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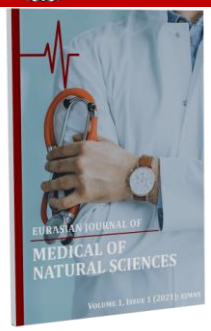

# BASICS OF MODERN PREVENTION OF NEPHROPATHY IN CHILDREN

**Akhmatova Yulduz Ablakulovna**
Assistant, PhD, Department of Pediatrics №2,
Samarkand State Medical University, Samarkand, Uzbekistan
E-mail: isomiddinov.1986@mail.ru
ORCID: 0000-0002-2895-8849
**Alimova Ozoda Bekmurodovna**
Assistant, Department of Physiology,
Samarkand State Medical University, Samarkand, Uzbekistan
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*Children, kidneys, dysmetabolic nephropathy, chronic kidney disease, chronic renal failure, preventive prophylaxis.*

**ABSTRACT**

*This study, based on our own research and recent literature sources, investigates the risk factors influencing the development and progression of nephropathies (genetic, teratogenic, environmental). Timely identification of these factors and adherence to simple preventive measures (diet, fluid regimen, maintaining a favorable microclimate, eliminating infectious, toxic, and allergic influences, and correcting dysmetabolism) can prevent complications such as interstitial nephritis (IN), urolithiasis (UL), secondary dysmetabolism (SDM), and secondary pyelonephritis. Environmental factors contributing to the manifestation of pathology in children with metabolic disorders include seasonal climate changes—adaptation to low and high temperatures, dietary errors, emotional and physical overloads, membranopathies, and intercurrent diseases. It has been established that the presence of hidden diathesis in a child from a family with a predisposition to certain diseases (family history, hereditary burden index) can be determined using biochemical, immunological, and functional tests. A scheme for preventive and metafilactic measures for nephropathies in uric acid diathesis has been developed.*

# ОСНОВЫ СОВРЕМЕННОЙ ПРОФИЛАКТИКИ НЕФРОПАТИЙ У ДЕТЕЙ

**Ахматова Юлдуз Аблакуловна**
Ассистент, PhD, кафедра Педиатрии №2, Самаркандский государственный медицинский университет, Самарканд, Узбекистан
E-mail: isomiddinov.1986@mail.ru
ORCID: 0000-0002-2895-8849
**Алимова Озода Бекмуродовна**
Ассистент, кафедра Физиологии,
Самаркандский государственный медицинский университет, Самарканд, Узбекистан.
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*Дети, почки, дизметаболические нефропатии, хроническая болезнь почек, хроническая почечная недостаточность, превентивная профилактика.*

**ABSTRACT**

*В данном исследовании на основе собственных данных и литературных источников последних лет изучены факторы риска, влияющие на развитие и прогрессирование нефропатий (наследственные, тератогенные, внешнесредовые). При своевременном выявлении этих факторов и соблюдении простых профилактических мер (диета, режим потребления жидкости, поддержание оптимального микроклимата, устранение инфекционных, токсических и аллергических воздействий, коррекция дизметаболизма) можно избежать осложнений, таких как интерстициальный нефрит (ИН), мочекаменная болезнь (МКБ), вторичный дизметаболизм (ДЗМ) и вторичный пиелонефрит. К факторам внешней среды, способствующим проявлению патологии у детей с обменными нарушениями, относятся сезонные климатические колебания, адаптация к низким и высоким температурам, ошибки в питании, эмоциональные и физические перегрузки, мембранопатии и интеркуррентные заболевания. Установлено, что наличие скрытого диатеза у ребенка из семьи с предрасположенностью к определенным заболеваниям (по родословной, индекс наследственной отягощенности) можно выявить с помощью биохимических, иммунологических и функциональных исследований. Разработана схема проведения превентивной профилактики и метафилактики нефропатий при мочекислом диатезе.*

# BOLALARDA NEFROPATİYANI ZAMONAVIY PROFILAKTIKASI ASOSLARI

**Axmatova Yulduz Ablakulovna**
Samarqand davlat tibbiyot universiteti 2-son Pediatriya kafedrasi assistenti,
PhD. E-mail: isomiddinov.1986@mail.ru
ORCID: 0000-0002-2895-8849
**Alimova Ozoda Bekmurodovna**
Samarqand davlat tibbiyot universiteti Fiziologiya kafedrasi assistenti
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**ABSTRACT**

*Ushbu tadqiqotda, so‘nggi yillarda o‘z tadqiqotlarimiz va adabiyot manbalariga asoslanib, nefropatiyalar (irsiy, teratogen, tashqi muhit omillari)ni rivojlanishiga va*

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*Bolalar, buyraklar, dismetabolik nefropatiya, surunkali buyrak kasalligi, surunkali buyrak etishmovchiligi, profilaktika profilaktikasi.*

*progressiyasiga ta'sir etuvchi xavf omillari o'rganildi. Ushbu xavf omillarini vaqtida aniqlash va oddiy profilaktik choralarni (diyeta, suyuqlik rejimi, mikroiqlimni saqlash, infeksion, toksik va allergik ta'sirlardan himoya qilish va dizmetabolizmni tuzatish) qo'llash orqali nojo'ya oqibatlarning oldini olish mumkin (interstitsial nefrit (IN), siydik tosh kasalligi (STK), ikkilamchi dizmetabolizm (DZM), ikkilamchi piyelonefrit). Tashqi muhit omillari, xususan, bolalarda metabolik buzilishlar mavjud bo'lgan hollarda patologiyaning namoyon bo'lishiga sabab bo'ladigan omillar sifatida fasllararo iqlim o'zgarishlari – past va yuqori haroratlarga moslashish, oziqlanishdagi xatolar, emotsional va jismoniy yuklar, membranopatiyalar va interkurrent kasalliklar keltiriladi. Boshqa tomondan, bola oilasida aniq bir kasalliklarga moyillik mavjudligini (nasl-nasab, meros bo'yicha yuklanganlik indeksi) biokimyoviy, immunologik va funksional tadqiqotlar yordamida aniqlash mumkin. Siydik kislota diatezi bo'lgan nefropatiyalarni oldini olish va metafilaktikasi bo'yicha profilaktik chora-tadbirlar sxemasi ishlab chiqilgan.*

**Introduction.** The primary strategy of preventive medical practice is not the diagnosis of early disease stages but active prevention of morbidity. This requires reorienting the activities of family doctors and primary healthcare providers toward identifying hereditary predispositions (diatheses), borderline conditions, and implementing preventive measures at this level [2, 11, 19].

The significant and increasing prevalence of urinary system diseases (USD) in both adult and pediatric populations, their tendency to recur and chronicize, leading to chronic renal failure (CRF) requiring replacement therapy in childhood and young adulthood, makes the development of preventive nephrology highly relevant [10, 13, 22, 23]. Risk factors influencing the formation and progression of nephropathies (hereditary, teratogenic, environmental) are intensively studied worldwide [9, 24].

In our context, the combination of natural climatic-geographic ecopathogenic factors (heat load, hyperinsolation) with high technogenic xenobiotic load and a high inbreeding coefficient (frequency of consanguineous marriages) are extreme risk factors for disease formation in predisposed individuals. Increasingly, it is noted that the prevalence of chronic somatic diseases, particularly chronic kidney disease (CKD), has reached epidemic proportions in recent decades [10, 13]. Primary prevention of nephropathies is emphasized as a priority, given the inevitable progression of CKD regardless of nosology, leading to CRF at varying intervals [22, 23].

In the existing system of specialized nephrological care, particular attention should be paid to the outpatient stage (polyclinic). It is here that the origins of the disease are first

identified, risk groups are formed, primary diagnosis of nephropathy is conducted, and children are monitored and rehabilitated [2]. Family doctors must maintain nephrological vigilance, paying close attention to minimal renal changes-isolated proteinuria, microhematuria, crystalluria, etc., as well as markers of potential predisposition to nephropathy.

Reorienting the dispensary service toward preventive prophylaxis and organizing specialized laboratories to identify individuals predisposed to certain diseases represent a qualitatively new level of dispensary care, requiring new approaches, particularly in laboratory services: improvement and centralization at the city or district level, considering the requirements of preventive medicine [8].

Currently, in the general nosological structure of kidney diseases, the frequency of various dysmetabolic nephropathies (DMN) is significantly higher than other kidney diseases [9]. However, with timely identification and adherence to simple preventive measures (diet, fluid regimen, maintaining a favorable microclimate, eliminating infectious, toxic, and allergic influences, and correcting dysmetabolism), complications such as interstitial nephritis (IN), urolithiasis (UL), secondary dysmetabolism (SDM), and secondary pyelonephritis can be prevented.

Environmental factors contributing to the manifestation of pathology in children with metabolic disorders include seasonal climate changes-adaptation to low and high temperatures, dietary errors, emotional and physical overloads, membranopathies, and intercurrent diseases [22]. It can be asserted that the current scientific concept meeting the requirements of preventive medicine involves actively identifying children with hereditary predispositions (diatheses), borderline conditions, and early correction to prevent clinical manifestation [2, 7].

Materials and Methods. Thus, life has dictated the necessity of developing and implementing principles of prenosological diagnosis and dispensary care in nephrology. For this, convincing prerequisites have been created to orient the activities of family doctors primarily toward prevention:

1. Primary prevention of nephropathies in children with diatheses (hereditary predisposition) is organized using non-invasive and predominantly non-pharmacological methods (regimen, microclimate, diet, herbal remedies, physical therapy, elimination of chronic infection foci - healthy lifestyle).

2. Priority of preventive prophylaxis of DMN involves implementing these measures at the preclinical stage.

3. CKD often originates in childhood, with objective signs of predisposition observable even in newborns (family history of nephropathy, maternal urinary system diseases, etc.). Early identification of risk factors, hereditary predisposition, and elimination of exogenous risk factors (avoiding nephrotoxic drugs, membrane-reparative therapy in early neonatal periods for nephropathic fetopathy, etc.) are significant but underutilized resources that can greatly enhance the effectiveness of family doctors' preventive activities [2, 11].

4. The role of family doctors in pediatric nephrological care is established, but priority in forming and qualitatively monitoring children at risk of urinary system diseases is still

lacking. The contingent of children requiring nephrological vigilance in dispensary care is significant.

Follow-up over six years of children who experienced nephropathy in the neonatal period showed complete recovery in only 15%, with the rest exhibiting various urinary system pathologies [13].

Recent studies have revealed pathological kidney immaturity in 62–74% of full-term pregnancies in children of mothers with chronic pyelonephritis complicated by OPG gestosis [7, 8]. Thus, maternal kidney pathology and gestosis are risk factors for impaired nephrogenesis, forming the basis for postnatal nephropathy development.

Observation of 68 children born to mothers with kidney pathology (GN, PN) over 13 years showed that 60% developed some form of kidney disease [2]. Newborns whose gestation occurred against OPG gestosis combined with chronic pyelonephritis, even without pronounced dysadaptation syndromes, require early neonatal antioxidant supplementation to prevent critical conditions and chronic somatic pathology development [18, 19]. The cornerstone of active prevention for all multifactorial diseases is early identification of hereditary predispositions (diatheses) and implementing preventive measures at this level [8]. "Diathesis is neither a disease nor a pre-disease nor a borderline condition; it is merely a predisposition to certain diseases, enabling the development of preventive pediatrics" [11]. However, there is no clear boundary between "predisposition" (diathesis) and so-called "borderline states," nor between the latter and early pathology manifestations. Regarding the urinary system, M.S. Ignatova (2013) defines it as follows: "Structural changes of anatomical, histological nature, biochemical shifts occurring at cellular and subcellular levels in the kidneys until they cause manifestations of syndromes characteristic of kidney pathology can be considered borderline states." Preventive measures, considering the nature of predisposing factors, are of a preventive nature. Determining the type of diathesis should dictate recommendations for preventing specific diseases [13], necessitating clear diagnostic criteria. Four variants of such predispositions are identified: allergic, dysmetabolic, organ (systemic), and neurotropic [5]. Within these groups, there are many more subtypes of diatheses than listed here. Thus, active monitoring of children with diatheses, organizing rational nutrition considering the diathesis type, and active hygienic education constitute elements of preventive morbidity prevention.

**Results.** Dysmetabolic nephropathies in these families often manifest against oxidative stress (OXSTR) during respiratory infections (ARVI, pneumonia, bronchitis), which is an important pathogenetic mechanism for the development and progression of urinary system diseases [8]. This mechanism is relevant for all types of diatheses, especially for families with calculous (oxalate-calcium) diathesis, characterized by familial cytomembrane instability.

Additionally, there is a known interrelationship between pulmonary ventilation and renal hemodynamics (respiratory-renal syndrome), i.e., maladaptive vascular reactions in bronchopulmonary diseases lead to reduced renal hemodynamics and glomerular filtration, causing nephrological issues in pulmonological patients, especially with hereditary predisposition.

For individuals with calculous diathesis, triggering factors for pathology onset may include:

- Hyperinsolation, promoting oxidative stress, and other factors with similar mechanisms, infections, etc.;
- Excessive consumption of oxalate-rich foods, excess vitamin C, and foods rich in it;
- Vitamin B6 deficiency;
- Reduced activity of intestinal microflora - Oxalobacter formigenes.

One pathway for preventive prophylaxis in these cases, alongside other measures, may involve developing dietary products limiting oxalagenic substances while enriching them with natural protective factors—vitamins F, E, etc. [2]. In situations promoting oxidative stress, alongside eliminating the primary factor, prescribing complex antioxidant preparations like Vetonon (containing water-soluble β-carotene, vitamins C and E) or Kudesan (containing ubiquinone and vitamin E) is indicated.

The priority of preventive clinical medicine necessitates elevating biochemical, immunological, and functional studies to a new level, enabling the identification of hereditary predisposition markers, achievable through creating large centralized laboratories [24].

The presence of hidden diathesis in a child from a family predisposed to certain diseases (family history, hereditary burden index) can be determined using biochemical, immunological, and functional tests. Preventive and metafilactic measures for nephropathies in uric acid diathesis are outlined as follows (Table 1):

**Table 1. Preventive and Metafilactic Measures for Nephropathies in Uric Acid Diathesis**

| Health Group | Markers | Preventive and Metafilactic Measures | Prevention Level |
|---|---|---|---|
| I – Healthy Children | No hereditary, biological, or social burden; normal pregnancy and delivery; normal physical and neuropsychic development; sufficient body resistance; no functional deviations in organs and systems; absence of chronic diseases and congenital anomalies | Monitoring and advice on feeding, care, and hardening at decreed times | I |
| II – Children with Uric Acid Diathesis | - Uricopathic spectrum in family history with hereditary index > 0.7; - Hyperuricemia > 0.230 mmol/L; - Hyperuricosuria, uraturia; - High xanthine oxidase activity | Low-purine diet, allopurinol in metabolic-type hyperuricemia, microclimate regulation, fluid regimen, vitamin therapy | I |

| | | | |
|---|---|---|---|
| III – Children with Uric Acid Diathesis Complicated by Pyelonephritis | Clinical-laboratory picture of pyelonephritis | 1. Potato diet for 2–3 weeks, followed by low-purine diet; 2. Allopurinol, potassium orotate as indicated; 3. Prevention of crystalluria, vitamin therapy; 4. Antibacterial therapy under bacteruria control | II |
| - IN | Clinical-laboratory picture of interstitial nephritis | 1, 2, 3, Delagil, antioxidants, membrane-protective therapy | II |
| - UL | Clinical-radiological and laboratory picture of urolithiasis | 1, 2, 3. Conservative therapy for uric acid lithiasis; 5. Surgical treatment as indicated | II |
| Autoimmune Overlay and Development of Hyperuricemic Glomerulonephritis in Compensated Stage | Extrarenal and renal clinical-laboratory syndromes of glomerulonephritis; renal function volume 80–50% of normal; blood creatinine 0.088–0.265 mmol/L; instrumental signs of pyelonephritis, interstitial nephritis, glomerulonephritis, urolithiasis; impaired partial and tubular renal functions | 1, 2, 3, glucocorticoids, cytostatics, heparin, antihistamines, symptomatic therapy | II |
| IV – All Listed Groups with Uric Acid Diathesis in Subcompensated Stage | Renal function volume 50–25%; active nephrons <30%; blood creatinine 0.12–0.53 mmol/L | Conservative therapy aimed at preserving residual renal function, | II |

| | | | |
|---|---|---|---|
| | | renoprotective therapy to slow nephrosclerosis | |
| V – All Listed Groups with Insufficient Renoprotective Therapy at Risk of CRF with Decompensated Renal Function | Renal function volume <30%; active nephrons <30%; frequent osteodystrophy, anemia, arterial hypertension, cardiovascular complications; blood creatinine 0.485–0.8 mmol/L | Conservative therapy aimed at correcting metabolic disorders, preventing complications; dialysis therapy if GFR <5 mL/min/1.73 $m^2$, creatinine >1.2 mmol/L, potassium >6.5 mmol/L | III |

Hereditary predisposition to many diseases (diatheses) remains latent for a long time and only under certain conditions transitions into a borderline state (appearance of microsigns of disease or its biochemical markers) or directly into disease. Even nephropathies in children living in ecologically unfavorable regions polluted with heavy metals primarily manifest in individuals with hereditary predisposition. Children with dyspurinosis constitute an immunocompromised contingent, as lymphocyte maturation and differentiation processes are involved [4], making 1–2 annual courses of immunocorrective agents (prodigiosan, lysozyme, levamisole) desirable. In dysmetabolic diatheses, the kidneys are primarily affected as the main elimination organ. However, without timely correction of metabolic disorders, various organs and systems may be affected (Fig. 1).

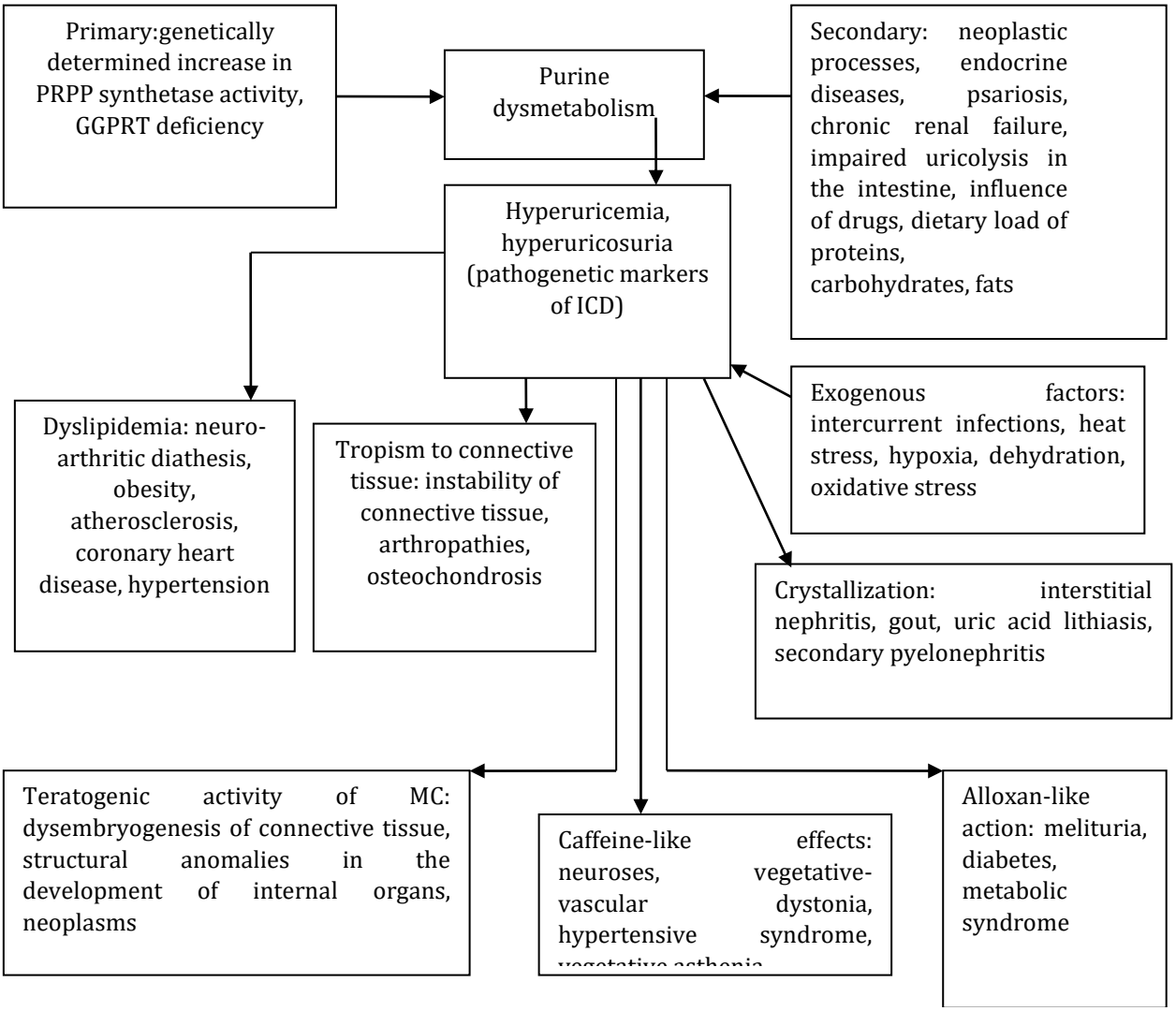


Fig. 1. Mechanisms of formation of multifactorial diseases with purine dysmetabolism

This is particularly evident in the formation of "uricopathies" in children and adults. Here, applying a low-purine diet before clinical manifestation, measures affecting purine metabolism and renal excretion through sequential use of allopurinol, magurlit, urodan, canephron, etc., in age-appropriate doses under urine reaction control, constitutes preventive prophylaxis of uricopathies, including urate nephropathies.

**Discussion.** The traditionally established system of specialized pediatric nephrological care is undoubtedly progressive but requires improvement based on scientific and practical achievements of 21st-century pediatric nephrology [24]. Reorienting the dispensary service toward preventive prophylaxis naturally requires organizational solutions: creating large preventive centers with appropriate equipment and staffing, utilizing large multidisciplinary hospitals for these purposes, etc., i.e., significant qualitative changes in both the structure and content of the dispensary service are necessary. A system of dispensary care for children who have experienced critical conditions at birth and mandatory long-term monitoring of children who have experienced nephropathy in the neonatal period using diagnostic methods accepted in nephrological practice is needed. The scope of preventive measures for nephropathies depending on the nature of the risk factor (predisposition) at various age periods is not yet

fully developed. Clear task lists must be formulated for each stage. Such a system should likely be multi-stage: antenatal, perinatal, neonatal, pediatric, and adolescent. Ensuring mutual acceptability among specialists (obstetrician-gynecologist, neonatologist, pediatrician, therapist) is necessary.

**Conclusion.**

1. The existing system of specialized pediatric nephrological care requires improvement with an emphasis on modern preventive nephrology achievements.

2. The priority of primary prevention of chronic urinary system diseases necessitates significantly strengthening specialized nephrological services at the primary level, creating diagnostic centers to identify pathogenetic markers of hereditary predisposition.

3. Strategically important is organizing preventive centers with corresponding biochemical, immunological, and genetic services to identify borderline states.

4. At the current level of scientific medicine, it is still difficult to assert the complete understanding of etiological and pathogenetic mechanisms in many chronic somatic diseases, making recommended preventive measures predominantly presumptive and requiring further refinement.

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