Urolithiasis as a clinical, epidemiological and socio-medical problem

B. F. Matkarimov[1], G. S. Khalimbetov[2]

[1]*Military Medical Institute of the University of Military Security and Defense of the Republic of Uzbekistan*

[2]*Center for the Development of Professional Qualifications of Medical Workers, Ministry of Health of the Republic of Uzbekistan*

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Abstract

Abstract. Urolithiasis is one of the most common urological diseases, and its prevalence varies considerably between climatic and geographical zones. Uzbekistan is among the regions where urolithiasis is endemic. Stone formation is strongly influenced by geographical, climatic, ethnic, dietary and genetic factors, whereas the risk of recurrence is determined by the underlying disease or metabolic disorder responsible for stone formation. The prevalence of urolithiasis ranges from 1% to 20% and continues to rise in both developing and developed countries owing to social, economic, dietary and environmental changes, as well as improved diagnostic methods. This review summarizes current data on the epidemiology, pathogenesis, diagnosis, treatment and metaphylaxis of urolithiasis and outlines unresolved problems in predicting its recurrence.

Keywords: urolithiasis; prevalence; minimally invasive endourological interventions; metaphylaxis; ureteral stenting; excretory urography; percutaneous nephrolithotomy; medical expulsive therapy.

Review

Urolithiasis (kidney stone disease) is one of the most common urological diseases. Its prevalence and incidence have been rising steadily over recent decades in virtually all regions of the world [10]. According to a meta-analysis of 22 epidemiological studies, the overall global prevalence of urolithiasis is approximately 10.8%. There are marked geographical differences: in population-based studies of adults, prevalence ranges from about 5% to 15% and is highest in regions with a hot climate and particular dietary habits. In industrialized countries, the lifetime risk of stone formation exceeds 12% in men and 6% in women [19]. Men are affected more often, with a peak incidence at 35-60 years of age [8], although the gap between the sexes has narrowed in recent years.

In the Republic of Uzbekistan, urolithiasis is very common, but its frequency varies between climatic and geographical zones, and the country is regarded as an endemic region. According to the Republican Center of Urology, the overall prevalence of urolithiasis in the country was already about 4.5% of the population in the late 1990s. In the arid southern and desert regions, rates are considerably higher: about 8.5% in Bukhara Region, 7.7% in the Republic of Karakalpakstan and 6.8% in Khorezm Region. By contrast, in areas with a more temperate climate, such as the city of Tashkent, prevalence is much lower (about 0.9%). These differences are explained by climatic factors (a hot, dry climate promotes dehydration and urine concentration), the composition of drinking water (high mineralization in some regions) and diet. Urolithiasis is also endemic in children, accounting for 44% to 61% of all urological diseases in childhood [14]. The climatic and geographical conditions of Uzbekistan therefore make it a high-risk zone for urolithiasis, which calls for particular attention to prevention in endemic areas.

Of particular concern to clinicians is the high risk of recurrence. Patients with urolithiasis frequently experience repeated episodes of stone formation. According to pooled data, after a first stone episode the risk of recurrence reaches 50% within 5 years and up to 80% within 10 years [13, 18]. In retrospective series, up to 60% of patients have a recurrent episode of nephrolithiasis in the following years [11]. Recurrence rates reported by different authors range from 30% to 70%, meaning that most patients are prone to repeated stone formation. Moreover, each new episode increases the likelihood of further stones, creating a vicious circle [16]. Factors associated with recurrence include young age at onset, male sex, metabolic disorders (obesity, diabetes mellitus), a positive family history, urinary tract infection and uncorrected anatomical abnormalities (strictures, congenital anomalies) [3, 4].

The etiological factors of urolithiasis are closely linked to the environment and lifestyle. A hot climate and insufficient fluid intake increase the risk of stone formation through dehydration and higher urinary salt concentrations. Drinking water also plays a role: in some regions, hard water contains excess calcium and sulfates, which may contribute to the formation of calcium oxalate and other calcium-containing stones.

Dietary and socioeconomic factors are also important. The traditionally high intake of meat and salt typical of several regional cuisines increases urinary excretion of uric acid and calcium and shifts urine pH toward acidity, raising the risk of urate and oxalate stones. A diet low in fresh vegetables and fruit leads to a deficiency of citrate, a natural inhibitor of crystallization [7]. Socioeconomic conditions play a particular role: in rural areas with a hot climate and heavy physical labor (for example, among farmers and outdoor workers), urolithiasis is more common precisely because of chronic mild dehydration. Urbanization and

industrialization have led to a rise in obesity and metabolic syndrome, which has also been reflected in a higher incidence of urolithiasis [5]. Finally, ethnic and genetic factors influence susceptibility: stones are somewhat more common in white populations than in Asian populations, whereas in South Asia and the Persian Gulf countries certain stone types (for example, urate stones) predominate owing to a combination of dietary preferences and genetics.

Urolithiasis is of great medical and social importance because of its high prevalence, its tendency toward a chronic, recurrent course and the cost of treatment. Its economic burden is considerable: in the early 2000s, between US$0.7 and 1.2 billion was spent annually on the diagnosis and treatment of urinary stones in the United States alone, and current estimates reach US$2 billion [12]. The high prevalence among people of working age (about 70% of cases occur between 20 and 50 years of age) results in lost working days because of attacks of renal colic and the need for hospitalization. Kidney and ureteral stones are a common reason for emergency visits, as an acute attack of renal colic requires emergency care and often hospital admission [1, 17]. Complications of urolithiasis (obstructive pyelonephritis, hydronephrosis, urosepsis) pose a direct threat to life and health and require costly intensive treatment [2, 9]. Urolithiasis often leads to a decline in renal function; large staghorn calculi can cause chronic renal failure and disability [6].

Urolithiasis also affects patients' quality of life. Recurrent episodes of renal colic are accompanied by severe pain, reduce work capacity and cause psychological distress. Patients have to follow dietary and preventive measures and attend regular check-ups, which adds to the burden of the disease. According to a study conducted in the Aral Sea region, where urological diseases are widespread, urolithiasis accounted for 22% of all urological conditions, second only to urinary tract infections [15]. This underlines the importance of the problem for the health care system. Urolithiasis is thus not only a medical but also a socioeconomic problem that requires better prevention, effective treatment and patient rehabilitation to reduce recurrence and complications.

The formation of urinary calculi is a multifactorial process resulting from an imbalance between factors that promote crystallization (lithogenic factors) and those that inhibit it (antilithogenic factors) [20, 27]. Normally, urine is a metastable solution supersaturated with salts, but natural crystallization inhibitors (citrate, magnesium, certain peptides) and regular emptying of the urinary tract prevent stone formation. The pathogenesis of urolithiasis involves a sequence of stages: crystal nucleation (formation of microcrystals where the solubility threshold is locally exceeded), crystal growth and aggregation, retention of crystal aggregates in the kidney or ureter, and the subsequent formation of a macroscopic calculus [31, 36]. A key role is played by abnormalities in urine composition: an excess of lithogenic substances (calcium, oxalate, phosphate, uric acid, cystine) or a deficiency of inhibitors (citrate, pyrophosphate, nephrocalcin, etc.). In each individual case, the balance of these factors shifts in a particular direction, leading to precipitation of a specific salt and formation of a stone of the corresponding composition.

Several complementary theories of stone formation have been proposed. The matrix theory regards the stone as the result of crystal deposition on an organic matrix of proteins capable of adsorbing minerals. The crystalloid-colloid theory proposes a loss of the colloidal stability of urine, in which protective colloids no longer prevent crystal aggregation. The interstitial theory explains the formation of some stones (particularly calcium stones) from calcified plaques in the renal papillae, which serve as a nidus for stone growth within the calyx. These plaques arise from the deposition of hydroxyapatite crystals in the renal interstitium; once exposed on the urothelial surface, they initiate the nucleation of calcium oxalate or calcium phosphate crystals from urine (the papillary, or Randall's, plaque theory of stone formation) [30]. Cellular mechanisms are also recognized: death and desquamation of tubular epithelial cells can create crystallization centers, and organic debris serves as a matrix for the stone [21].

Recent studies indicate that stone formation is not a purely local process but is associated with systemic metabolic disorders and even inflammatory responses. Calcium oxalate crystalluria is associated with injury to the tubular epithelium and activation of local inflammation in the renal parenchyma. Khan et al. described how oxalate crystals induce the production of reactive oxygen species and attract macrophages, triggering an inflammatory cascade in the kidney. This leads to subclinical tubulointerstitial injury, which in turn promotes further stone formation [2, 3, 29]. Urolithiasis is therefore currently regarded as a systemic metabolic and, in part, inflammatory disease underpinned by a variety of pathophysiological mechanisms.

Metabolic disorders are among the most important groups of risk factors for urolithiasis. An increased urinary concentration of stone-forming components is the main direct pathway to crystallization. Hypercalciuria is found in about 30-50% of patients with calcium stones; it may be primary (hereditary or associated with hyperparathyroidism) or secondary (a diet high in salt and protein, or metabolic acidosis, increases calciuria). Hyperoxaluria is often associated with excessive dietary oxalate (spinach, sorrel, etc.), impaired intestinal absorption (enteric hyperoxaluria in bowel disease) or inborn errors of metabolism (primary hyperoxaluria). Hyperuricosuria and low urine pH are the main factors in urate nephrolithiasis, which often accompanies metabolic syndrome. Low urinary citrate (hypocitraturia) is an important independent risk factor, because citrate binds calcium and inhibits crystal growth; hypocitraturia occurs in metabolic acidosis, potassium deficiency and excessive consumption of animal protein. In addition, dehydration and a low urine volume (<1 L/day) markedly increase the overall lithogenicity of urine [173].

Metabolic syndrome (MetS), a combination of obesity, insulin resistance, hypertension and dyslipidemia, is recognized as a significant risk factor for urolithiasis. Patients with MetS have a markedly higher incidence of uric acid stones and calcium oxalate nephrolithiasis. Insulin resistance reduces renal ammonium production and consequently leads to persistently acidic

urine. At a pH below 5.5, uric acid remains poorly soluble and precipitates as uric acid or sodium urate crystals. Obesity is accompanied by dietary changes (excess purines and protein) and increased urinary excretion of oxalate and urate. Hyperinsulinemia and concomitant hyperparathyroidism can enhance bone resorption, raising calcium levels in the blood and urine. Dyslipidemia and elevated free fatty acid levels may damage the renal tubules, indirectly contributing to stone formation. Metabolic syndrome thus creates a combination of conditions (low urine pH, hyperuricosuria, hypercalciuria and hypocitraturia) that together sharply increase the risk of urolithiasis [25].

The role of urine pH and acid-base balance deserves special attention. Acidic urine (pH <5.5) promotes the formation of urate stones, because uric acid is poorly soluble in an acidic environment. At pH 5.0, uric acid solubility is minimal, whereas at pH >6.5 most of it is in the dissolved, ionized form [37]. Persistently low urine pH is therefore a key factor in urate nephrolithiasis. Conversely, excessively alkaline urine (pH >7.0) predisposes to the precipitation of phosphates (struvite, carbonate apatite). Urine pH also modifies the excretion of lithogenic substances: at low pH, the excretion of uric acid and cystine increases, whereas at high pH more calcium and phosphate are excreted.

Supersaturation, which occurs when the urinary concentration of a substance exceeds its solubility, is the main prerequisite for crystallization. Each stone type has its own lithogenic factors: hyperoxaluria and hypercalciuria in calcium oxalate nephrolithiasis, hyperphosphaturia and infection in phosphate stones, hyperuricosuria and acidic urine in urate stones, and cystinuria (a hereditary disorder) in cystine stones. Common factors include low urine volume, high urine specific gravity (>1.020) and high urinary sodium (which reflects excess salt intake and promotes calciuria). The antilithogenic properties of urine are provided by substances that inhibit crystal growth. The most important of these is citrate, which forms complexes with calcium and reduces the concentration of free Ca2+ in urine; an adequate urinary citrate level (>320 mg/day) substantially reduces the risk of calcium stones. Magnesium competes with calcium for binding to oxalate, forming readily soluble salts. Urinary glycoproteins such as uromodulin (Tamm-Horsfall protein) and nephrocalcin can adsorb crystals and prevent their aggregation, although their role is dual: at excessive concentrations they may themselves become a stone matrix. Peptides and small molecules such as pyrophosphate also inhibit calcium phosphate crystallization. The balance between all these factors is complex and dynamic, which explains why some people form stones despite relatively mild abnormalities, whereas others remain stone-free even with marked hypercalciuria if their inhibitor levels are compensatorily increased. Assessment of the urinary metabolic profile (concentrations of lithogenic substances, citrate, pH, etc.) is fundamental to understanding the individual pathogenesis of urolithiasis in each patient.

Urinary tract infection not only complicates the course of urolithiasis but can also directly cause stone formation. Infection (struvite) stones consist mainly of struvite, i.e., magnesium ammonium phosphate ($MgNH_4PO_4 \cdot 6H_2O$), and carbonate apatite [34]. They form only in the presence of urease-producing bacteria, which hydrolyze urea to ammonia. Ammonia alkalinizes the urine, raising its pH above 7.0 and causing the precipitation of poorly soluble magnesium ammonium phosphate and calcium phosphate. The classic causative organisms are *Proteus mirabilis*, *Klebsiella* and *Pseudomonas* species and, less commonly, *Staphylococcus* and other genera [35]. Struvite stones are more common in women over 50 years of age and account for 10-15% of all urinary stones in developed countries. They often take the form of staghorn calculi filling the renal pelvis and calyces. Infection stones grow rapidly (large calculi can form within a few months) and tend to recur if the infection is not eradicated. Inflammation also acts as a pathogenetic factor: bacteria form biofilms on the stone surface, and the protective layer of mucus and cellular debris becomes a matrix for mineralization [22]. The chronic pyelonephritis that accompanies such stones leads to scarring of the renal parenchyma. Infection and stone formation therefore sustain each other: the calculus favors bacterial persistence, and the infection accelerates stone growth. Complete stone removal and long-term antibacterial therapy are critical for the treatment and prevention of struvite nephrolithiasis [24, 38, 41].

Even non-infectious stones often have an inflammatory component. Microtrauma of the calyceal and pelvic mucosa by sharp-edged crystals triggers a local inflammatory response with leukocyte infiltration and cytokine release. Kidney biopsy specimens from patients with urolithiasis often show foci of tubulointerstitial inflammation and fibrosis around crystal deposits, and lymphocytic and plasma cell infiltration is observed around calcified papillary plaques. Chronic pyelonephritis may both precede stone formation (by causing urinary stasis and changes in pH) and result from it. Inflammatory changes are thus a frequent companion of urolithiasis and aggravate kidney damage [26].

A kidney stone causes a range of morphological and functional disturbances. Mechanical obstruction of the urinary tract impairs urine outflow and raises hydrostatic pressure above the obstruction. Acute complete ureteral obstruction causes acute hydronephrosis, whereas chronic partial obstruction leads to dilation of the pelvicalyceal system and atrophy of the renal parenchyma. Even after stone removal, many patients retain signs of injury, such as reduced glomerular filtration in the previously obstructed kidney and scarring. Bilateral obstruction may lead to acute renal failure. In addition, stone migration and renal colic are accompanied by vasospasm and renal ischemia, which can also damage nephrons [28, 32].

At the microscopic level, nephrolithiasis is characterized by crystal deposits in the collecting ducts and interstitium (nephrocalcinosis), degeneration and squamous metaplasia of the tubular epithelium, and focal tubular necrosis. Microliths forming in the tubular lumen damage the epithelium and cause its desquamation. Dilation of the tubular lumen and tubular acidosis are often found in the affected nephrons. Interstitial fibrosis develops, particularly around calcium deposits. In children with long-standing urolithiasis, severe diffuse parenchymal changes (nephrosclerosis) may develop. Superimposed infection leads to purulent and destructive processes (renal carbuncle, and pyonephrosis in advanced staghorn stone disease).

The pathogenesis of urolithiasis is thus complex and multifactorial. Stone formation is determined by the interplay of metabolic changes, local conditions in the kidney, infectious agents and genetic predisposition. Identifying the leading pathogenetic factors in an individual patient makes it possible to develop a targeted plan for preventing recurrence.

Modern diagnosis of urolithiasis is based on a combination of clinical data, laboratory tests and imaging [32, 40]. When urinary stones are suspected, imaging is the standard approach. In outpatient practice, the first step is usually ultrasonography of the kidneys and urinary tract, which is a safe, non-invasive and affordable screening method. Ultrasound can detect stones of about 3-4 mm or larger in the kidneys, the upper and distal thirds of the ureters and the bladder. It shows the number and approximate size of stones, as well as indirect signs of obstruction (pelvic dilation, hydronephrosis). However, ultrasonography has limitations: small stones (<3 mm) and stones in the middle third of the ureter may not be visualized. For this reason, plain abdominal radiography (a plain film of the kidneys, ureters and bladder) has traditionally been used to detect radiopaque stones (oxalate, phosphate). It allows rapid assessment of the presence, number and location of large stones and of the anatomy of the kidneys and ureters. However, about 10-15% of stones (urate and xanthine stones) are radiolucent and are not visible on plain films. In emergencies (renal colic), plain radiography can help to rule out other causes of pain and identify conditions requiring urgent treatment.

Excretory urography, a contrast-enhanced X-ray examination, was long considered the gold standard for diagnosing urinary stones. Contrast administration shows not only the stone itself (as a filling defect or contrast retention above the obstruction) but also the function of both kidneys and the degree and level of obstruction. In recent years, however, excretory urography has given way to computed tomography. Non-contrast computed tomography (CT) is currently the method of choice for diagnosing urinary stones. Low-dose multislice CT detects stones of any chemical composition and size, in any part of the urinary tract, with a sensitivity approaching 100%. CT precisely determines the location of a stone relative to anatomical structures, its size and its density in Hounsfield units (HU), which indicates its likely composition (for example, a density >1000 HU is typical of calcium oxalate and about 400 HU of urate). CT also reveals associated changes (hydronephrosis, ureteral wall thickening, renal anomalies) and helps to differentiate urolithiasis from other diseases with similar symptoms (appendicitis, cholecystitis, peptic ulcer, etc.). According to clinical guidelines, CT should be performed to confirm the diagnosis when a ureteral stone is suspected, especially if ultrasound findings are inconclusive. In children and pregnant women, however, CT is avoided because of radiation exposure, and ultrasound or MRI is preferred.

Laboratory investigations in urolithiasis aim to identify metabolic disorders and complications. Urinalysis is mandatory; it usually reveals microhematuria (resulting from mucosal injury by the stone) and crystalluria (salt crystals in the urine). Bacteriuria and leukocyturia indicate urinary tract infection, which is particularly important in obstructive pyelonephritis, a combination that requires urgent renal drainage. If a stone has passed spontaneously or has been removed, its composition is determined by X-ray diffraction or infrared spectroscopy of a fragment. This provides valuable information: for example, uric acid in the stone prompts a search for disorders of purine metabolism, whereas struvite indicates chronic infection. In renal colic, blood tests may show signs of inflammation (leukocytosis, elevated C-reactive protein) or impaired renal function (raised creatinine) [33]. A comprehensive metabolic evaluation is recommended for all patients with urolithiasis, particularly those with recurrent stone formation, young patients and those with multiple or unusual stones. It includes 24-hour urine analysis for calcium, oxalate, uric acid, citrate, magnesium, phosphorus, pH and volume, as well as serum biochemistry (calcium, phosphorus, uric acid and parathyroid hormone). Studies have shown that the vast majority of patients with recurrent nephrolithiasis have at least one abnormality of urinary metabolic parameters. Correction of these abnormalities, by diet or medication, forms the basis of metaphylaxis [39].

Beyond standard tests, specific biomarkers of the lithogenic process are of scientific interest. For example, a number of authors from Uzbekistan have studied urinary enzyme activity as an indicator of stone formation and proposed measuring the activity of the leucine aminopeptidase fractions LAP-C and LAP-M. All patients with urolithiasis were found to have elevated LAP-C levels, whereas LAP-M was markedly elevated in patients with calcium phosphate and mixed stones, reflecting an inflammatory process in the kidneys. This is an interesting example of the search for markers of renal tissue damage and stone-forming activity. Although such tests are not yet in widespread use, research in this area continues [43].

The treatment of urolithiasis has changed dramatically in recent decades with the introduction of minimally invasive and non-invasive technologies. Whereas open surgery (pyelolithotomy, nephrolithotomy) was formerly the main method of stone removal, today more than 90-95% of stones are removed without an open incision. Extracorporeal shock wave lithotripsy (ESWL) [46] uses externally generated shock waves focused on the stone to fragment it. ESWL requires no incision and is performed on an outpatient basis; the stone fragments then pass spontaneously with the urine. According to Uzbek urologists, ESWL is used in most cases for stones ≤2 cm. However, its effectiveness is reduced for dense oxalate stones, large stones (>2 cm) and unfavorable locations (the lower calyceal group). In such cases, endourological methods are used.

Transurethral ureterorenoscopy with laser lithotripsy is used to treat ureteral and kidney stones. A thin flexible or rigid endoscope is passed through the urethra into the ureter (ureteroscopy) or even into the renal pelvis (flexible retrograde intrarenal surgery, RIRS). The stone is fragmented under direct vision with a laser fiber (holmium laser), and small fragments are extracted with special baskets [48]. This method is particularly effective for stones in any segment of the ureter and for renal calculi up to about 2 cm. It is gentle and organ-preserving, and patients recover quickly [49].

For large kidney stones (more than 2 cm, including staghorn calculi), percutaneous nephrolithotomy (PCNL) is the method of choice. Under fluoroscopic or ultrasound guidance, a tract is created through the skin of the lumbar region directly into the renal collecting system, and a nephroscope, an instrument about 5-10 mm in diameter, is inserted. The stone is visualized through the nephroscope and fragmented with an ultrasonic or laser lithotripter, and the fragments are removed with forceps. Percutaneous access allows even very large stones to be removed in one or two procedures. Modern modifications such as mini-PCNL, which use smaller-caliber instruments, reduce the invasiveness of the procedure [47].

Minimally invasive surgery has thus almost completely replaced open surgery, which is now rarely performed, mainly for complex staghorn stones associated with renal anomalies or when endoscopic methods have failed. In Uzbekistan, as elsewhere, considerable experience has been accumulated with minimally invasive treatment. The widespread introduction of ESWL, ureterorenoscopy and PCNL has made the treatment of urolithiasis much safer and more routine. Mortality after elective stone removal is now close to zero, and the risk of serious complications is low. Hospital stay and rehabilitation have been shortened considerably, and most patients return to normal life within a few days of the procedure [20, 32].

Another important aspect of treatment is stone dissolution, or litholytic therapy. Urate stones can be dissolved conservatively: with prolonged alkalinization of the urine using citrate mixtures (potassium citrate, sodium bicarbonate), uric acid is converted into a soluble form and the stone gradually decreases in size. For cystine stones, alkalinization and penicillamine or tiopronin are used to reduce the urinary cystine concentration. Unfortunately, oxalate and phosphate stones are virtually impossible to dissolve, which limits the scope of conservative therapy.

Metaphylaxis: prevention of recurrence. Metaphylaxis refers to a set of measures aimed at preventing recurrent stone formation in patients whose stones have already been removed or have passed spontaneously. Given the high propensity for recurrence, metaphylaxis is the cornerstone of the modern management of urolithiasis. It is based on the results of metabolic evaluation: knowing the stone composition and the abnormalities identified on testing, the physician develops an individualized prevention program [44, 45].

General preventive measures include increasing fluid intake (to achieve a urine output of about 2.5 L/day), dietary restrictions tailored to the type of metabolic disorder and maintenance of an optimal urine pH. All patients are advised to drink at least 8-10 glasses of water a day, distributed evenly throughout the day, and even more in hot climates. Adequate hydration reduces urinary salt concentrations and the risk of crystallization.

Dietary recommendations depend on the stone type. For oxalate stones, patients are advised to limit oxalate-rich foods (sorrel, rhubarb, chocolate), to reduce fat intake (which lowers intestinal oxalate absorption) and to combine calcium- and oxalate-containing foods in the same meal, since calcium binds oxalate in the intestine. For urate stones, a low-purine diet is recommended: offal, red meat, legumes, strong broths and alcohol should be excluded, and the proportion of vegetables and dairy products increased. For phosphate stones, dairy products and highly alkaline mineral waters should be limited, while meat and acidic juices help to acidify the urine. Restricting table salt (to 5 g/day) and animal protein (to 0.8-1 g/kg) is recommended for most patients, because excess salt and protein increase calciuria and decrease citraturia. The meal pattern also matters: overeating and long intervals between meals are undesirable, and regular, small meals are preferred.

Pharmacological metaphylaxis is aimed at correcting the metabolic disorders identified. Thiazide and thiazide-like diuretics (hydrochlorothiazide, indapamide) are effective in hypercalciuria: they reduce urinary calcium excretion by enhancing its tubular reabsorption and thus lower the risk of calcium stones. For hypocitraturia, potassium citrate or potassium sodium citrate is prescribed; these agents alkalinize the urine and correct the citrate deficiency, significantly reducing the recurrence of calcium oxalate stones. In patients with low baseline citrate levels, citrate therapy more than halves the recurrence rate. In uric acid diathesis, allopurinol, a xanthine oxidase inhibitor that reduces uric acid synthesis, is used in addition to citrates; it is particularly indicated when urolithiasis is combined with gout or in patients with very high uric acid levels. In cystinuria, penicillamine or tiopronin, which form soluble complexes with cystine, are used. For infection stones, the most important metaphylactic measure is eradication of the infection with prolonged (up to 3-4 weeks) courses of antibiotics guided by urine culture, together with urinary antiseptics and acidifying agents (methenamine, ascorbic acid) to inhibit bacterial growth [42].

Regular follow-up is an essential part of prevention. Patients with a history of urolithiasis are advised to undergo urinalysis every 3-6 months and renal ultrasonography at least once a year (every 6 months in complicated cases). This allows early detection of newly forming stones or microliths. Herbal remedies are also widely used for prevention: preparations based on madder extract, phytoverzhinia and bearberry increase diuresis and have antispasmodic and anti-inflammatory effects, which may reduce the likelihood of stone formation. However, the evidence base for herbal medicines remains limited, and they should be regarded only as supportive measures.

Despite all these advances, current treatment and prevention methods do not guarantee freedom from recurrence. Data show that over 5 years of follow-up, up to half of patients develop new stones even with metaphylaxis. This may be due both to poor adherence (not all patients follow the diet and fluid regimen over long periods) and to the limitations of the methods themselves. For example, ESWL often fails to clear the stone completely: residual fragments (≤4 mm) remain in the kidney in 20-50% of cases and may form a steinstrasse ("stone street") in the ureter or serve as nuclei for new stone growth. If left untreated, such residual fragments lead to recurrence within months. Endoscopic procedures, although effective, do not address the underlying cause of stone formation, namely metabolic abnormalities. Without metabolic correction, the problem may

therefore recur even after complete stone removal. There are also difficult cases in which standard treatments are ineffective, for example multiple recurrent stones in primary hyperoxaluria or cystinuria, where even the most intensive prophylaxis reduces stone formation only partially. In infection-related nephrolithiasis, eradicating chronic infection is challenging: bacteria in the biofilm on the stone are resistant to most antibiotics, and a latent reservoir of infection may persist in the renal parenchyma after stone removal.

In recent years, efforts have been made in urology to develop mathematical models that predict the likelihood of recurrence in an individual patient. Such personalized prediction could help to identify high-risk groups that particularly need active metaphylaxis and, conversely, spare low-risk patients unnecessary interventions.

The development of reliable prognostic algorithms for the course of urolithiasis is therefore a pressing task for modern urology. Such algorithms would allow treatment to be personalized: patients at high risk of recurrence could receive the most intensive metaphylaxis and closer monitoring, whereas low-risk patients could avoid overtreatment. Prognostic tools would also help to evaluate the effectiveness of new preventive interventions. Equally important is the development of algorithms for choosing the optimal treatment method according to the characteristics of the stone and the patient. Current clinical guidelines provide detailed decision-making algorithms, for example flexible retrograde intrarenal surgery for a 1-cm stone in the lower calyx or staged PCNL for a staghorn stone. In complex cases, however, the choice of treatment may be ambiguous, and computerized decision support systems drawing on the experience of many centers may be helpful.

In conclusion, urolithiasis remains one of the most complex and challenging conditions in urology and requires a multidisciplinary approach. Modern diagnostic methods, especially CT and extended laboratory panels, make it possible in most cases to establish an accurate diagnosis and identify the causes of stone formation. Minimally invasive technologies have revolutionized treatment, making it less traumatic and more effective. However, the high recurrence rate calls for greater attention to metaphylaxis, and the limitations of current preventive approaches warrant further research, including the development of prognostic models and new pharmacological and non-pharmacological preventive measures. These promising directions can improve outcomes for patients with urolithiasis. Ultimately, the goal of modern urology is not only to remove stones effectively but also to prevent their formation, ensuring patients a long, stone-free life with preserved quality of life.

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