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Review Article

Nephrolithiasis - A Short Review

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Nephrolithiasis, or kidney stones, is the most common condition affecting the urinary system, affecting about 12% of the world population, with a yearly incidence of 600,000 in America. Kidney stones correlate with an increased risk of chronic kidney diseases, end-stage renal failure, cardiovascular diseases, diabetes, and hypertension. [1-2].

Epidemiology

A study based on the National Health and Nutrition Examination Survey (NHANES) estimated that 19 percent of males and 9 percent of females would be diagnosed with a kidney stone by the age of 70 years. Incidence rates are also similar in males and females below age 40 years, but above age 40 years, the rates are higher in males than in females. Stone disease is most common in White patients who are not Hispanic, followed by White patients who are Hispanic, and is least common in Black patients and Asian patients. The tendency in the United States to develop stones also depends on geographical location, with an increasing prevalence from north to south and, to a lesser degree, from west to east. The increase in nephrolithiasis rates from north to south may be due to increased environmental temperatures and greater sunlight exposure leading to an increase in insensible losses through sweating and more concentrated urine [3].

Types and Composition of Stone

The stone type varies with worldwide geography and genetic predisposition. In the Mediterranean and Middle East, 75% of stones are composed of uric acid. In the United States, most stones are calcium oxalate or calcium phosphate (>70%), with less than 10% being pure uric acid stones.

Magnesium ammonium phosphate (struvite) stones account for 10% to 25% of stones formed (with a higher incidence in the United Kingdom), and cystine stones constitute 2% of all stones formed. [4-5]

Pathophysiology (Fig.1 & 2)

The pathogenetic mechanisms of kidney stone formation is complex and involve both metabolic and environmental risk factors. Stones occur in urine that is supersaturated with respect to the ionic constituents of the specific type of stone. When the solution becomes supersaturated with respect to a solid phase, ions can join together to form the more stable, solid phase, a process termed nucleation. Homogeneous nucleation refers to the joining of similar ions into crystals. The more common and thermodynamically favored heterogeneous nucleation results when crystals grow adjacent to crystals or other substances in the urine, such as sloughed epithelial cells. [6]

Clinical Manifestations

The two most characteristic symptoms of nephrolithiasis are pain and hematuria. Other presentations include urinary tract infections (UTIs) and acute kidney injury caused by obstructive uropathy if stones cause bilateral renal tract obstruction or unilateral obstruction in a single functioning kidney, sometimes kidney stone remains asymptomatic, although stone size can be large.[6]

Figure: 1

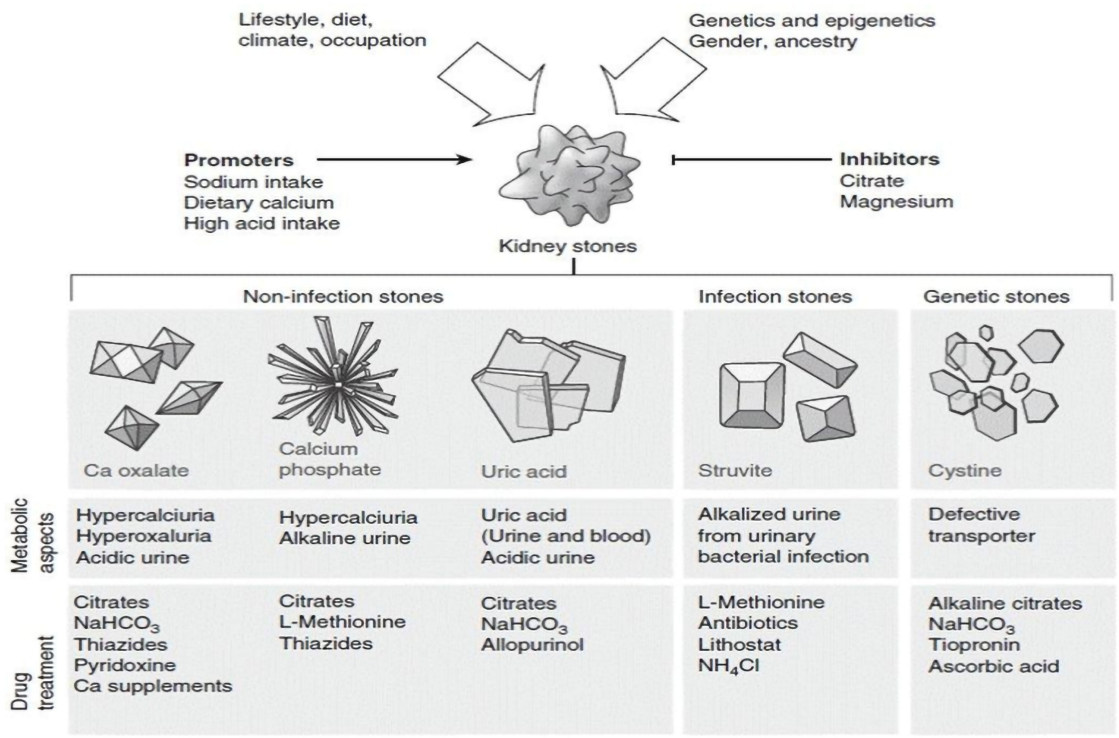
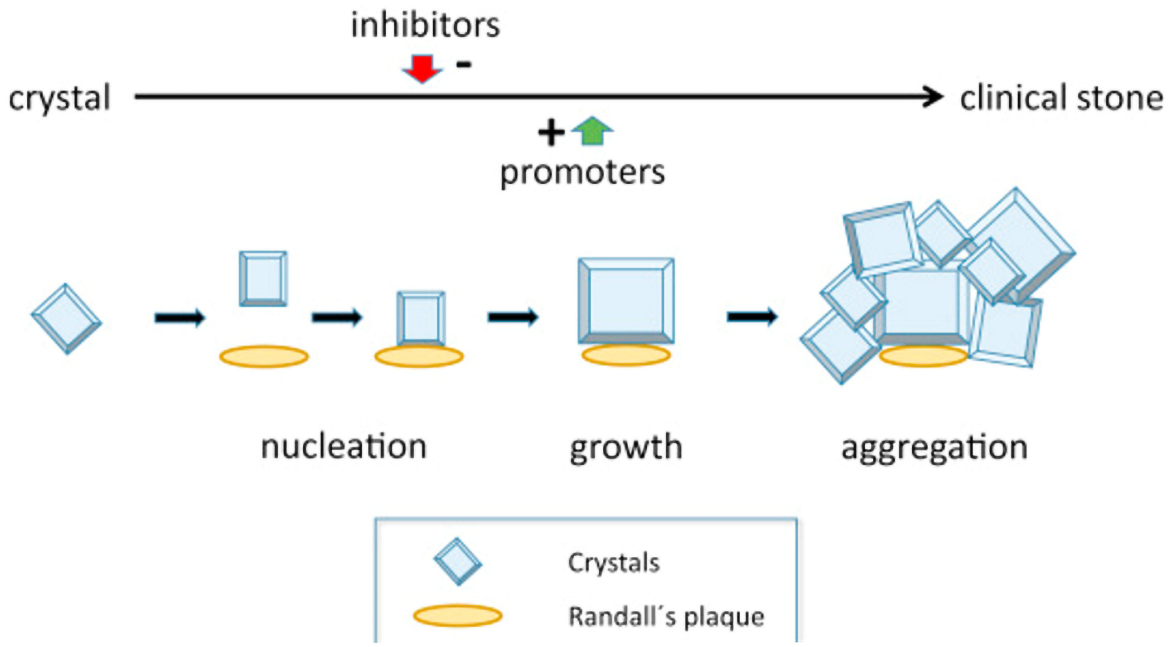


Figure: 2



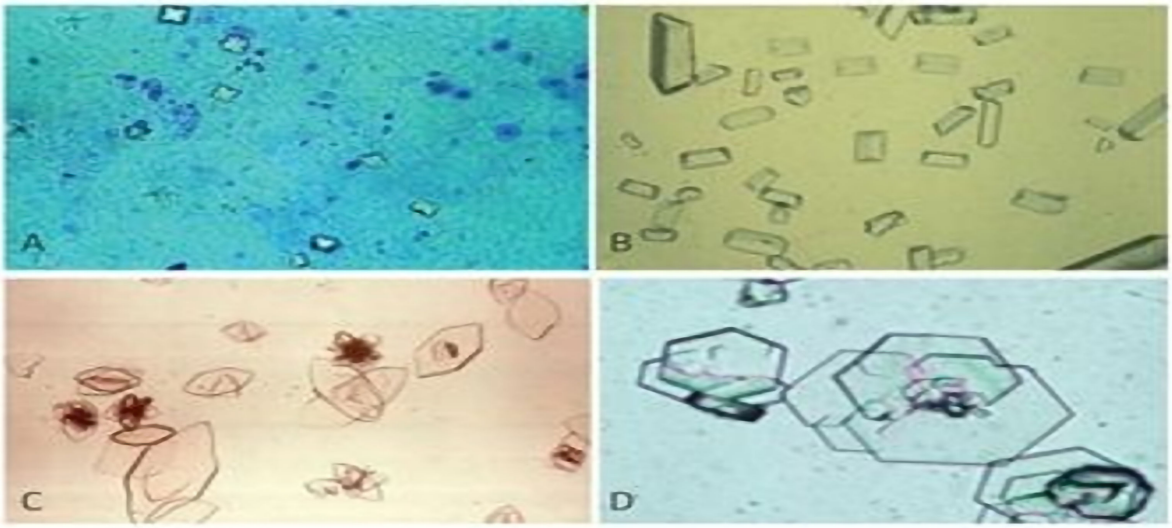
Clinical Evaluation of Stone Formers (Box.1 & 2)

Patients with underlying characteristics merit complete metabolic evaluation to determine the cause of their kidney stones.

Pertinent medical history, including medications in use, family and social history, and physical examination are important to evaluate kidney stone disease. Basic Investigations include UA with micro (to look for Crystals, Specific gravity, PH, and any presence of infections), Urine Chemistry also Basic Metabolic Profile.

Box: 1

- First stone episode under the age of 25
- Recurrent stones
- Bilateral or multiple stones, or nephrocalcinosis
- Strong family history of stones
- Impaired renal function (eGFR <60 ml/min/1.73m2) associated with stones
- Non–calcium oxalate stones
- Radiolucent stones (may be urate or cystine)
- Stone episode associated with underlying condition (eg inflammatory bowel disease, gastric bypass surgery or metabolic syndrome)



Microscopic appearance of common urine crystals: A. calcium oxalate, B. triple phosphate, C. uric acid, D. cystine

Box: 2

Medications Associated With Nephrolithiasis and Nephrocalcinosis

Calcium Stone Formation

- Loop diuretics
- Vitamin D
- Corticosteroids
- Calcium supplements
- Antacids (calcium and noncalcium antacids)
- Theophylline
- Acetazolamide *
- Amphotericin *
- Topiramate

Uric Acid Stone Formation

- Salicylates
- Probenecid
- Melamine (in contaminated infant formula and milk products)

Medications That May Precipitate Into Stones

- Triamterene
- Acyclovir (if infused rapidly intravenously)
- Indinavir
- Nelfinavir

Diagnostic Radiological Evaluation of Nephrolithiasis (Algorithm. 1)

CT of the abdomen and pelvis without contrast performed using low-radiation-dose protocols is the preferred examination for most adults with suspected nephrolithiasis. If CT technology is not available, ultrasound of the kidneys and bladder, sometimes in combination with abdominopelvic radiography, is the second-line option for initial imaging. Following is a radiological diagnostic algorithm for Nephrolithiasis.

A complete evaluation should be undertaken in patients with multiple or metabolically active stones (i.e., stones that increase in size or number within a year), in all children, in patients from demographic groups not typically prone to stone formation, and in those with stones other than those containing calcium.

The complete evaluation should include a measure of urine volume and the quantity of calcium, oxalate, phosphorous, uric acid, sodium, citrate, and creatinine excreted in a 24-hour urine collection.

General Treatment

Non-Pharmacological Treatment

Fluid intake: An increase in urine volume to more than 2 to 2.5 liters daily has been proven to reduce the incidence of stones.{7]

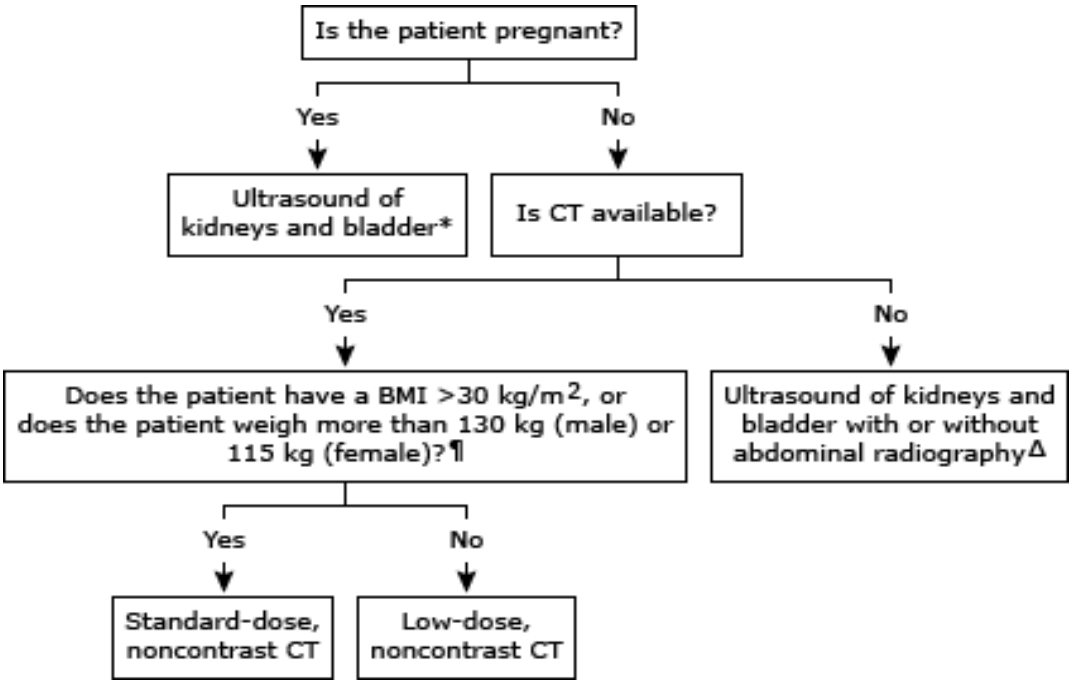
Salt intake: Dietary salt restriction is associated with decreased urine calcium excretion.

Patients: should be instructed to limit daily sodium intake to 2 g (87 mmo l sodium). [7] Dietary protein. Animal protein ingestion increases the frequency of renal stone formation. [7]

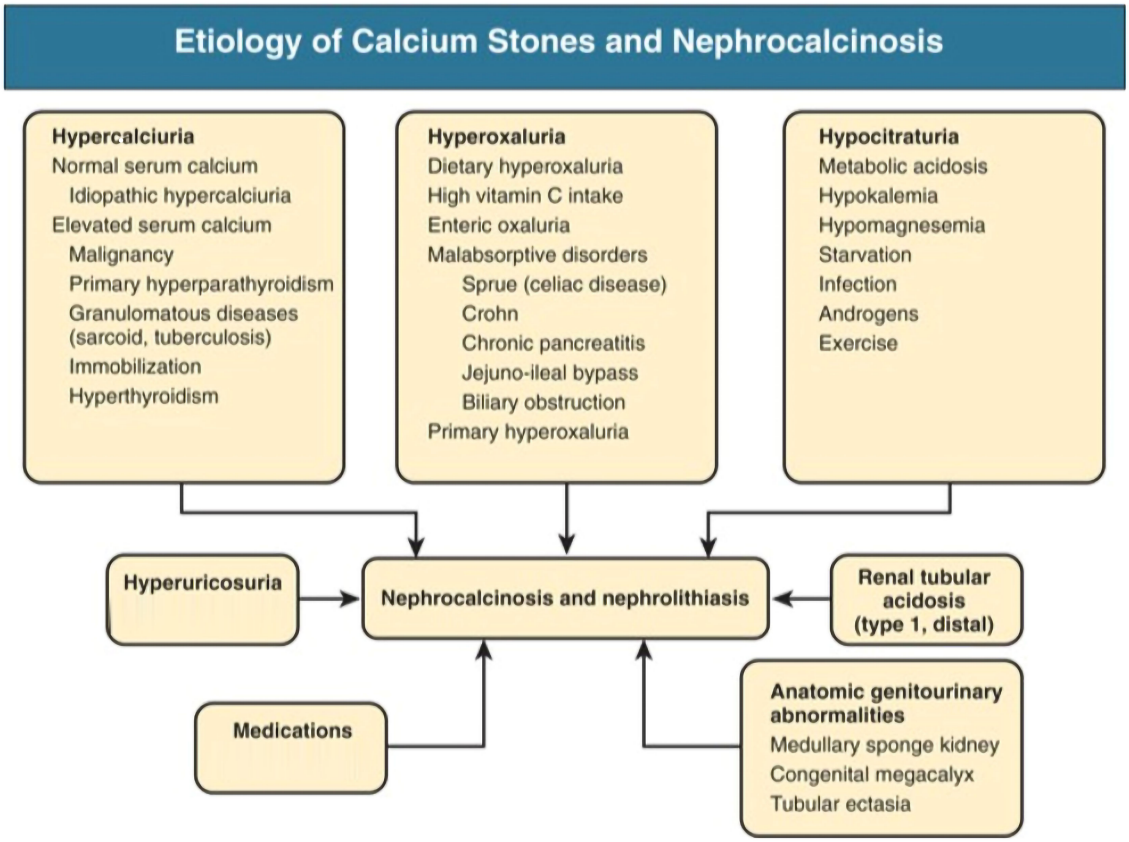
Dietary calcium: Despite conventional wisdom, several studies have demonstrated a decrease in stone incidence when people consume diets adequate in calcium. [8]

Fruit and Vegetable: Increase Citrate concentration.[8]

Algorithm. 1



Box: 3



Specific type of Stone and Treatment (Algorithm. 2)

Calcium Oxalate

Calcium-based stones most often develop as a result of hypercalciuria. Other causes of calcium stones are hyperoxaluria, hyperuricosuria, hypocitraturia, renal tubular acidosis, certain medications, and congenital abnormalities of the genitourinary tract. Specific therapy for patients with calcium stones depends on the underlying metabolic abnormalities detected on evaluation. General therapy, as outlined earlier, always should be instituted; however, more definitive treatment is often required to significantly decrease the rate of recurrent stone formation. [6]

Treatment

For hypercalciuria the usual first-line therapy is a thiazide diuretic, which acts to reduce urinary calcium. In the United States, chlorthalidone 25 to 50 mg is the drug of choice. On commencing these medications, patients should be instructed to increase their dietary potassium intake and as needed supplement with Potassium Citrate.

Hyperoxaluria

Elevated urinary oxalate results from excessive dietary intake (dietary oxaluria), gastrointestinal disorders that can lead to malabsorption (enteric oxaluria), or an inherited enzyme deficiency that results in excessive metabolism of oxalate (primary hyperoxaluria) [9]

Treatment of dietary and enteric hyperoxaluria: Consists of dietary oxalate restriction. Patients should be given a list of foods that have high oxalate content to avoid or eat in moderation. Calcium-containing food may be included at each meal to bind intestinal oxalate and prevent its absorption.

Treatment of primary hyperoxaluria: Primary hyperoxaluria type 1 (PH1) is a severe disorder that can be cured only with liver transplantation. [12]

Hypocitraturia

Citrate inhibits stone formation. A number of conditions reduce urinary citrate excretion, predisposing to stone formation. Excessive protein intake, hypokalemia, metabolic acidosis, exercise, hypomagnesemia, infections, androgens, starvation, and acetazolamide have all been implicated in decreased urinary citrate excretion. Increased supplement of dietary Citrate (Lemon) or oral sodium/potassium citrate is the treatment of choice. [6]

Hyperuricosuria

Calcium oxalate crystals often nucleate around other crystal types, such as uric acid. Hyperuricosuria contributes to nephrolithiasis in 10% to 15% of calcium stones. If uric acid excretion remains elevated, allopurinol should be initiated at 100 to 300 mg/day. [6]

Uric Acid Stones

The stones are radiolucent and, therefore, poorly visible on plain radiographs. In Mediterranean and Middle Eastern countries, uric acid stones may constitute up to 75% of stones.

Three major factors influence uric acid stone formation: low urine pH, low urine volume, and elevated urinary uric acid levels.

Treatment: Treatment of uric acid stones involves increasing urine pH and volume as well as decreasing uric acid excretion. Alkaline urine not only can prevent uric acid stone formation but also may result in stone dissolution. To raise urine pH, potassium citrate is recommended. [6]

Struvite Stones

Struvite stones are also referred to as infection stones or triple phosphate stones. The stones grow rapidly to a large size, can reduce renal function in the affected kidney, and are difficult to eradicate.

Most staghorn calculi, large stones that penetrate more than one renal calyx, are composed of struvite. Their formation requires the presence of urease-producing bacteria in the urine, like Proteus Mirabilis.

Treatment: Struvite stones require aggressive medical and surgical management. Antibiotic therapy is important to reduce further stone growth and for stone prevention.

Given the need for complete stone removal to effect a cure, early urologic intervention is advised. Stones smaller than 2 cm may respond well to ESWL; however, larger stones will likely require percutaneous nephrolithotomy, often in combination with ESWL [10]

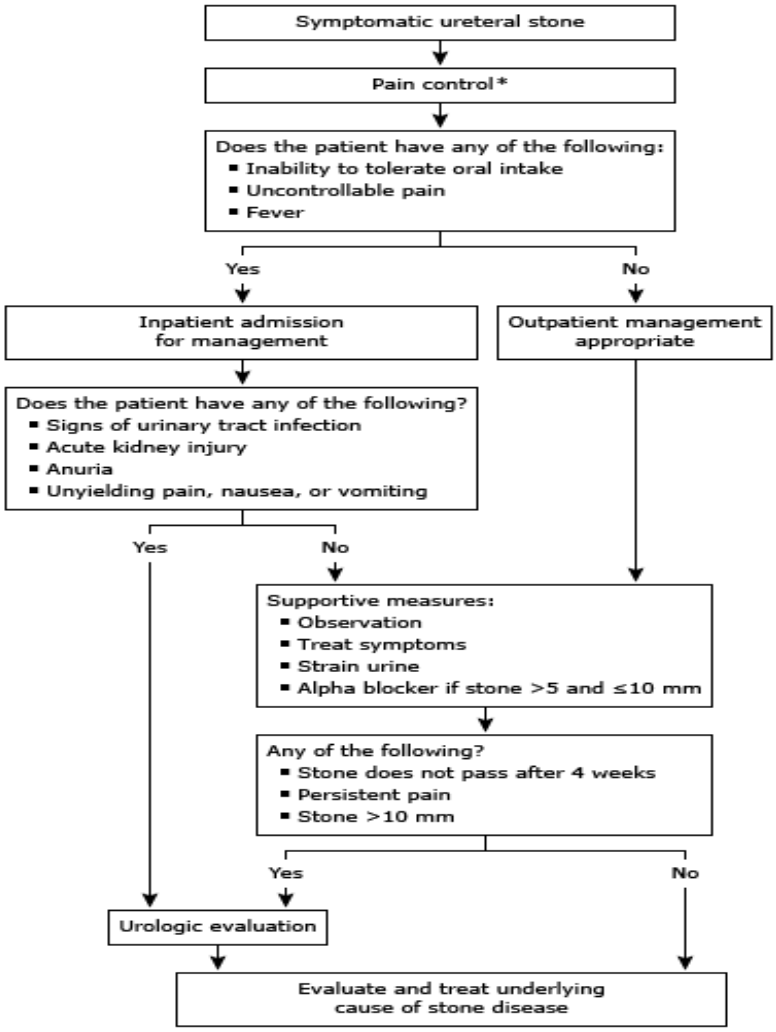
Cystine Stones

Cystinuria is an autosomal disorder with a tubular defect in dibasic amino acid transport, resulting in increased cystine, ornithine, lysine, and arginine excretion.

Stone disease is usually clinically manifested in the second and third decades of life. Because of the high sulfur content of the cystine molecule, the stones are apparent on plain radiographs. Treatment is directed at decreasing the urinary cystine concentration below the limits of solubility. [11]

Management of acute symptomatic nephrolithiasis

Algorithm. 2



NSAID: nonsteroidal antiinflammatory drug; eGFR: estimated glomerular filtration rate.

* For most patients with acute renal colic, we suggest NSAIDs rather than opioids as the initial choice for pain control. We reserve opioids for patients who have contraindications to NSAIDs, have severe

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