MEDICAL CARE OF CHILDREN WITH UROLITHIASIS

Learning guide for the 5th- and 6th-year students, trainee physicians, pediatricians, general practitioners

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

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МЕДИЧНА ДОПОМОГА ДІТЯМ З СЕЧОКАМ'ЯНОЮ ХВОРОБОЮ

Методичні вказівки для здобувачів вищої освіти 5–6-х курсів за спеціальністю «Медицина», лікарів-інтернів, лікарів-педіатрів, лікарів загальної практики – сімейної медицини

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Introduction and Definitions

Urolithiasis (UL) is a disease characterized by interstitial kidney processes caused by metabolic disorders. Kidney stones form due to a complex process involving metabolic, anatomical, and infectious factors.

Dysmetabolic nephropathy (DN) is a group of diseases of varying etiology and pathogenesis, marked by multiple metabolic disorders. The prevalence of DN in children has fluctuated between 11 % and 13 % in recent years. **Urolithiasis** is a common kidney disease characterized by the formation of stones (concrements) in the kidney's calyx-pelvic system. Kidney stones can develop at any age, including childhood.

Key Causes Leading to the Development of Urolithiasis:

- Hot climates or seasons (ambient temperature above 30 °C), which cause excessive sweating and increased concentration of salts in urine.
- Cold climates with prolonged insufficient sunlight.
- Vitamin D deficiency or excess in the diet.
- Limited fluid intake.
- Hard water, which contains high concentrations of calcium salts.
- Unbalanced and irregular diet: excessive intake of meat and fatty foods, leading to urate accumulation. Consistent consumption of dairy or plant-based foods can result in phosphate salt accumulation. Spicy foods, marinades, and seasonings contribute to the accumulation of oxalate salts.
- Sedentary lifestyle.
- Severe illnesses and injuries that lead to prolonged bed rest.
- Metabolic and water-salt imbalances.

Endocrine system disorders (parathyroid and gonadal glands).

Classification

Genetic Causes of Stone Formation:

- **Cystinuria**: Aminoaciduria, characterized by impaired tubular reabsorption of cystine, ornithine, arginine, and lysine.
- **Xanthinuria**: A hereditary deficiency of the enzyme xanthine oxidase.

Infectious Stones:

- Magnesium ammonium phosphate (struvite)
- Apatite
- Ammonium urate

Non-infectious Stones:

- Calcium oxalate
- Calcium phosphate
- Uric acid

Drug-Induced Stones:

- Allopurinol, amoxicillin, ceftriaxone, ciprofloxacin, ephedrine, indinavir, magnesium trisilicate, sulfonamide, triamterene.

Stone Size Classification:

- Stones are measured in millimeters and classified as follows: < 5 mm, 5–10 mm, 10–20 mm, and > 20 mm.

Stone Localization:

- Stones are classified based on their location within the urinary tract: upper, middle, or lower calyx, renal pelvis, upper, middle, or distal ureter, and the bladder.

Radiological Characteristics:

- **Radiopaque** and **radiolucent** stones.

ICD-10 Coding:

- Kidney and ureter stones (N20)
  - N20.0 – Kidney stones
  - N20.1 – Ureter stones
  - N20.2 – Stones in both kidney and ureter
  - N20.9 – Unspecified urinary stones
- Lower urinary tract stones (N21)
  - N21.0 – Bladder stones
  - N21.1 – Urethral stones
  - N21.8 – Other stones in lower urinary tract
  - N21.9 – Unspecified stones in lower urinary tract
- Urinary tract stones in diseases classified in other headings (N22)
- Unspecified renal colic (N23)

Diagnosis

Symptoms and History:

Main Symptom of Urolithiasis:

Pain, which can vary in nature. An attack of acute pain in the lower back, side, or upper abdomen is often accompanied by fever, nausea, vomiting, abdominal distension, and changes in the color and volume of urine.

If the following symptoms appear, children must be consult a doctor (pediatrician, pediatric nephrologist, or urologist) immediately:

- Pain (persistent or sharp) in the side, lower back, or groin.
- Changes in urine color (red tint of varying intensity, dark urine), urine cloudiness, or the presence of sediment and impurities.
- Fever accompanied by changes in urine color or transparency and pain in the lower back, side, or groin.
- Sudden onset of sharp pain after intense physical exertion, prolonged walking, riding on rough roads, or extended bed rest.

The leading signs of urolithiasis include pain, dysuria, hematuria, pyuria, and the passage of urinary salt crystals or stones. Of these, only the last is an absolute indicator. Pain is the most common symptom of nephrolithiasis, with varying characteristics depending on the stone's size, shape, and location. Vomiting and fever may also be present in some patients, though asymptomatic cases are possible.

When gathering patient history, it is essential to consider:

- A family history of urolithiasis or urinary system diseases
- Presence of urinary tract anomalies in the child
- Environmental factors
- Unhealthy lifestyle habits (smoking, alcohol consumption)
- The mother's pregnancy course

Etiopathogenesis:

Factors contributing to stone formation are both **endogenous** and **exogenous**.

Endogenous Factors:

- Parathyroid gland hyperfunction
- Vitamin imbalances
- Electrolyte disturbances (K, Ca, Mg)
- Diabetes
- Uric acid metabolism disorders
- Cystine and oxalate metabolism disorders
- Genetic predisposition
- Embryonic tissue development disorders

Exogenous Factors:

- Dietary habits
- Hydration levels
- Environmental factors
- Medications
- Climatic conditions in the region

Diagnostic Criteria for Crystalluria:

Phase of Metabolic Disorders	Laboratory Urinalysis
Salt Diathesis (Preclinical Phase)	Crystalluria, decreased urinary osmolality, elevated excretion of lipids, ethanolamine, and phosphoethanolamine without significant reduction in renal function
Dysmetabolic Nephropathy (DN)	Signs of salt diathesis + urinary syndrome (minimal hematuria, proteinuria, bacterial leukocyturia), increased urinary specific gravity
Tubulointerstitial Nephritis	Pronounced hematuria and proteinuria (tubular type proteinogram), eosinophiluria, non-selective hyperaminoaciduria, elevated excretion of urinary enzymes, microalbuminuria, decreased urinary specific gravity
Urolithiasis	Stone passage, hematuria (micro- or macroscopic), leukocyturia, elevated phospholipid excretion

Physical Examination:

- In renal colic, the patient may exhibit restlessness, struggling to find a comfortable position. The "psoas sign" is common. Younger children may present with more general symptoms of the pathological process and less specific local symptoms.

Laboratory Indicators:

Urine Testing:

- Sediment analysis or test strip analysis for:
  - Red blood cells
  - White blood cells
  - Nitrites
  - pH (approximate value)
  - Amino acid spectrum
  - Urinary uric acid

Bacterial culture or microscopic urine examination.

Blood Analysis:

- Serum creatinine
- Uric acid
- Ionized calcium
- Sodium
- Potassium
- Magnesium
- Parathyroid hormone, Vitamin D

General blood test

C-reactive protein

For planned or possible surgical treatment: **coagulation profile** (APTT and INR).

In all cases of newly diagnosed urolithiasis, it is recommended to conduct an analysis of the stone composition using analytical methods such as X-ray diffraction or infrared spectroscopy. (Strength of recommendation 1; evidence level B).

Instrumental Diagnostics:

- **Ultrasound (US)** of the urinary system is recommended as the primary diagnostic tool (Strength of recommendation 1; evidence level B).
- **X-ray** of the urinary system is recommended to differentiate radiopaque and radiolucent stones and for dynamic monitoring (Strength of recommendation 2; evidence level C).
- **Spiral computed tomography (CT)** of the urinary system is recommended in cases of acute lumbar pain to determine the presence, size, and density of the stone (Strength of recommendation 1; evidence level A).

Indications for Hospitalization:

- Severe pain, the presence of stones > 15 mm with a low likelihood of spontaneous passage, or impaired renal function.

Treatment Recommendations:

Conservative Treatment:

If stones are asymptomatic, it is recommended to begin treatment conservatively. **Litholytic therapy** can facilitate the passage of stones and reduce the need for surgery (Strength of recommendation 1; evidence level C).

Fluid Intake:

There is an inverse relationship between stone formation and high fluid intake. Patients at risk for stone formation are recommended to maintain high diuresis and drink plenty of fluids.

Diet Recommendations:

- **Oxalates**: Limit foods high in oxalates to avoid excessive intake, especially in patients with elevated oxalate excretion.
- **Vitamin C**: While Vitamin C is a precursor to oxalate, its role as a risk factor for calcium oxalate stone formation is controversial. However, it is advisable to recommend that patients at risk for calcium oxalate stones avoid excessive Vitamin C intake.

- **Animal proteins**: Avoid excessive consumption. A diet high in animal proteins promotes factors that contribute to stone formation.
- **Calcium**: Calcium intake should not be restricted unless contraindicated, as a low-calcium diet can promote calcium stone formation. Calcium supplements should only be prescribed in cases of intestinal hyperoxaluria. Calcium intake recommendations for children:
  - Under 3 years: 600 mg/day
  - 4–10 years: 800 mg/day
  - 10–13 years: 1000 mg/day
  - 13–16 years: 1200 mg/day
  - Over 16 years: 1000 mg/day.
- **Sodium**: High sodium intake negatively affects urine composition by increasing calcium excretion and lowering citrate levels, raising the risk of sodium urate stone formation. Limiting sodium and animal protein intake (to 2 g/kg/day) can reduce the risk of calcium stone formation.
- **Uric acid**: Limit foods rich in purines in patients at risk of calcium oxalate stones caused by hyperuricosuria, as well as in patients at risk of uric acid stones.

Lifestyle:

Certain studies indicate that stone formation is linked to lifestyle factors such as excessive body weight and obesity.

Renal Colic:

Initial treatment of renal colic should focus on pain relief. Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended due to their high effectiveness (Ibuprofen can be prescribed for children weighing over 20 kg (6 years and older) and adults. The recommended daily dose is 20–30 mg/kg, not exceeding 30 mg/kg/day. Children weighing 20–30 kg (6–11 years) should take 200 mg (one tablet) per dose, with repeat doses every 6 hours if necessary. The daily dose should not exceed 600 mg (three tablets). Adults and children over 30 kg should take 200–400 mg per dose, with repeat doses every 4–6 hours. The daily dose should not exceed 1200 mg) (Strength of recommendation 1; evidence level C).

Oral Litholytic Therapy:

This approach is effective with a high level of compliance from parents, caregivers, and the patient. The treatment involves **alkalizing urine** using nitrate mixtures or sodium bicarbonate (sodium bicarbonate is prescribed for children over 1 year at a dose of 5–7 ml per kg of body weight). The urine pH should be adjusted to 7.0–7.2, with the alkalizing dose individualized. Urine pH should be measured regularly using test strips throughout the day.

Hyperoxaluria:

Early diagnosis and proper management can significantly influence the course of the disease. It is recommended to consider prescribing **Vitamin B6** (orally, at a dose of 10 mg/kg/day) in cases of hyperoxaluria, as most patients exhibit a positive response to this treatment (Strength of recommendation 1; evidence level C).

Prolonged administration of **citrate** (Blemaren, with parental consent) is recommended for hyperoxaluria, which significantly reduces the recurrence of

urolithiasis (Strength of recommendation 1; evidence level C). The highest solubility of calcium oxalate is achieved at a pH of 6.2–6.8. Therapeutic doses of citrate range from 0.1 to 0.15 g/kg/day (Blemaren, with parental consent).

Dietary calcium should not be restricted in hypercalciuria, as a deficiency in the intestine leads to increased oxalate absorption, raising the risk of urolithiasis recurrence (Strength of recommendation 1; evidence level C).

Nephrocalcinosis:

This condition involves the diffuse deposition of calcium salts in the kidney's interstitium, glomeruli, and renal arterioles, accompanied by inflammatory and sclerotic changes, and renal failure. Therapy includes increasing water intake, excluding calcium-rich foods, and prescribing medications that disrupt calcium reabsorption in the loop of Henle and promote calcium excretion in the urine (Furosemide, Calcitonin). Citrate mixtures can also be used.

Treatment of Calcium-Phosphate Stones:

Therapy is only effective if the stones are fully removed.

Struvite and (e.g., uroantiseptics in prophylactic doses – Furagin, Furamag, Trimethoprim) (Strength of recommendation 1; evidence level C).

Treatment of Cystine Stones:

To prevent cystine crystallization, the primary recommendation is to maintain urine pH above 7.5 to increase cystine solubility and ensure adequate fluid intake – at least 1.5 liters per m² of body surface area in children (Strength of recommendation 1; evidence level C).

It is recommended to use the following regimen for cystine stones: **citric acid/potassium bicarbonate/sodium citrate** (Blemaren, with parental consent), with dosage adjusted individually according to the medication instructions to maintain urine pH above 7.5 for 6 months, under medical supervision, with regular urinalysis at least once a month (Strength of recommendation 1; evidence level C).

Surgical Treatment:

Effective methods for removing stones in children currently include **extracorporeal shock wave lithotripsy (ESWL)**, **contact lithotripsy with lithoextraction**, and **percutaneous nephrolithotomy** (Strength of recommendation 1; evidence level C).

Recommendations for Active Stone Removal:

- Stones with a low probability of spontaneous passage
- Persistent pain despite adequate analgesia
- Persistent obstruction
- Renal function impairment (renal failure, bilateral obstruction, solitary kidney).

Active stone removal is also recommended for kidney stones in the following cases:

- Stone growth
- Stones in patients at high risk of stone formation
- Stones causing obstruction
- Stones accompanied by infection

- Stones causing clinical symptoms (e.g., pain, hematuria)
- Stones larger than 15 mm
- Stones smaller than 15 mm if observation is not preferred
- Stones persisting for more than 2–3 years

Prevention and Follow-Up:

Medication Prevention of Recurrence:

Patients at high risk of recurrent stone formation should undergo pharmacological treatment. Medical treatments are usually combined with general preventive measures. It is recommended to prescribe medications that prevent stone formation, have minimal side effects, and are easy to use. These factors are critical for ensuring patient adherence to the treatment regimen (Strength of recommendation 1; evidence level C).

Alkaline Citrates:

Common alkalizing agents include **potassium citrate**, **sodium citrate**, **potassium magnesium citrate**, **potassium bicarbonate**, and **sodium bicarbonate**. Sodium citrate and potassium bicarbonate are components of **Blemaren** (prescribed with parental consent).

Magnesium:

Magnesium (Magnesium B6 for children over 6 years weighing over 20 kg: 10–30 mg/kg/day or 0.4–1.2 mmol/kg/day, corresponding to 4–6 tablets daily, divided into 2–3 doses during meals). Magnesium oxide, magnesium hydroxide, potassium magnesium citrate, and magnesium aspartate are prescribed to increase magnesium excretion in the urine. Elevated urinary magnesium levels decrease calcium oxalate ion activity and inhibit calcium phosphate crystal growth. However, magnesium should not be prescribed as monotherapy.

Allopurinol:

Allopurinol is used to prevent the recurrence of calcium oxalate stones, as hyperuricosuria is associated with such stones. Children and adolescents weighing ≥ 45 kg should take 10 mg/kg/day, divided into three doses. The maximum daily dose is 400 mg (tablets of 100 mg).

Pyridoxine:

Pyridoxine is recommended at a dose of 1–2 mg/kg/day for one month. Since no other effective treatments exist, pyridoxine is used to reduce oxalate excretion in patients with primary hyperoxaluria type 1.

L-methionine:

Urine acidification can be achieved with the sulfur-containing amino acid **L-methionine** at a dose of 600–1500 mg/day. Methionine lowers urine pH by acting as a proton donor (hydrogen ions). However, maintaining consistently low pH levels is difficult, and prolonged urine acidification is not recommended in children.

Canephron N:

Canephron N has a complex action: it is diuretic, anti-inflammatory, antispasmodic, antioxidant, and nephroprotective, reducing capillary permeability and enhancing the effects of antibiotics.

Follow-Up:

Follow-up lasts at least 5 years and includes:

- Specialist evaluations:
  - Pediatrician: once a month.
  - Nephrologist: every 2–3 months.
  - Urologist: every 3–6 months.
  - Dentist: every 6 months.
  - Ophthalmologist: annually.
  - ENT specialist: annually.
- Laboratory tests:
  - General urine analysis: every 3 months and as needed.
  - Blood biochemistry: every 3 months during the first year, then every 6 months.
  - Ultrasound of the urinary system: every 3 months during the first year, then every 6 months.
  - X-ray: abdominal overview and excretory urography as needed.
  - Urine culture with antibiotic sensitivity testing: after therapy and periodically.
  - pH measurement of urine: once every 3 months during the first year, for 3–5 days. Keep a diary of urine pH values.

Prevention of Urolithiasis:

Preventing the disease is easier than treating it. Effective preventive measures include:

- **Physical activity**: Exercise improves blood circulation in the pelvic region, preventing stone formation.
- **Adequate fluid intake**: Ensure a good hydration regime, especially in hot weather. Water balance is closely related to mineral balance, and a lack of fluids leads to a higher concentration of salts in the urine.
- **Balanced diet**: The diet should include sufficient vitamins D, C, and A.
- **Consult a doctor immediately**: If any suspicion of urolithiasis arises, seek medical advice promptly.

SELF-ASSESSMENT TESTS

1. A 16-year-old patient experiences acute paroxysmal pain in the right lumbar region radiating along the ureter, with frequent urges to urinate. Urinanalysis shows protein at 0.033 g/L, leukocytes 2–3 per field of vision, and fresh erythrocytes 10–20 per field of vision. Which of the following is the diagnosis?

A. Acute appendicitis. *C. Right-sided renal colic.* *E. Acute adnexitis.*
B. Perforated gastric ulcer. *D. Acute cholecystitis.*

2. A 12-year-old patient has had acute paroxysmal pain in the right lumbar region radiating to the genitals for three days. On the second day, fever up to 40°C, chills, and profuse sweating appeared. The right kidney is palpable, lumbar muscles are tense, and the Pasternatsky symptom is positive. Urine analysis shows protein at 0.033 g/L, and leukocytes present throughout the field of vision. Ultrasonography reveals an enlarged right kidney with dilated pelvis and ureter. Which of the following is the diagnosis?

A. Acute appendicitis . *D. Acute cholecystitis.*
B. Intestinal obstruction. *E. Right-sided renal colic.*
C. Acute pyelonephritis.

3. A 14-year-old patient had a boil on the back two weeks ago. Three days ago, high fever up to 39 °C with chills and pain in the right lumbar region began. The condition is moderately severe, pulse 100 bpm, BP 130/80, dry tongue. The abdomen is soft but painful in the right lumbar region. Urination is frequent. Urinanalysis shows protein at 0.033 g/L, 24-35 leukocytes per field of vision, bacteria, and 0-1 erythrocytes per field of vision. Blood analysis reveals leukocytosis at 15,000 with 15 % band neutrophils and ESR of 28 mm/hour. Which of the following pathological process caused this condition?

A. Right-sided acute pyelonephritis. *D. Acute pancreatitis.*
B. Acute appendicitis. *E. Acute pyelonephritis.*
C. Acute cholecystitis.

4. Which of the following is primary stone formation site:

A. Renal pelvis and calyces. *C. Urethral orifice.* *E. Bladder.*
B. Ureter. *D. Urethra.*

5. Which of the following is the leading diagnostic method for kidney stone disease:

A. Radioisotope investigation methods. *D. Laboratory blood tests.*
B. Laboratory urine tests. *E. Medical history collection.*
C. Ultrasound examination.

6. Which of the following types of urinary stones are characyetrized by an intense acoustic shadow on ultrasound examination:

A. Oxalates. *C. Urates.* *E. All answers are correct.*
B. Phosphates. *D. Cystine stones.*

7. Which of the following is the most characteristic treatment for relieving renal colic:

A. Antibiotics. *C. Herbal preparations.* *E. Diuretics.*
B. Analgesics and antispasmodics. *D. Antispasmodics.*

8. Which of the following is the absolute sign of urolithiasis:

A. Dysuria. *B. Hematuria.* *C. Passage of stones.* *D. Pyuria.* *E. Leukocyturia.*

9. Which of the following can secondary hematuria indicate:

A. Chronic pyelonephritis. *D. Glomerulonephritis.*
B. Kidney stone disease. *E. All answers are correct.*
C. Renal cancer.

10. A 13-year-old patient presents with dull pain in the lumbar region, fatigue, and polyuria. She has been ill for a year. The patient's mother has a kidney development anomaly. On examination, the condition of the patient is moderately severe, the skin is, the tongue is dry, BP is 170/100 mmHg, and pulse is 80 bpm. The lungs and heart are normal. The abdomen is soft; enlarged, firm, nodular kidneys are palpable in both the right and left lumbar regions. Urination is normal, with up to 3 liters of urine output. Urinanalysis shows protein at 0.099 g/L, specific gravity 1010, leukocytes up to 100 in urine, fresh erythrocytes 5–6, and bacteria present. Blood creatinine is 240 μmol/L. Which of the following is the diagnosis?

A. Kidney hydronephrosis. *C. Kidney stone disease.* *E. Renal colic.*
B. Polycystic kidney disease. *D. Kidney tumor.*

1	2	3	4	5	6	7	8	9	10
C	*C*	*E*	*A*	*C*	*E*	*B*	*C*	*C*	*B*

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Навчальне видання

МЕДИЧНА ДОПОМОГА ДІТЯМ З СЕЧОКАМ'ЯНОЮ ХВОРОБОЮ

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