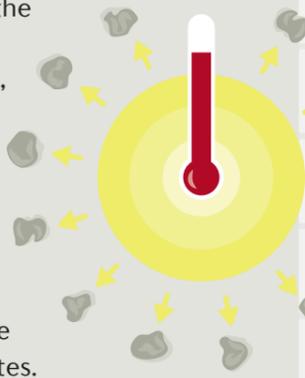


For the Primer, visit [doi:10.1038/nrdp.2016.8](https://doi.org/10.1038/nrdp.2016.8)

→ Kidney stones (nephrolithiasis) form when urine becomes supersaturated with respect to a mineral, leading to crystal formation, growth, aggregation and retention within the kidneys. Stones range in size and can be as small as a grain of sand. A stone does not have to cause symptoms in the patient to be a stone.

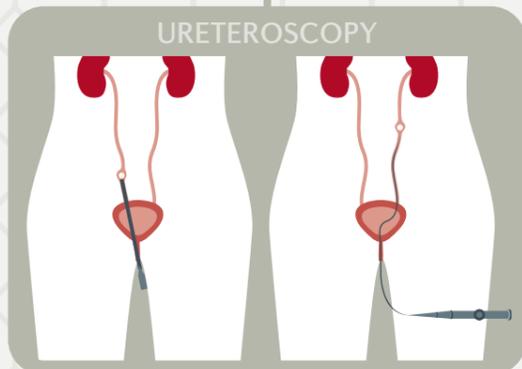
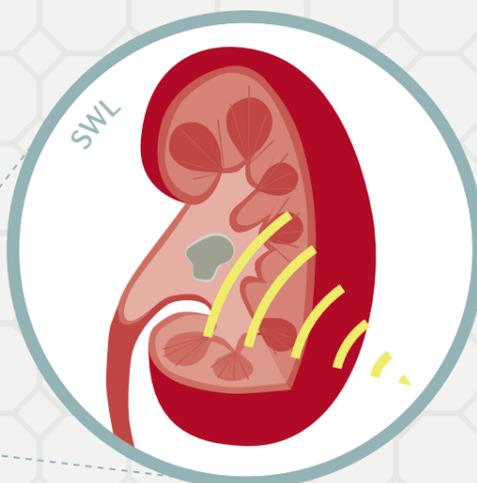
EPIDEMIOLOGY

Data from seven countries places the incidence of kidney stones at 114–720 per 100,000 individuals and the prevalence at 1.7–14.8%. In nearly all countries surveyed, the rates are rising. The propensity to form stones varies according to sex, ethnicity and geography. For example, stone disease can reflect environmental risk factors, with higher stone prevalence in hot, arid climates.



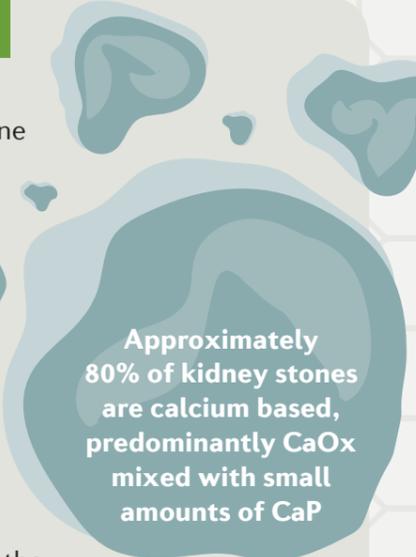
Rx MANAGEMENT

Surgery to remove stones from the kidney is the mainstay of treatment. The main procedures for stone treatment are extracorporeal shockwave lithotripsy (SWL), rigid or flexible retrograde ureteroscopic stone fragmentation and retrieval and percutaneous nephrolithotomy.



DIAGNOSIS

Diagnosing kidney stone disease requires an understanding of the metabolic background that promotes lithogenesis. The metabolic evaluation of patients aims to estimate the propensity of urine to crystallize, investigate the metabolic mechanisms of nephrolithiasis, diagnose underlying systemic causes of nephrolithiasis, determine the risk of chronic kidney disease and metabolic bone disease and to achieve insights on nutritional habits. Stone composition should be determined, and laboratory assessments to determine metabolic activity include measurement of serum levels of creatinine, calcium, potassium, inorganic phosphate and other ions; estimation of glomerular filtration rate; and measurement of urinary volume, pH and stone substrate levels.



Approximately 80% of kidney stones are calcium based, predominantly CaOx mixed with small amounts of CaP

MECHANISMS

On the basis of experimental and available clinical data, stone formation can be viewed as a multistep process involving the formation of mineral plugs and plaques in the kidneys. For example, calcium phosphate (CaP) crystals deposited in the interstitium grow outwards towards the papillary surface. This growth can become exposed to the pelvic urine and provides a nidus for calcium oxalate (CaOx) nucleation, leading to stone formation. At the same time, CaP crystals can form in the renal tubules and can aggregate to form a plug. Deposition of CaOx crystals on the plugs in the ducts of Bellini leads to the formation of kidney stones.

OUTLOOK

Emerging therapies in kidney stones include methods to deal with residual fragments after SWL, which could act as foci for regrowth of the stone. For example, stents and other intracorporeal devices loaded with digestive

enzymes (with slow-release functionality) might eliminate these fragments. Inversion therapy is a procedure carried out with the aim of changing the position of fragments in the lower pole of the kidneys, which have a low rate

! The majority of stone formers will form only a single symptomatic stone in their lifetime or over a long observation period.

of spontaneous expulsion. The altered position of the kidneys combined with applied vibrational energy is thought to help eliminate the fragments, but further research is needed to assess its efficacy.

PREVENTION

For some individuals, stone formation can be a recurring disease that has consequences such as chronic kidney disease and metabolic bone disease. The aim of preventive strategies should also focus on preventing these outcomes. Calcium stone prevention relies on increasing water intake, controlling calcium intake and reducing intake of meat, poultry and salt. For other stone compositions, such as uric acid stones, supersaturation in the urine must be decreased. Strategies here include increasing urinary volume and modulating urinary pH.