

**MINISTRY OF HEALTHCARE OF UKRAINE  
HSEEU "Ukrainian Medical Stomatological Academy"**

**"Approved"**  
at the meeting of internal  
medicine №1 department  
Head of Department  
**Prof. Skrypnyk I.M.**

---

Protocol № 4 from 13.10.2016

**GUIDELINES  
FOR STUDENTS  
INDEPENDENT WORK  
IN THE PRACTICAL CLASSES PREPARING**

<i>Academic discipline</i>	Internal medicine
<i>Module</i>	Current practice of internal medicine
<i>Content module</i>	Management of the patients with main symptoms and syndromes in nephrology clinic
<i>Study subject</i>	<b>Management of the patients with urinary syndrome</b>
<i>Course</i>	VI
<i>Faculty</i>	of foreign students training

### 1. Actuality of the topic

An urinary syndrome is observed at the different pathologies, that does this theme actual in professional activity of all specialities physicians.

Necessity of study of the "Urinary syndrome" theme in the clinic of internal diseases was conditioned by considerable prevalence of clinical displays, clinical course severity, possibility of latent clinical course, more often in the the young and middle aged persons.

### 2. The aims of the training course:

#### To Know:

1. Definition and classification.
2. Etiological factors.
3. Classification.
4. Pathogenesis of lesions in organs and systems, their clinical manifestations.
5. Clinic and laboratory parameters.
6. Differential treatment at different stages.
7. Weather and performance.

#### To be able to:

- Conduct surveys and examination of patients with major nephrological syndromes
- Know the basic invasive and noninvasive diagnostic techniques used in nephrology, indications and contraindications for their conduct, possible complications
- Identify major and atypical variants of the course and complications of urinary system diseases• draft examination of patients with major nephrological syndromes
- Based on analysis of laboratory and instrumental examination to conduct differential diagnosis, justify and formulate diagnoses for diseases of urinary system
- Prescribe treatment, determine prognosis, to conduct primary and secondary prevention
- Diagnose and assist in renal insufficiency

### 3. Basic knowledge, abilities and skills necessary for studying theme.

#### Interdisciplinary integration:

Subject	To know	To be able to
Previous subject (pathophysiology, propedeutics; internal medicine (IV, V years of education), urology, pharmacology	Basic terms Etiopathogenesis Pathogenesis Skills Clinics, diagnostics, principles of treatment Pharmacokinetic-dynamic	To use information gained previously
Following subject	etiopathogenesis, classifications, clinics, diagnostics, principles of treatment	to derive clinical diagnosis, to interpret the results of additional data; to prescribe the treatment

### The contents of the topic:

#### Text

Urinary syndrome - the most constant symptom of renal and urinary tract. Its diagnostic value is particularly high in the absence of extrarenal symptoms of kidney disease (edema, hypertension), when changes in the urine are the only diagnostic criterion for renal disease or urinary tract, such

as glomerulonephritis with isolated urinary syndrome, chronic pyelonephritis with a latent course, at the initial stage of renal amyloidosis etc. The term urinary syndrome include proteinuria, hematuria, and leucocyturia, cylindruria. Below are brief characteristics, diagnostic value and the current understanding of the mechanism of their origin.

### ***Urinalysis***

The analysis of the urine sample involves simple observation and separate measurements using specific tools or commercially available dipsticks.

### ***Appearance and Color***

The normal color of the urine is derived from urochromes, which are pigments excreted in the urine. Abnormal color or appearance of the urine may be explained by many conditions.

### ***Specific Gravity***

The specific gravity of the urine generally is related linearly with osmolality. However, it can be raised by the presence of molecules with relatively high molecular weight, such as glucose or contrast dye. A fixed specific gravity of 1.010, so called isosthenuria, is characteristic of chronic kidney disease.

### ***pH***

Urine pH typically is 5 as a result of daily net acid excretion. An alkaline pH often is noted after meals, when an “alkaline tide” to balance gastric acid excretion increases urine pH. A high urine pH also is seen in patients who are on a vegetarian diet. An exceptionally high urine pH is indicative of an infection with a urea-splitting organism, such as *Proteus* species. An inappropriately high urine pH in the setting of systemic non-anion gap metabolic acidosis may be seen in certain forms of renal tubular acidosis (RTA). In a proximal RTA, the urine pH is high until the tubular reabsorption threshold for bicarbonate, which is abnormally low, is reached. At this point, the urine pH decreases to 5. In distal RTA, the inability to create a sufficient gradient for hydrogen ions results in a urine pH that is always higher than 5.5; the urine net charge gives complementary and confirmatory information. In type 4 RTA, the urine pH is often 5, and the urine net charge is often positive, thereby confirming the absence of significant amounts of ammonium in the urine; this defect is exacerbated by the accompanying hyperkalemia.

### ***Glucose***

Glucose in the urine is detected by an assay using dipsticks impregnated with the enzyme glucose oxidase. Glycosuria is seen in diabetes mellitus, when pregnancy causes the tubular threshold for glucose reabsorption to change, and in tubular diseases that affect the proximal convoluted tubule and cause tubular glycosuria. Evidence for pan-proximal tubular dysfunction (e.g., glycosuria, aminoaciduria, phosphaturia) indicates that Fanconi’s syndrome is present.

### ***Protein***

The dipstick for protein is a sensitive assay based on color change induced by the presence of proteins at a given pH. It is most sensitive to the presence of albumin and is much less sensitive to other proteins, such as the light chains of Bence Jones protein. The presence of 1+ protein correlates with about 30 mg/dL of albuminuria, and 3+ protein correlates with greater than 500 mg/dL of proteinuria. Because the dipstick is not a quantitative measurement, small amounts of proteinuria in an oliguric patient may give the false appearance of high-grade proteinuria.

### ***Heme***

The dipstick for heme uses the peroxidase-like activity of hemoglobin and myoglobin molecules to detect the presence of heme pigment. The reaction occurs on exposure to hemoglobin, myoglobin, or intact red blood cells (RBCs). The presence of myoglobin, which is found in patients with rhabdomyolysis, or free hemoglobin, which is seen in patients with intravascular hemolytic anemias, is suspected if the heme reaction is intensely positive and there is a paucity of cellular elements in the sediment.

### ***Leukocytes***

The dipstick detection of leukocytes depends on the presence of leukocyte esterase. Leukocyte esterase is usually present in infections and in inflammatory conditions.

## ***Urine Sediment***

### ***Cells***

RBCs, white blood cells (WBCs), tubular cells, transitional cells, and squamous epithelial cells may be seen in the urine. Casts are formed in tubules and may contain cells or cellular debris, or may be acellular.

RBCs may originate from intrarenal vessels, glomeruli, tubules, or anywhere in the urogenital tract. Dysmorphic RBCs are cells that have been deformed by transit through the glomerulus and through the medullary interstitium, as opposed to RBCs from the remainder of the genitourinary tract; these cells are often lysed and less refractile than nonglomerular RBCs. Dysmorphic RBCs often fragment with poikilocytosis and with blebs, forming so-called Mickey Mouse RBCs. Phase contrast microscopy aids in the identification of dysmorphic RBCs. The presence of a majority of dysmorphic RBCs in a urine sediment points to a glomerular origin of the hematuria. The presence of RBC casts is often conclusive evidence for the presence of glomerulonephritis.

WBCs are seen most commonly in urinary tract infections, but they also can be seen in acute interstitial nephritis, with *Legionella* and *Leptospira* species infections, chronic infections such as tuberculosis, allergic interstitial nephritis, atheroembolic diseases, and granulomatous diseases such as sarcoidosis and tubulointerstitial nephritis uveitis syndrome. Mononuclear cells often appear with transplant rejection. Tubular cells, which are seen in many conditions involving tubulointerstitial diseases, also are seen in ischemic and nephrotoxic injury, such as with myeloma kidney or cast nephropathy. Eosinophils require special stains, with the Giemsa stain being much less sensitive than the Hansel stain. Urine eosinophils classically are seen in allergic interstitial nephritis, but they also are seen in atheroembolic disease, prostatitis, and vasculitis.

### ***Other Elements***

Bacteria may be seen in the urine sediment. A spun urine sediment may show rods or cocci in chains, but bacteria are identified best by Gram staining of the urine sediment. Budding yeast forms, which are highly refractile, trichomonads, and spermatozoa also may be seen in the urinary sediment.

### ***Casts***

Casts, which are formed in tubules, are characterized by the arrangement of the cells in a clearly formed matrix composed of Tamm-Horsfall protein. Because casts are formed in the renal parenchyma, they may give a clue to the origin of accompanying cellular elements.

*Hyaline casts* are composed of Tamm-Horsfall proteins that are formed normally and are seen in increased numbers after exercise. *Granular casts* are degenerated tubular cell casts that are seen in the setting of tubular injury. *Pigmented granular casts* are seen in rhabdomyolysis with myoglobinuria or, rarely, hemoglobinuria. *RBC casts* are rarely seen in allergic interstitial nephritis and diabetic nephropathy, but they are frequently seen in acute glomerulonephritis. The presence of RBC casts in a patient with microscopic hematuria can narrow the focus of the evaluation to a glomerular lesion. *WBC casts* are seen commonly in pyelonephritis and in acute and chronic nonbacterial infections. They also are seen in other conditions in which WBCs are associated with parenchymal renal processes, such as allergic interstitial nephritis, atheroembolic diseases, and granulomatous diseases such as sarcoidosis. Rarely, WBC casts can be a dominant feature of many diseases that traditionally are thought of as glomerular diseases, such as SLE and Wegener's granulomatosis. *Tubular cell casts* are seen with any acute tubular injury and are the dominant cellular casts in ischemic acute tubular necrosis. They also can be seen with nephrotoxic injury, such as with aminoglycosides and cisplatin. Some casts may contain both leukocytes and tubular cells or be difficult to distinguish.

### ***Crystals***

Crystals can be a normal finding in the urine or serve as clues to pathophysiologic processes. Certain crystals, such as the hexagonal crystals seen with cystinuria, are always abnormal.

Others, such as the octahedral calcium oxalate crystals, may be a normal finding or may be evidence for ethylene glycol intoxication. Triple phosphate crystals, which are composed of ammonium magnesium phosphate and are coffin shaped, are seen in urinary tract infections with urea-splitting organisms. Uric acid crystals, sodium urate crystals, and calcium phosphate amorphous crystals are common and do not have pathologic significance.

#### 4. Materials for self-training

4.1. The main terms, subjects and its introductions: urinary syndrome, leukocyturia, haematuria, proteinuria, cystinuria, glycosuria, aminoaciduria, phosphaturia

4.2. Self-control materials Questions to be answered:

1. Introduction
  2. The modern views at etiology and pathogenesis
  3. Classifications.
  4. Diagnostics.
  5. Differential diagnostic.
  6. Complications
  7. The main principles of treatment.
  8. Further outpatient care, prognosis.
- 4.3. Self preparation at class. Practical skills the student must be able to do:
1. To survey a patient.
  2. To make a differential diagnostic and formulate the clinical diagnosis.
  3. To estimate the results of lab studies and procedures.
  4. To write out the recipe:

Theme contents:

#### **Materials for self-control:**

##### ***A. The questions for self-control:***

1. Name the main aetiological factors of urinary syndrome.
2. Make the plan of additional investigation of the patient with urinary syndrome.
3. Name the main principles and ways of treatment of urinary syndrome.

##### ***B. Tests for self-control:***

#### ***Questions:***

1. A caucasian girl aged 18 years developed haematuria. At cystoscopy the bladder was normal. Investigations: urine microscopy – granular and red cell casts, sterile, on culture; glomerular filtration rate (GFR) 118 ml/min (corrected for surface area); protein excretion 0,2 g/day; serum IgA 158% of normal reference sera; antistreptolysin titre (ASOT) 150 Todd units.

- (a) Suggest two possible diagnosis.  
(b) What additional features of history were needed?

2. A man aged 51 years took medical advice because of two episodes of haematuria. The blood pressure was 175/122 mmHg. Investigations: urea 5,9 mmol/l (35 mg/100 ml); plasma electrolytes normal; urine microscopy – epithelial cells only; urine culture – sterile. The blood pressure was successfully treated. Two months later he felt unwell and reinvestigated urea 32.1 mmol/l (193 mg/100 ml); plasma sodium 130, potassium 5,5, bicarbonate 16 mmol/l (mEq/l); urine microscopy – many erythrocytes and white blood cells; no casts, urine culture sterile; IVp – poor opacification and dilatation of right renal pelvis, left kidney not demonstrated; total serum acid phosphatase 6.5 iu/l (3.6 King-Armstrong units/100 ml).

- (a) What was the probable diagnosis?  
(b) What urgent investigation was needed?

(c) Comment upon initial management.

**Recommended literature:**

**A. Main:**

1. "Harrison's principles of internal medicine", Editors: Dan L. Longo, Dennis L. Kasper, J. Larry Jameson, Anthony S. Fauci, Stephen L. Hauser, Joseph Loscalzo, 18th ed. McGraw Hill. – 2012, 1-2 volumes. CURRENT Medical Diagnosis and Treatment 2012, Fifty-First Edition (LANGE CURRENT Series) by Stephen McPhee, Maxine Papadakis and Michael W. Rabow (Paperback - Sep 12, 2011)
2. Davidson's Principles and Practice of Medicine: With STUDENT CONSULT Online Access, 21e (Principles & Practice of Medicine (Davidson's)) by Nicki R. Colledge BSc FRCP(Ed), Brian R. Walker BSc MD FRCP(Ed) and Stuart H. Ralston MB ChB MD FRCP FMedSci FRSE (Paperback - Mar 11, 2010) Kumar and Clark's Clinical Medicine, 7e (Kumar, Kumar and Clark's Clinical Medicine) by Parveen J. Kumar (Paperback - Jul 2, 2009)
3. 1000 Questions and Answers from Kumar & Clark's Clinical Medicine, 2e [Paperback] Parveen Kumar CBE BSc MD FRCP FRCP(Edin) (Editor), Michael L Clark MD FRCP (Editor)
4. Differential Diagnosis in Internal Medicine: From Symptom to Diagnosis by Walter Siegenthaler (Mar 21, 2007)
5. Symptom to Diagnosis: An Evidence Based Guide, Second Edition (LANGE Clinical Medicine) by Scott D. C. Stern (Sep 16, 2009)
6. CURRENT Diagnosis and Treatment Emergency Medicine, Seventh Edition (LANGE CURRENT Series) by C. Keith Stone (May 23, 2011)
7. Harrison's Gastroenterology and Hepatology by Dan Longo and Anthony Fauci (May 3, 2010)
8. Mayo Clinic Gastroenterology and Hepatology Board Review (Mayo Clinic Scientific Press) by Stephen Hauser (Jun 23, 2011)
9. Clinical Nephrology 2012 (The Clinical Medicine Series) by M.D., C. G. Weber (Sep 19, 2011) - Kindle eBook
10. Goldman's Cecil medicine / [edited by] Lee Goldman, Andrew I. Schafer.—24th ed. Elsevier Sanders. Rev. ed. of: Cecil medicine. 23rd ed. – 2012. p.
11. Sonographer's Handbook of Diagnostic Ultrasound by Jason R. Young M.D. (Feb 23, 2011)

**Additional literature:**

1. Kovalyova O.M., Asheulova T.V. Propedeutics to internal medicine. Part 1, Diagnostics. Vinnytsya, Nova Knyha, 2006, 424 p

**Answers:**

1. (a) Haematuria of glomerular origin in an adolescent is likely to be an expression of one of four nephritides: Berger's C3/IgA (recurrent haematuria), Henoch-Schönlein purpura, membranoproliferative glomerulonephritis (mesangiocapillary glomerulonephritis) or acute post-streptococcal nephritis. In this question the discriminating features are a normal GFR, the very low protein excretion and the raised IgA. Berger's lesion is the only one of the four possibilities which usually has a normal GFR at presentation. It is also associated with minimal urinary protein loss and often with a raised serum IgA.  
(b) The history should be expanded to include recent infections. Berger's nephritis often occurs at the height of or shortly after an upper respiratory tract infection and acute post-streptococcal infection of the throat or skin. Acute post-streptococcal nephritis is now uncommon in Western Europe. Henoch-Schönlein nephritis tends to follow joint, skin and gut lesions.

2. (a) A sudden deterioration in renal function associated with haematuria is very suggestive of cancer of the lower urinary tract with bleeding, and obstruction of one or both ureters. This man's GFR declined by about 75% in 2 months. While renal impairment follows hypertension this is usually found in the patient with accelerated hypertension, and is unusual and gradual in a severe essential hypertensive. In this man's IVP the right kidney with a dilated pelvis suggested a bladder tumour which had previously obstructed the left ureter and had encroached upon the right ureteric orifice.

(b) Cystoscopy is essential and showed in this patient an extensive bladder tumour. The left ureteric orifice could not be identified with difficulty. Injection of contrast demonstrated a hydro-ureter above the bladder.

(c) While hypertension is occasionally a cause of haematuria it is a diagnosis by exclusion. Virtually all middle-aged patients with haematuria require an IVP and cystoscopy regardless of their blood pressure.

Methodical recommendations made by

Kulishov S.K.