who are so motivated.

One approach to evaluating patients is to gauge the extent of the evaluation according to the estimation of potential or risk for new stone formation. First-time stone-formers without increased risk for recurrence can undergo an abbreviated diagnostic evaluation, whereas patients with recurrent stone disease or those first-time stone formers who are at risk for recurrence should generally undergo a more extensive diagnostic evaluation. Patients at risk include children, middle-aged white males with a family history of stones, and patients with intestinal disease (chronic diarrheal or malabsorptive states), gout, nephrocalcinosis, osteoporosis, pathologic skeletal fractures, or urinary tract infection (UTI). Any patients with stones composed of cystine, struvite, or uric acid should also undergo a complete metabolic work-up. As stone disease is less common in non-Caucasian patients, a search for underlying derangements in these individuals is recommended.

The primary objective of a diagnostic evaluation of nephrolithiasis should be to efficiently and economically identify the particular physiological defect present in a given patient in order to enable the selection of specific and rational therapy. It is generally agreed that selective medical therapy is indicated to prevent further stone formation and to correct underlying physiological disturbances that may result in non-renal complications.

Evaluating the Patient with a First-time Stone – Abbreviated Diagnostic Evaluation

The decision to thoroughly investigate a first-time stone former should be shared by the physician and the patient. While some first-time stone formers will readily accept following conservative therapy, others may elect to undergo a more thorough evaluation. In single-stone formers without increased risk, the following abbreviated protocol may be applied (see *Table 1*). A



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Table 1: Abbreviated Diagnostic Evaluation for Single-stone Formers Without Risk for Recurrence

History	Underlying predisposing conditions Medications (calcium, vitamin C, vitamin D, acetazolamide, steroids) Dietary excesses, inadequate fluid intake or excessive fluid loss	
Multichannel blood screen	Low potassium and bicarbonate, high chloride – distal renal tubular acidosis High uric acid – gouty diathesis High calcium – primary hyperparathyroidism Low phosphorus: renal phosphate leak	
Urine	Urinalysis pH >7.5 – infection lithiasis pH <5.5 – uric acid lithiasis Sediment for crystalluria Urine culture Urea-splitting organisms – suggestive of infection lithiasis Qualitative cystine	
X-ray	Radiopaque stones	calcium oxalate, calcium phosphate, cystine, magnesium ammonium phosphate (struvite)
	Radiolucent stones	triamterene, uric acid, xanthine, 2-hydroxyadenine
	Intravenous pyelogram	radiolucent stones, anatomic abnormalities
Stone analysis		

thorough history should be obtained on such patients, including dietary habits, fluid consumption, and medications. A multi-channel blood screen can be helpful in identifying underlying systemic problems, such as distal renal tubular acidosis (hypokalemic, hyperchloremic metabolic acidosis), gouty diathesis (hyperuricemia), primary hyperparathyroidism (high serum calcium, low serum phosphorus), and renal phosphate leak (hypophosphatemia).

Voided urinary specimens should be obtained for comprehensive urinalysis and culture. The urinalysis should include pH determination (by electrode) since a pH greater than 7.5 is suggestive of infection lithiasis, whereas a pH less than 5.5 may be indicative of gouty diathesis. The urine sediment must be examined since particular crystal types may provide a clue to the composition of certain stones. Urine cultures that are positive for urea-splitting organisms are consistent with struvite stones. In addition, urine should be examined for the presence of cystinuria using a qualitative examination (nitroprusside test). Abdominal plain films should also be obtained to document any residual urinary tract calculi.

Finally, all available stones should be analyzed to determine their crystalline composition. The presence of cystine crystals is diagnostic of cystinuria, whereas uric acid crystals suggest the presence of gouty diathesis. The finding of carbonate apatite or magnesium ammonium phosphate suggests infection lithiasis. A predominance of hydroxyapatite (calcium phosphate) suggests the presence of distal renal tubular acidosis or primary hyperparathyroidism. Stones composed purely or predominantly of calcium oxalate are less useful diagnostically, since they may occur in several conditions.

Evaluating the Patient with Recurrent Stones – Extensive Diagnostic Evaluation

A more extensive evaluation, directed at the identification of underlying physiologic derangements, should be performed in patients with recurrent nephrolithiasis, as well as in stone formers at increased risk for further stone formation or with evidence of multisystem involvement (see *Table 2*). Three 24-hour urine samples should be collected, two of which are obtained with the patient on a random diet that is reflective of their usual dietary intake. The third 24-hour sample should be collected after one week on a diet restricted in calcium, oxalate, and sodium. The ‘fasting calcium’ test, is performed on the second visit. Fasting urinary calcium is expressed as milligrams per deciliter of glomerular filtrate as it is reflective of renal function. Normal fasting urinary calcium is <0.11mg/dl glomerular filtrate. Blood samples are collected at both visits.

Recent progress in pathophysiological elucidation, paralleled by advances in analytical methodology, have allowed identification of physiological or environmental causes of renal calculi in more than 97% of patients. Various diagnostic categories and their relative frequency are shown in *Table 3*.

Medical Management

Conservative Management

Certain conservative recommendations should be made for all patients regardless of the underlying etiology of their stone disease. Patients should be instructed to

Table 2: Outline of Extensive Diagnostic Evaluation

	Blood		Urine					Total			Qualitative	
	Complete Blood Count	Chemistry	PTH	Calcium	Uric Acid	Creatinine	Sodium	pH	Volume	Oxalate	Citrate	Cystine
VISIT 1*	X	X		X	X	X	X	X	X	X	X	X
VISIT 2+		X	X	X	X	X	X	X	X	X	X	
FAST				X		X			X			
LOAD				X		X			X			

*History and physical examination, diet history, radiologic evaluation, two 24-hour urine specimens on random diet and dietary instruction for restricted diet.

+24-hour urine specimen on restricted diet (400mg calcium and 100mEq sodium/day), fast and calcium load test.

PTH=parathyroid hormone.

increase their fluid intake to at least three liters/day, in order to maintain a urine output of at least 2,500ml/day. In addition, all patients should be instructed on limiting their dietary oxalate and sodium intake, which should help decrease the urinary excretion of oxalate and calcium. In patients with suspected absorptive hypercalciuria without evidence of bone loss, a dietary limitation of dairy products may also be enforced. A restriction of animal proteins in those with ‘purine gluttony’ and hyperuricosuria should be encouraged.

With these conservative measures, a significant number of patients may be able to reduce their risk factors for urinary stone formation. In some patients, these measures alone might be necessary to keep their stone disease under control. It is believed that six-month follow-ups are essential not only to monitor the efficiency of treatment, but also to encourage patient compliance. If a metabolic or environmental defect persists while the patient is on conservative therapy, selective medical therapy should be considered.

Selective Medical Therapy

Improved elucidation of the etiology and pathophysiology of nephrolithiasis has made the adoption of selective treatment programs quite feasible. Treatment programs should:

- reverse the underlying physicochemical and physiological derangements;
- inhibit further stone formation;
- overcome non-renal complications of the disease process; and
- be without serious side effects.

The rationale for the selection of certain treatment programs is the assumption that the particular aberrations identified with given disorders are etiologically important in the formation of stones, and that the correction of these disturbances would prevent stone formation. Moreover, such a selected treatment program should be more effective and safe than ‘random’ treatment. For many pharmacological agents recommended for the management of nephrolithiasis,

Table 3: Classification of Nephrolithiasis

	Percent Sole Occurrence	Percent Combined Occurrence
Absorptive hypercalciuria Type I	20	40
Type II		
Renal hypercalciuria	5	8
Resorptive hypercalciuria (primary hyperparathyroidism)	3	8
Unclassified hypercalciuria	15	25
Hyperoxaluric calcium nephrolithiasis	2	15
Dietary hyperoxaluria		
Enteric hyperoxaluria		
Primary hyperoxaluria		
Hyperuricosuric calcium nephrolithiasis	10	40
Hypocitraturic calcium nephrolithiasis	10	50
Distal renal tubular acidosis		
Chronic diarrheal syndrome		
Thiazide-induced hypocitraturia		
Idiopathic hypocitraturia		
Hypomagnesuric calcium nephrolithiasis	5	10
Gouty diathesis	15	30
Cystinuria	<1	
Struvite (infection) lithiasis	1	5
Low urine volume	10	50
No pathological disturbance and miscellaneous	<3	
	100	

sufficient information is now available to characterize their physicochemical and physiological actions. Unfortunately, it is beyond the scope of this editorial to present a complete discussion of selective medical management. A listing of physicochemical and physiological effects of pharmacological therapy is presented in Table 4.

Summary

Selective medical therapy of nephrolithiasis is highly effective in preventing new stone formation. A remission rate of greater than 80% and overall reduction in individual stone formation rate of greater than 90% can be obtained in patients with

Table 4: Physicochemical and Physiological Effects of Pharmacologic Therapy

	Sodium Cellulose Phosphate	Thiazide	Allopurinol	Potassium Citrate
Urinary calcium decrease	Marked decrease	Moderate decrease	No change	Mild No change
Urinary phosphorus	Mild increase	Mild increase/ no change	No change	No change
Urinary uric acid	No change	Mild increase/ no change	Marked decrease	No change
Urinary oxalate	Mild increase	Mild increase/ mild decrease	No change	No change
Urinary citrate increase	No change	Mild decrease	No change	Marked
Calcium oxalate saturation decrease	Mild decrease/ no change	Mild decrease	No change	Moderate
Brushite saturation	Moderate decrease	Mild decrease	No change	No change

nephrolithiasis. In patients with mild–moderate severity of stone disease, virtually total control of stone disease can be achieved with a remission rate of greater than 95%.

Selective pharmacologic therapy of nephrolithiasis also encompasses the advantages of overcoming non-renal complications as well as averting certain side

effects that may be caused by non-selective medical therapy. Despite these advantages, it is clear that selective medical therapy cannot provide total control of stone disease. A satisfactory response requires continued, dedicated compliance by patients to the recommended program, and a commitment of the physician to provide long-term follow-up and care. ■

Further Reading

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