MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE
ODESA NATIONAL MEDICAL UNIVERSITY

Medical Faculty

Department of Internal Medicine #2 with postgraduate training

APPROVED

Vice-rector for scientific and pedagogical work

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«____» September 2024

METHODICAL GUIDE
for independent applicant's work (IAW) in educational discipline

International Faculty, V-th course

Educational discipline: **Internal Medicine**

Theme: **Basics of diagnostics, treatment and prophylaxis of main diseases of the urinary system**

Approved

At the meeting of the Department of Internal Medicine #2 with postgraduate training

Protocol № 1 dated «02» September 2024

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Methodical recomendations for independent students work (iws)

Topic: "Basic of diagnosis, treatment and prevention of major urinary system diseases "

Theme № № 8-11, the number of hours - 6.

Object: To teach students to master the method of examination of patients with nephrology diseases with the selection of the main syndromes. To study probable etiological factors, pathogenesis of Glomerulonephritis and Renal Amyloidosis, their main clinical forms, variants of disease course, differential diagnosis, treatment tactics, determination of prognosis and efficiency of patients.

Students must acquired the following special competencies:
- Communication skills and clinical examination of the patient with major urinary system diseases (SC1).
- Ability to determine the necessary list of clinical, laboratory and instrumental studies and evaluate their results in major urinary system diseases (SC2).
- Ability to establish a preliminary and clinical diagnosis of major urinary system diseases (SC3).
- The ability to determine the principles of treatment, the required regime of work/rest and alimentary regime of patients with major urinary system diseases (SC4).
- Ability to diagnose emergencies in the clinic of major urinary system diseases: Nephrotic syndrome, Acute kidney injury, etc. (SC5).
- Ability to determine tactics and provide emergency medical care to patients with major urinary system diseases (SC6).
- Ability to perform medical manipulations in a case of major urinary system diseases such as BP measurement, ECG registration, drugs administration, etc. (SC8).

List of base terminology, parametrs, characteristics, that the student must learn during preparing for the lesson.
1. Urinary syndrome
2. Nephrotic syndrome
3. Nephritic syndrome
4.Syndrome of arterial hypertension
5.Syndrome of tubular dysfunction
6. Syndromes of acute and chronic renal failure

Plan

I. Theoretical questions:

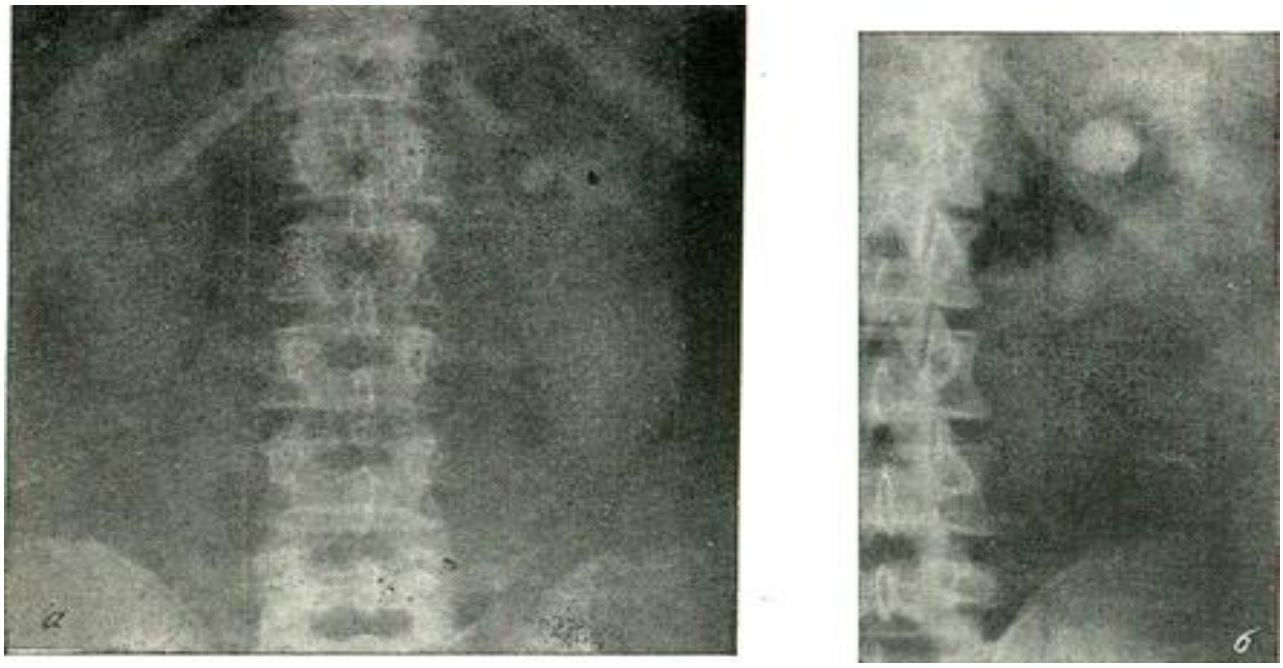
1. The main symptoms in nephrology
2. Research Methods in nephrology
3. Glomerulonephritis and nephrotic syndrome: etiology, pathogenesis, practical classification, clinical manifestations, diagnostic criteria, differential diagnosis, the value of laboratory and instrumental methods studies, treatment, prognosis, complications.
4. Pyelonephritis, tubulointerstitial nephritis and renal amyloidosis: etiology, pathogenesis, classification, clinical manifestations, diagnostic criteria, differential diagnosis, the value of laboratory and instrumental methods studies, treatment, prognosis, complications.
5. Chronic renal failure. Chronic kidney disease: etiology, pathogenesis, classification, clinical manifestations, diagnostic criteria, differential diagnosis, laboratory and instrumental data value, methods of treatment (renal replacement therapy), the prognosis, complications.
6. Acute renal failure: etiology, pathogenesis, classification, clinical manifestations, diagnostic criteria, differential diagnosis, the value of laboratory and instrumental research methods, treatment, prognosis, complications.

II Contents of the theme:

1. Mastering the skills of the urinary system X-ray data interpretation

X-ray examination of the kidneys used to determine the morphological changes in the kidneys and urinary tract, evaluating their functional state.
In clinic are most requently used:
* overview Renography - gives an idea of the location and size of the kidneys, the number and availability of radiopaque inclusions;
* excretory (intravenous) Renography - imaging of the kidneys and urinary tract;
* retrograde pyelography - in case of impossibility of excretion (intravenous) renography.

In a healthy person, the right kidney is located lower than the left on 2-3 cm, its shadow is a bit wider and shorter. X-ray signs of kidney disease are change the value and contour contrast ratio of kidney, the pyelocaliceal system, urinary tract, placing of vessels.



Plain film of kidney and ureter (a), kidney stone shadow (b).

Excretory (intravenous) urography

Excretory urography: method based on the ability of the kidneys excrete the contrast agent which is administered intravenously. The term of the making plain film after the administration of radiography contrast agent depends on the functional ability of the kidneys, the patient's age, concomitant diseases and research objectives.

Indications:

* imaging the kidneys and urinary tract;
* identify the causes of recurrent urinary tract infection, obstruction, hydronephrosis, vesicoureteral reflux, kidney stones, hypertension, congenital anomalies, hematuria.

Contraindications:

* Shock, collapse;
* Significant azotemia;
* Hypersensitivity to iodine;
* Severe hypertension;
* Multiple myeloma;
* Severe hyperthyroidism;
* Severe disturbances of liver and kidney functions.

Preparing the patient for study:

* for 1 - 2 days prior to the study limit the amount of carbohydrates, is prescribed activated charcoal to 2 tablets 3 - 4 times a day, camomile tea 0.5 cups 3 times a day;
* the night before and 2 hours prior to studies carried out a cleansing enema. If there is no constipation in young patients, only one enema is quite enough 2 hours

prior to the study. In the morning, before examining the patient can afford a light breakfast - a sandwich and sweet tea to reduce the number of "hungry gases";
* selection of radiopaque substance.

For contrasting is used: - high-osmolar ionic substances (Sergozin, Urografin, Verografin, Urotrast, Hypaque, etc.); - nonionic low-osmolar agents (omnipak). On the eve of the study (within 24h) is carried out sample for sensitivity to the contrast. If there are absent disturbances of cardiac activity, no reduction in blood pressure, no skin rash, you can recommend the entire dose.

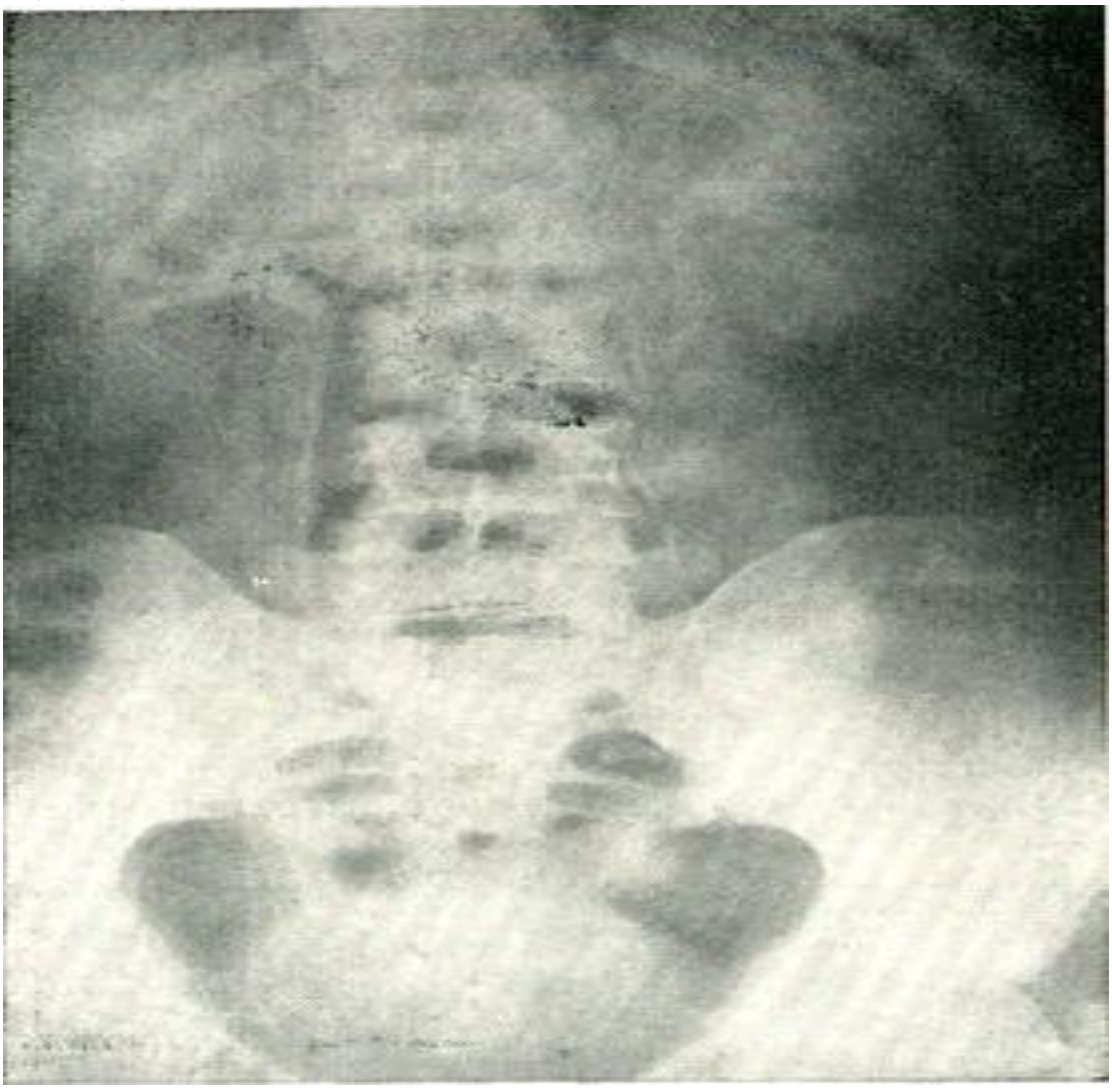
In normal renal function is used 300 - 350 mg of iodine per 1 kg body weight. In a case of reduction of the glomerular filtration rate, dose is increase. However, no more than 600 - 700 mg of iodine per 1 kg of body weight with simultaneous i/v injection of 120 - 150 ml 5% glucose solution or isotonic sodium chloride solution.

Phase of the excretory urography:
1 - minute - nephrogramme - shows the status of the parenchyma, is usually not recorded, but allows evaluating kidney function (normal, low, absent);
5th minute - pyelogram - demonstrates the contrast of the renal pelvis, calyces, the upper part of the ureter - 1 phase filling the pyelocaliceal system. Determine the shape, size of the kidneys, the pyelocaliceal system architectonics, quantitative characteristics;
10th minute - pyelogramme - maximum contrasting the pyelocaliceal system and ureter;
15th minute - urogramme - exhibits a contrast of ureter. Is carried out on inspiration. Determine the mobility of the kidneys;
20 th minute – cystogramme - demonstrates contrast of the urine bladder

X-rays of the patient at standing position is performed if is the doubt about presence Nephroptosis, and to determine the degree of emptying of the urinary system.

Late urography (30 - 60 min.) Is carried out to clarify the renal function, to identify more clearly position of stones, ureteral filling defect detection, their expansion or contraction.

Excretory urogramme.

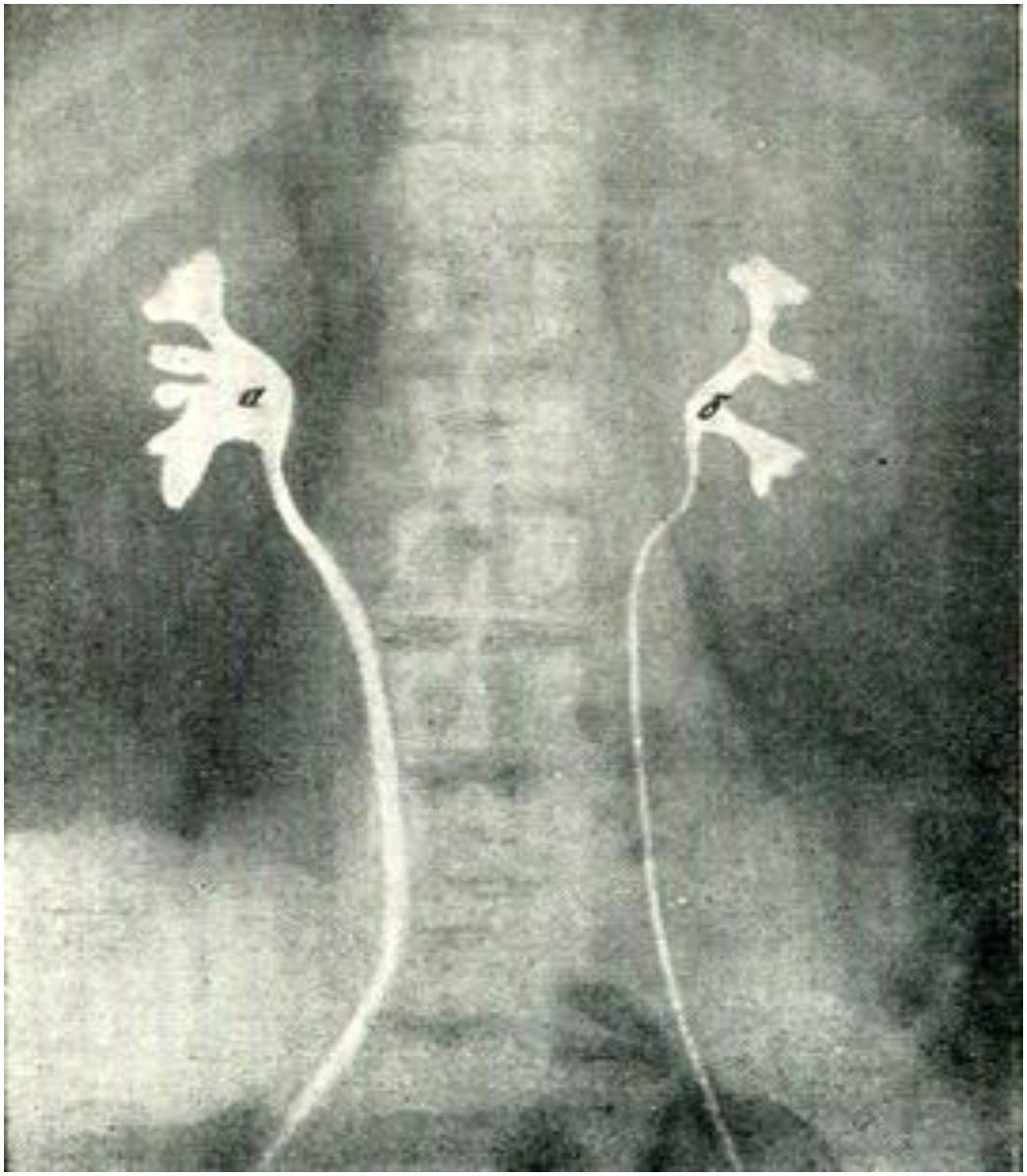


Retrograde pyelography:

Retrograde pyelography - examination method of kidneys in which the contrast is injected into the kidney pelvis through the urinary tract. The method is particularly valuable for careful examination of morphological changes of the urinary tract. Are used the same contrast agents that in excretory urography, but with a lower iodine content. Increasingly performed unilateral pyelography (depending on the location of the lesion) .

After insertion a ureteral catheter into the renal pelvis, warmed to body temperature sterile solution of 20% contrast agent (sergozinom, urokon etc.) 8-10 ml is slowly injected through a catheter into the pelvis by the 10 – 20 ml syringe with appropriate caliber needle, till the appearance of heaviness in the kidneys and then produce an X-ray.

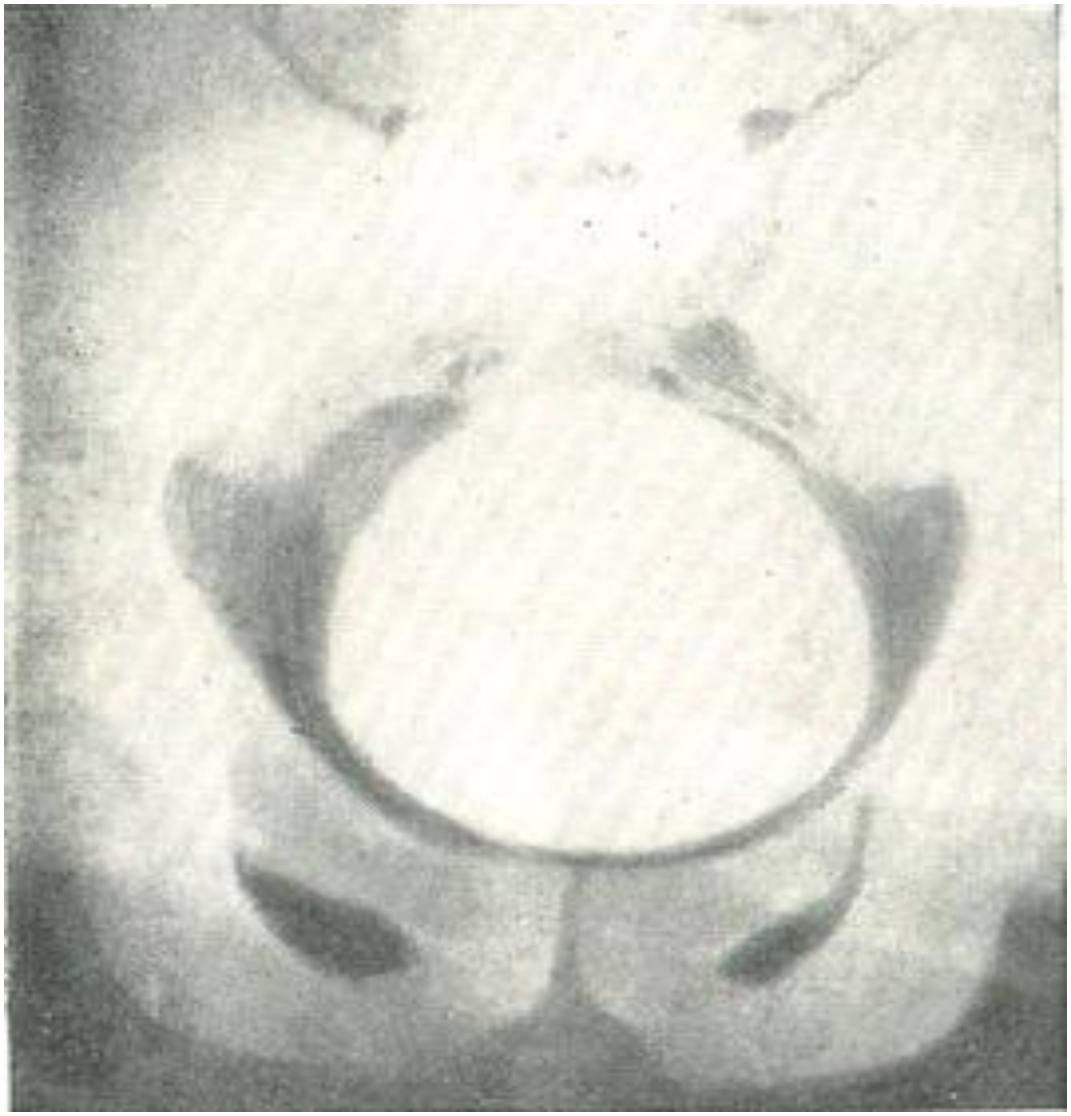
To avoid excessive intraglomerular pressure and reflux should not use ureteral catheter thicker # 5 by Charriere scale in order to a contrast fluid can flow back out of the pelvis by a catheter into the bladder. For the prevention of attacks of pyelonephritis after retrograde pyelography recommended injection is 200,000 units of penicillin. Normal pyelogram is represented as follows: pelvis is at the level thoracic XII - II lumbar vertebra, located lateral to the kidney pelvis, XII edge intersects the left pelvis in the middle of it, and the right on the border of the upper and middle thirds. Ureter runs parallel to the spine, forming an arc in the pelvic department facing bulge in the lateral direction. There are two basic types of renal pelvis. The first type ampoule-shaped is relatively large with three short and wide cups top, middle and bottom; a pelvis is located outside the renal parenchyma,



medially from it; its capacity is about 8-10 ml. In the second, branched, type it size dimensions; is positioned within the renal parenchyma, its capacity is 3-4 ml. Extrarenal (right) and intrarenal (left) type of the renal pelvis. retrograde pyelogram.

Cystography

If urine bladder fill with Sergozine solution or gas (oxygen) can be found cavity on X-ray image. This method is called cystography. Normally urine bladder, filling with contrast agent, has a rounded shape, density of contrast is the same. Bladder's contours are equal.

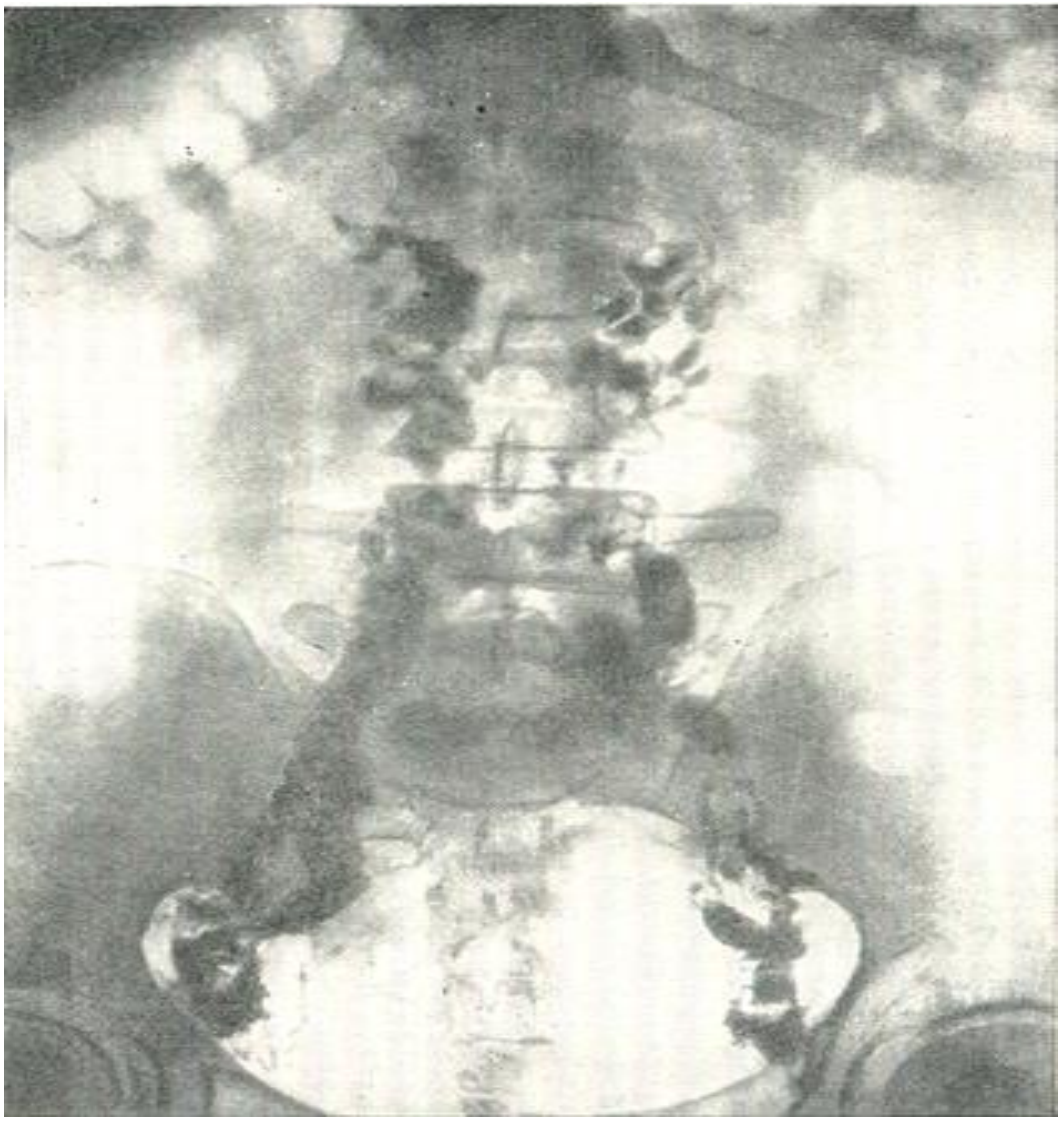


Normal cystograme

Lymphography:

For detection the metastases of malignant tumors of the genitourinary system testes, prostate, urine bladder, kidney in the inguinal and retroperitoneal lymph nodes used lymphangiography. In the interdigital skin folds between the I and II of each foot finger injected 0.5 ml of ink (blue by Evans). After a few minutes the staining of lymphatic vessels stop. In the middle third of of each rear foot under local anesthesia over colored lymph vessel cut through the skin. Fine forceps of vessel is isolated take it under a thin thread and pulling it creates lymph stagnation and expansion of vessel. In the expanded portion of the vessel through a fine needle IV slowly for 3

hours with 10 ml administered Iodolipol. Uniformity and duration of injection is achieved by the pressure on the syringe plunger by using a fine thread screw. Filling the inguinal and retroperitoneal lymph nodes with Iodolipol comes after 20-24 hours. Lymph nodes affected by tumor metastasis, increased in size, they are defined filling defects or uneven accumulation of contrast material.



Lymphogramme: tumor of urine bladder.

Tomography:

X-ray examination of kidneys, ureters and adrenal glands in wich layerimages are made. Kidneys are located in a layer distant an average of 5-10 cm from the plane of the x-ray table when the patient is on the back. Sometimes are identified stones or kidney tumors that are not detected by conventional images. Tomography makes it easy to differentiate kidney stones from gall bladder stones, as they are located in different planes.

2. Mastering the skills to analyze laboratory data:
General urine test in glomerulonephritis:

Patient B., 25 years old, was admitted for hospital care with complaints of recurrent headaches, dizziness, facial swelling, weakness. From history we know that 17 months ago after suffering a tonsilitis acute glomerulonephritis was diagnosed. Objectively: pale skin, puffy face. Lung auscultation - vesicular breathing. Border of cardiac dullness not changed. Cardiac sounds are muffled, rhythmic, accentuated II sound on aorta. BP 150/100 mmHg.

Urinanalysis
Color: light yellow
Transparency: cloudy
Specific gravity 1024
pH reaction acidic
Protein 3,6 g / l,
Glucose absent
Leukocytes 8-12 in f/v
Erythrocytes 20-30 in f/v
Flat epithelium 2-3 in f/v
Transient epithelium 8-10 in f/v
Cylinders hyaline, granular

This patient has:
Urinary syndrome as a proteinuria, microscopic hematuria, cylindruria.
You can suggest the presence of chronic glomerulonephritis.

General urine test in pyelonephritis:
Patient M., 26 years old, addressed to the family doctor with complaints of recurrent rise in temperature to 38-39^{0}C, accompanied by chills, pain in the left lumbar region, swelling of the face. Objectively: skin and visible mucous membranes of normal color, swelling of the face. Pulse 94 beats per minute, regular. BP 152/104 mmHg. Sizes of relative cardiac dullness extended to the left. Cardiac sounds clear, rhythmical. Vesicular breathing. Abdomen soft, painless. Stabbing on the lumbar region – tenderness from the left.

Urinanalysis
Color: light yellow
Transparency: cloudy
Specific gravity 1014
pH reaction alkaline
Protein 0.33 g / l
Glucose absent
Leukocytes cover entire sight
Leukocytes with granules motion (active) 65%
Erythrocytes 2-3 in f/v

Epithelium: flat 3-4 in f/v
transition 6-8 in f/v
Cocci bacteria - a significant amount
Microbial count 120,000 in 1 ml
Cylinders absent

This patient has:
Urinary syndrome has a severe leukocyturia, proteinuria, moderate bacteriuria.
You can suggest the presence of chronic pyelonephritis.

Nicheporenko urine test:
Patient N., 30 years old, turned to the family doctor with complaints of recurrent rise in temperature to 38-39^{0}C, accompanied by chills , pain in the left lumbar region , swelling of the face. An objective examination: skin and visible mucous membranes of normal color , swelling of the face . Pulse 85 beats per minute, regular. BP 152/104 mmHg. Sizes of cardiac dullness extended to the left. Cardiac sounds clear, rhythmical. Vesicular breathing. Abdomen soft, painless. Stabbing on the lumbar region – tenderness from the left.

alkaline pH
Leukocytes 8000 / ml
Red blood cells 550/ ml
Hyaline cylinders 20 / ml

This patient has:
Urinary syndrome as a leukocyturias, cylindruria.
You can suggest the presence of chronic pyelonephritis.

Zimnitskiy urine test:
Patient P., 25 years old with complaints of weakness, headaches, recurrent fevers with chills. Last 2 months developed nausea, vomiting, diarrhea. At he age of 17 was diagnosed with polycystic kidney disease, chronic pyelonephritis. Objectively: skin and visible mucous membranes pale. Puffy face, swollen eyelids. BP 165/105 mmHg. Abdomen - soft and painless, liver and spleen not palpable. Stabbing on lumbar region is negative. Minor edema of legs and feet.

Urinalysis by Zimnitskiy

Time	Amount of urine	Specific gravity
06.00-09.00	250 ml	1012
09.00-12.00	200 ml	1011
12.00-15.00	100 ml	1011

15.00-18.00	200 ml	1012
Daily diuresis	750 ml	
18.00-21.00	350 ml	1011
21.00-24.00	400 ml	1009
24.00-03.00	350 ml	1010
03.00-06.00	300 ml	1009
Night diuresis	1400 ml	

Microbiological examination of urine:
Man, 30 years old. Complaints of general weakness, edema of the eyelids in the morning. Suffers from chronic pyelonephritis for 3 years. Three days ago noticed increased body temperature, headache. OBJECTIVE: temperature 37.8 ^{0}C. RR - 18 per min., Pulse 86 beats / min, blood pressure 150/95 mmHg. Skin pale, pasty foot. Took ceftriaxone. Condition did not improve.

Result of microbiological test
Bacteriological examination of urine microflora found: microorganisms - B. Klebsiella, 5 million microbial cells in 1 ml of urine.
Sensitivity to antibiotics:

Gentamicine- resistant	Imipenem- resistan
Chloramphenico resistant	Macropen resistant
Lincomycin resistant	Nevigramon resistant
Lomefloxacin resistant	Norbaktin resistant
Fortum resistant	Tobramycin resistant
Cefazolin resistant	FURAMAG resistant
Cefotaxime resistant	Cefoperazone resistant
Tsifran resistant	Ceftriaxone resistant
Clotrimazole resistant	Cefuroxime resistant
Nystatin resistant	Ciprofloxacin resistant
Fluconazole resistant	Levofloxacin sense

According to the results of urine culture detected bacteriuria 5 million microbes B. Klebsiella in 1 ml of urine with a sensitivity to the antibiotic levofloxacin.

Complete blood count with determination of total protein and protein fractions, blood electrolytes:
Patient D., 54 years old, was admitted to the medical department in the direction of GP_ complaining headaches, palpitations, nausea, loss of appetite, shortness of breath, severe weakness, drowsiness, decrease in daily urine output of 300 ml, swelling of the face and lower extremities. Disease has developed gradually for about 1.5 years ago, especially deteriorated over the past 2 months. In a polyclinic was performed urine analysis: relative density 1002, Protein 0.99 g / l Glucose - no,

Leucocytes - 20-25 in f/v. The family doctor diagnosed - chronic pyelonephritis, nephrotic syndrome and sent to hospital. From history we found that within 14 years the patient suffers from diabetes, blood sugar ranges 6,8-12,4 mmol / l, the patient was in diet. The last 3-4 years has worsened vision, blood pressure began to rise to 180/110 mmHg.

Blood analyses
Creatinine 145 mcmol / L
GFR 72 ml / min
Urea 18.9 mmol / l
Potassium 5,7 mmol / l
Sodium 126 mmol / l
Magnesium 1,21 mmol / l
Chlorine 86 mmol / l
Calcium 1.94 mmol / l
Total protein 49 g / l
Albumin 28 g / L
Total cholesterol 10.4 mmol / l

Is determined increased creatinine, urea, reduction in glomerular filtration rate, electrolyte disturbances as a hyperkalemia, hyponatremia, hypermagnesemia, hypochloremia, hypocalcemia, hypoalbuminemia, hypercholesterolemia, suggesting that there is one degree of chronic renal insufficiency.

Create tests with values of creatinine and calculated glomerular filtration rate at different stages of chronic kidney disease (CKD)

Patients P, 22 year old, is in hospital due to acute glomerulonephritis for 7 days. From history we know that 10 days after undergoing tonsillectomy patient began to complain of pain in the lumbar region, increased body temperature, change in urine color to color "meat slops", headache, dizziness, weakness, swelling of the face, decrease in urine output, whereby the patient was sent to hospital treatment. A month ago, the patient noted the sudden appearance of anuria, which was preceded by 2 overnight weakness, oliguria, the patient didnot visit the doctor. Despite ongoing therapy in the hospital, the patient's condition worsened: sleepiness and the past 12 hours the urine does not depart. Objectively: the patient is lethargic, pale skin, swelling of the face, waist, lower extremities. Body weight - 70 kg. Border of cardiac dullness extended to the left. Cardiac sounds are muffled, rhythmic, accentuated II sound on aorta. HR - 104 beats per minute..

$$\text{GFR (ml / min)} = \frac{88 \times (140 - \text{age}) \times \text{body weight, kg}}{72 \times \text{Cr serum, mmol / l}}$$

GFR of the patient 28.3 ml / min.

Make general and biochemical blood tests with nonspecific signs of inflammation, blood test for uric acid.

Patient M., 55 years old, the driver. During hospitalization complains with swelling and pain in the right ankle and small joints of the right foot, redness of the skin over them, limitation of movement in them.

From history we found that he suffers from sudden attacks of pain in the joints of the right foot about 8 years when night appeared intense pain in the first finger of his right foot. At the same time it was discovered swelling, redness and increased local temperature in the affected area. Self-administration of analgesics has led to a significant decrease in pain and restore joint function. It was further noted that the recurrence of arthritis 1 - first metatarsophalangeal phalanx joint occurs after the holiday feasts or intense physical work. Pain in the right shin joint joined in the past 6 months. Periodically affected joints crack notes while walking, especially on nervious surfaces.

Objectively: the right body type, high power. In the cartilaginous part of the external ear painless palpable dense formations magnitude 0.3 x 0.2 cm, whitish at the bend. Skin clean, adequate moisture. Tissue turgor was maintained. Marked bony deformity in 1 - and 2 first metatarsophalangeal metacarpophalangeal joint of the right foot with the formation hallus valgus, combined with swelling, redness and increased local temperature over the same joints.

Symptom lateral compression of the right foot positive. Slight limitation of movement 1 - and 2 of the fingers of the right foot. Right ankle shin, hot and painful on palpation. Volume of active and passive movements in it is limited because of the pain. Internal organs without significant changes.

Urinalysis: Specific gravity 1015, pH reaction is weakly acidic, protein - 0.066 g / l, Er. 0-2 in f/v, Leuk. 0-2-4 in f/v. Ultrasound of the kidneys: kidneys are located typically, mobility saved, the pyelocalicial complex is not changed. In the cortical area of the left kidney observed mild hyperechogenicity foci and symptoms of microlithiasis. CT of the kidney: detected foci of interstitial fibrosis and microconcrements in the cortex of the left kidney.

Complete blood count:

HB – 160g/l
Erytrocytes – $6.6x10^{12}$/l
ESR - 10 mm / min
Platelets $406x10^9$ / l
Leukocytes 12.2 x 10^9 / l
Eosinophils 5%
Basophils - 1% Myelocytes - 10%
Banded - 10%
Segmented 47%
Lymphocytes - 10%
Monocytes 3%

According to clinical analysis of blood, it can be assumed the presence of inflammatory process in the patient.

Biochemical analysis of blood:
Bilirubin 13.5 mcmol / l
Cholesterol 7.8 mmol / l
Creatinine - 65 mcmol / l
Residual nitrogen 16.5 mmol / l
Sialic acid 2.99 mmol / l
Seromucoid 0.37 units.
Fibrinogen 6.0 g / l
C reactive protein + + +
Total protein 77, 5 g / l
Protein fractions albumins - 53% globulins α_1 - 3%, α_2 - 9%, β - 14%, γ - 21%
Rheumatoid factor negative
LE cells negative
Uric acid 589 mcmol / l

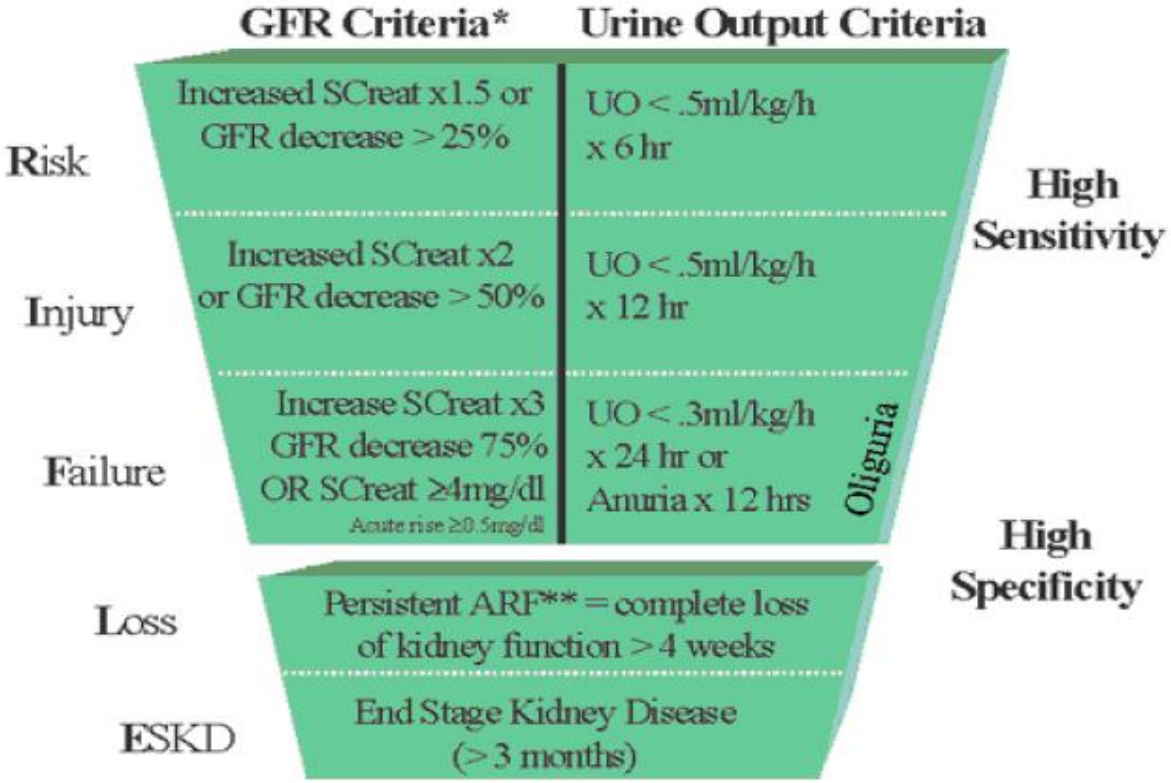
According to the biochemical analysis of blood, we can assume the presence of inflammation due to Gout.
This patient has can establish the diagnosis: Gout, a mixed form, oligoarthritis 1st and 2nd right metacarpophalangeal joint, the activity of 1-2 degrees. Gouty nephropathy. Secondary oligoosteoartrosis 1st and 2nd metacarpophalangeal and metatarsophalangealright ankle. Joint disability of the 1-st degree.

5.3. Mastering the emergency care skills health in acute kidney injury (AKI): Describe an algorithm for assistance.
I. Identify AKI. According to KDIGO 2013, AKI is defined as any of the following (not graded):
• increase in serum creatinine (SCr) by ≥0.3 mg/dl (≥26.5 μmol/l) within 48 hours; or
• increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
• urine volume <0.5 ml/kg/hour for 6 hours.
II. Assess the stage of AKI severity.

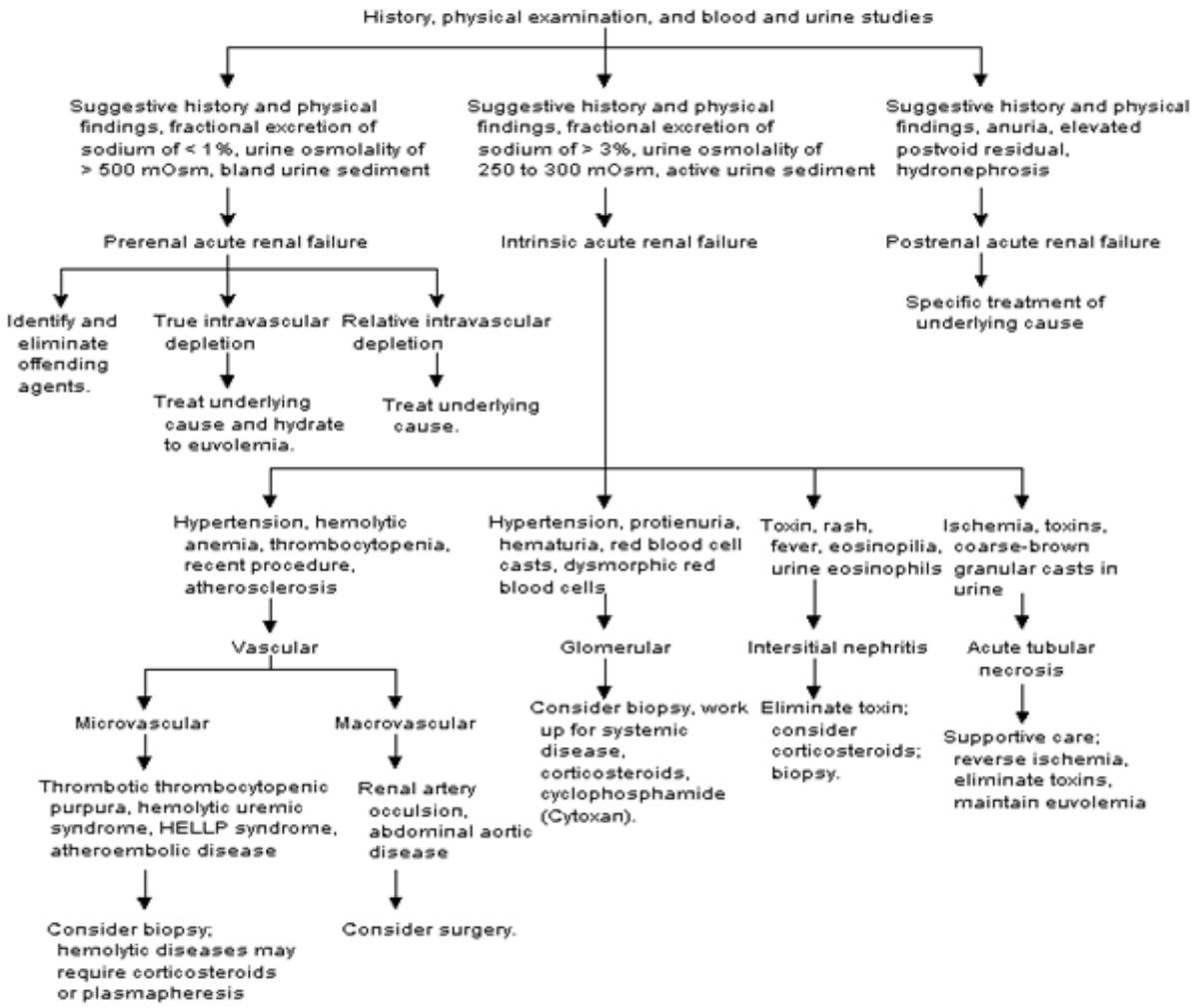
Stage	**Serum creatinine**	**Urine output**
1	1.5 to 1.9 times baseline *or* ≥0.3 mg/dl (≥26.5 μmol/l) increase	<0.5 ml/kg/hour for 6 to 12 hours
2	2.0 to 2.9 times baseline	<0.5 ml/kg/hour for ≥12 hours

3	3.0 times baseline *or* increase in serum creatinine to ≥4.0 mg/dl (≥353.6 μmol/l) *or*initiation of renal replacement therapy *or* in patients <18 years a decrease in eGFR to <35 ml/minute per 1.73 m^2	<0.3 ml/kg/hour for ≥24 hours *or* anuria for ≥12 hours

RIFLE classification



III. Determine the cause of AKI and risk assessment



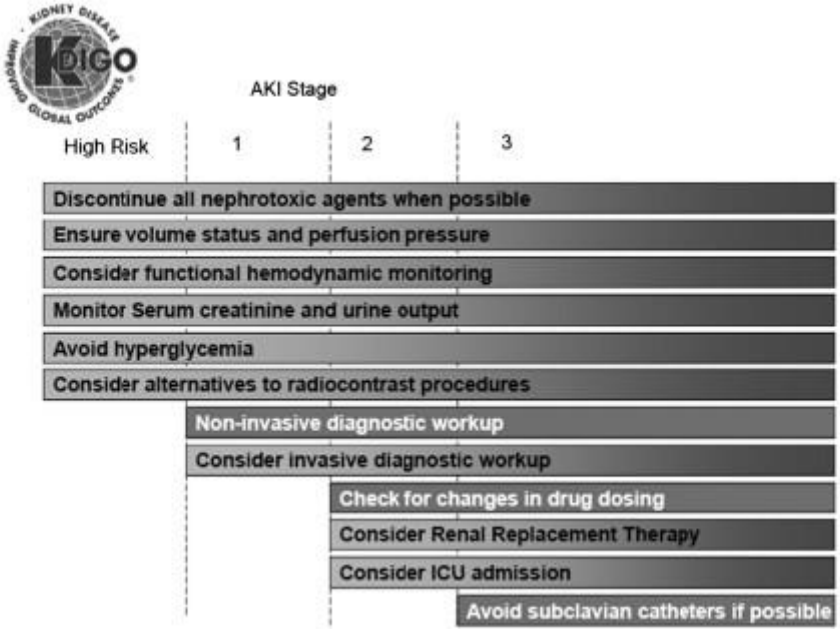
Algorithm for the diagnosis and treatment of acute renal failure. (HELLP = *h*emolysis, *e*levated *l*iver enzymes and*l*ow *p*latelets.)

Causes of acute kidney injury: exposures and susceptibilities for nonspecific acute kidney injury

Exposure	**Susceptibility**
Sepsis	Dehydration or volume depletion
Critical illness	Advanced age
Circulatory shock	Female gender
Burns	Black race
Trauma	Chronic kidney disease
Cardiac surgery (especially with cardiopulmonary bypass)	Chronic diseases (heart, lung, liver)

Major noncardiac surgery	Diabetes mellitus
Nephrotoxic drugs	Cancer
Radiocontrast agents	Anemia
Poisonous plants and animals	

IV. Stage-based management of acute kidney injury



General Treatment of Acute Renal Failure / KDIGO recommendations

1. Initial treatment should focus on correcting fluid and electrolyte balances and uremia while the cause of acute renal failure is being sought. A volume-depleted patient is resuscitated with saline. More often, however, volume overload is present, especially if patients are oliguric or anuric.

KDIGO: **In the absence of hemorrhagic shock, we suggest using isotonic crystalloids rather than colloids (albumin or starches) as initial management for expansion of intravascular volume in patients at risk for AKI or with AKI (Grade 2B)**

Results of the Saline vs. Albumin Fluid Evaluation study - a RCT comparing 4% human albumin in 0.9% saline with isotonic saline in ICU patients - indicated that albumin is safe, albeit no more effective than isotonic saline for fluid resuscitation. The study demonstrated no difference in need for and duration of RRT. Very few patients in the trial received large volume fluid resuscitation (>5 l) and thus the results may not be applicable to all patients.

Hydroxyethylstarch (HES) is a widely used, relatively inexpensive alternative to human albumin for correcting hypovolemia. A recent Cochrane review concluded that there is no evidence that resuscitation with colloids, instead of crystalloids, reduces the risk of death in patients with trauma, burns, or following surgery. In

addition to some negative effects on coagulation, particularly with older forms of HES, development of renal dysfunction has been a concern associated with the use of mainly hypertonic HES. A recent meta-analysis described 11 randomized trials with a total of 1,220 patients: seven trials evaluating hyperoncotic albumin and four trials evaluating hyperoncotic starch. Hyperoncotic albumin decreased the odds of AKI by 76% while hyperoncotic starch increased those odds by 92% (odds ratio (OR) = 1.92; 95% confidence interval (CI) = 1.31 to 2.81; *P* = 0.0008). Parallel effects on mortality were observed. The renal effects of hyperoncotic colloid solutions appeared to be colloid specific, with albumin displaying renoprotection and hyperoncotic starch showing nephrotoxicity. A 7,000-patient study comparing 6% HES 130/0.4 in saline with saline alone was scheduled to begin in Australia and New Zealand in 2010. This study will provide further high-quality data to help guide clinical practice. The use of isotonic saline as the standard of care for intravascular volume expansion to prevent or treat AKI is thus based upon the lack of clear evidence that colloids are superior for this purpose, along with some evidence that specific colloids may cause AKI, in addition to their higher costs. It is acknowledged that colloids may be chosen in some patients to aid in reaching resuscitation goals, or to avoid excessive fluid administration in patients requiring large volume resuscitation, or in specific patient subsets (for example, a cirrhotic patient with spontaneous peritonitis, or in burns). Similarly, although hypotonic or hypertonic crystalloids may be used in specific clinical scenarios, the choice of crystalloid with altered tonicity is generally dictated by goals other than intravascular volume expansion (for example, hypernatremia or hyponatremia). *In addition, isotonic saline solution contains 154 mmol/l chloride and when administration in large volumes will result in relative or absolute hyperchloremia.* Buffered salt solutions approximate physiological chloride concentrations and cause less acid-base disturbances and other side effects associated with hyperchloremia. Whether the use of buffered solutions results in better clinical outcomes, however, is uncertain.

2. Furosemide (Lasix) administered intravenously every six hours is the initial treatment for volume overload. Depending on whether the patient takes furosemide regularly, the initial dose can be between 20 and 100 mg. If an inadequate response occurs in one hour, the dose is doubled. This process is repeated until adequate urine output is achieved. A continuous furosemide drip may be required. The last resort is ultrafiltration via dialysis.

KDIGO: **“We recommend not using diuretics to prevent AKI (Grade 1B)**

We suggest not using diuretics to treat AKI, except in the management of volume overload (Grade 2C)”.

Specifically, prophylactic furosemide was found to be ineffective or harmful when used to prevent AKI after cardiac surgery, and to increase the risk of AKI when given to prevent contrast-induced AKI.

Epidemiologic data suggest that the use of loop diuretics may increase mortality in patients with critical illness and AKI, along with conflicting data that suggest no harm in AKI. Finally, furosemide therapy was also ineffective and possibly harmful when used to treat AKI. A systematic review and meta-analysis by Ho and Power

also included six studies that used furosemide to treat AKI, with doses ranging from 600 to 3,400 mg/day. No significant reduction was found for in-hospital mortality or for RRT requirement. Furosemide may be useful in achieving fluid balance to facilitate mechanical ventilation according to the lung-protective ventilation strategy in hemodynamically stable patients with acute lung injury. However, a beneficial role for loop diuretics in facilitating discontinuation of RRT in AKI is not evident from clinical studies.

The often retrospective and/or underpowered studies using prophylactic mannitol did not meet the criteria of the Work Group to be included in formulation of recommendations. Mannitol is often added to the priming fluid of the cardiopulmonary bypass system to reduce the incidence of renal dysfunction, but the results of these studies are not very convincing. Two small randomized trials - one in patients with pre-existing normal renal function, the second in patients with established renal dysfunction - did not find differences for any measured variable of renal function. More convincing are the results obtained with the preventive administration of mannitol, just before clamp release, during renal transplantation. The sparse controlled data available have shown that 250 ml of 20% mannitol given immediately before vessel clamp removal reduces the incidence of post-transplant AKI, as indicated by a lower requirement of post-transplant dialysis. However, 3 months after transplantation, no difference is found in kidney function compared with patients who did not receive mannitol. Finally, it has been suggested that mannitol is beneficial in rhabdomyolysis by stimulating osmotic diuresis and by lowering the intracompartmental pressure in the affected crushed limbs; again, these studies were either not randomized or were underpowered. A separate guideline on crush injury associated with disasters, mainly earthquake victims, has now been published by the International Society of Nephrology Renal Disaster Relief Task Force.

3. The main electrolyte disturbances in the acute setting are hyperkalemia and acidosis. The aggressiveness of treatment depends on the degree of hyperkalemia and the changes seen on the electrocardiogram. Intravenously administered calcium (10 mL of a 10 percent solution of calcium gluconate) is cardioprotective and temporarily reverses the neuromuscular effects of hyperkalemia.

Potassium can be temporarily shifted into the intracellular compartment using intravenously administered insulin (10 units) and glucose (25 g), inhaled beta agonists or intravenously administered sodium bicarbonate (three ampules in 1 L of 5 percent dextrose). Potassium excretion is achieved with sodium polystyrene sulfonate (Kayexalate) and/or diuretics. Sodium polystyrene sulfonate is given orally (25 to 50 g mixed with 100 mL of 20 percent sorbitol) or as an enema (50 g in 50 mL of 70 percent sorbitol and 150 mL of tap water). If these measures do not control the potassium level, dialysis should be initiated.

4. Acidosis is treated with intravenously or orally administered sodium bicarbonate if the serum bicarbonate level is less than 15 mEq per L (15 mmol per L) or the pH is less than 7.2. The amount of supplemental bicarbonate needed is determined on the basis of the bicarbonate deficit equation: bicarbonate deficit (mEq per L) = 0.5 × weight (kg) × (24 – actual serum bicarbonate level).

Sodium bicarbonate ampules are available in two concentrations: 44.6 and 50 mEq per 50 mL. Patients can also be treated orally with sodium bicarbonate tablets (a 300-mg tablet contains 3.6 mEq of sodium bicarbonate), Shohl's solution in 30-mL doses (1 mEq of sodium bicarbonate per mL) or powdered sodium bicarbonate (Arm and Hammer baking soda provides approximately 50 mEq of sodium bicarbonate per rounded teaspoon). Serum bicarbonate levels and pH should be followed closely. Intractable acidosis requires dialysis.

5. Because acute renal failure is a catabolic state, patients can become nutritionally deficient. Total caloric intake should be 30 to 45 kcal (126 to 189 kJ) per kg per day, most of which should come from a combination of carbohydrates and lipids. In patients who are not receiving dialysis, protein intake should be restricted to 0.6 g per kg per day. Patients who are receiving dialysis should have a protein intake of 1 to 1.5 g per kg per day.

KDIGO: **We suggest achieving a total energy intake of 20 to 30 kcal/kg/day in patients with any stage of AKI (Grade 2C)**

We suggest avoiding restriction of protein intake with the aim of preventing or delaying initiation of RRT (Grade 2D) We suggest administering 0.8 to 1.0 g/kg/day protein in noncatabolic AKI patients without need for dialysis (Grade 2D), 1.0 to 1.5 g/kg/day in patients with AKI on RRT (Grade 2D), and up to a maximum of 1.7 g/kg/day in patients on CRRT and in hypercatabolic patients (Grade 2D)

Patients should receive 100 to 130% of the basal energy expenditure, which can be estimated with acceptable precision and accuracy by the Caldwell-Kennedy equation:

Resting energy expenditure(kcal/kg/day)=22+31.05×weight(kg)+1.16×age(years)

6. Glycemic control.

KDIGO: **In critically ill patients, we suggest insulin therapy targeting plasma glucose 110 to 149 mg/dl (6.1 to 8.3 mmol/l) (Grade 2C)**

Use insulin for preventing severe hyperglycemia in critically ill patients but in view of the danger of potentially serious hypoglycemia, we suggest that the average blood glucose should not exceed 149 mg/dl (8.3 mmol/l), but that insulin therapy should not be used to lower blood glucose to <110 mg/dl (6.1 mmol/l)

7. Vasodilator therapy: dopamine, fenoldopam, and natriuretic peptides.

KDIGO: **We recommend not using low-dose dopamine to prevent or treat AKI (Grade 1A)**

We suggest not using fenoldopam to prevent or treat AKI (Grade 2C)

We suggest not using ANP to prevent (Grade 2C) or treat (Grade 2B) AKI

Three systematic reviews have reached identical conclusions that dopamine does not provide any benefit for prevention or early treatment of AKI. There is also limited evidence that the use of dopamine to prevent or treat AKI causes harm. Dopamine can trigger tachyarrhythmias and myocardial ischemia, decrease intestinal blood flow, cause hypopituitarism, and suppress T-cell function. Fenoldopam mesylate is a pure dopamine type-1 receptor agonist that has similar hemodynamic renal effects as low-dose dopamine, without systemic α-adrenergic or β-adrenergic stimulation. A meta-analysis found that fenoldopam reduces the need for RRT and in-hospital death

in cardiovascular surgery patients. However, the pooled studies included both prophylactic and early therapeutic studies, as well as propensity-adjusted case-matched studies (rather than purely randomized trials). A 1,000-patient RCT of fenoldopam to prevent the need for RRT after cardiac surgery is currently underway (ClinicalTrials.gov: NCT00621790); meanwhile, this remains an unproven indication for fenoldopam therapy.

Nesiritide (b-type natriuretic peptide) is the latest natriuretic peptide introduced for clinical use, and is approved by the US Food and Drug Administration only for the therapy of acute, decompensated congestive heart failure. Meta-analysis of outcome data from these and some other nesiritide congestive heart failure trials has generated some controversy. Sackner-Bernstein and colleagues analyzed mortality data from 12 randomized trials; three trials provided 30-day mortality data, and found a trend towards an increased risk of death in nesiritide-treated subjects. In another meta-analysis of five randomized trials that included 1,269 subjects, the same investigators found that there was a relationship between nesiritide use and worsening renal function, defined as SCr increase >0.5 mg/dl (>44.2 μmol/l). Nesiritide doses ≤0.03 μg/kg/minute and even at doses ≤0.015 μg/kg/minute significantly increased the risk of renal dysfunction compared with non-inotrope-based controls or compared with all control groups (including inotropes). There was no difference in dialysis rates between the groups. Another retrospective study determined independent risk factors for 60-day mortality by multivariate analysis in a cohort of 682 older heart-failure patients treated with nesiritide versus those who were not. When patients were stratified according to nesiritide usage, AKI emerged as an independent risk factor for mortality only among patients who received the drug. Strikingly, among these heart-failure patients who developed AKI, nesiritide usage emerged as the only independent predictor of mortality.

8. Avoiding nephrotoxins

KDIGO: We suggest not using aminoglycosides for the treatment of infections unless no suitable, less nephrotoxic, therapeutic alternatives are available (Grade 2A)

We suggest that, in patients with normal kidney function in steady state, aminoglycosides are administered as a single dose daily rather than multiple-dose daily treatment regimens (Grade 2B)

We recommend monitoring aminoglycoside drug levels when treatment with multiple daily dosing is used for more than 24 hours (Grade 1A)

We suggest monitoring aminoglycoside drug levels when treatment with single-daily dosing is used for more than 48 hours (Grade 2C)

We suggest using topical or local applications of aminoglycosides (for example, respiratory aerosols, instilled antibiotic beads), rather than intravenous application, when feasible and suitable (Grade 2B)

We suggest using lipid formulations of amphotericin B rather than conventional formulations of amphotericin B (Grade 2A)

In the treatment of systemic mycoses or parasitic infections, we recommend using azoleantifungal agents and/or the echinocandins rather than conventional amphotericin B, if equal therapeutic efficacy can be assumed (Grade 1A)

Finally, all medications should be reviewed, and their dosages should be adjusted based on the glomerular filtration rate and the serum levels of medications.

Between 20 and 60 percent of patients require short-term dialysis, particularly when the BUN exceeds 100 mg per dL (35.7 mmol per L of urea) and the serum creatinine level exceeds the range of 5 to 10 mg per dL (442 to 884 μmol per L). Indications for dialysis include acidosis or electrolyte disturbances that do not respond to pharmacologic therapy, fluid overload that does not respond to diuretics, and uremia. In patients with progressive acute renal failure, urgent consultation with a nephrologist is indicated.

Table 3: Recommended relative and absolute indications for RRT in critically ill patients with AKI.

Dialysis indication	Criteria	Absolute/relative
Metabolic	Urea > 27 mmol/L	Relative
	Urea > 35.7 mmol/L	Absolute
	Hyperkalaemia > 6 mmol/L	Relative
	Hyperkalaemia > 6 mmol/L plus ECG changes	Absolute
	Dysnatraemia	Relative
	Hypermagnesaemia > 4 mmol/L	Relative
	Hypermagnesaemia > 4 mmol/L plus anuria or areflexia	Absolute
Acidosis	pH > 7.15	Relative
	pH < 7.15	Absolute
Anuria/oliguria	Risk (RIFLE class)	Relative
	Injury (RIFLE class)	Relative
	Failure (RIFLE class)	Relative
	UO < 200 mL for 12 hrs or anuria	Absolute
Uraemic complication	Encephalopathy	Absolute
	Pericarditis	Absolute
	Myopathy	Absolute

	Neuropathy	Absolute
	Bleeding	Absolute
Fluid overload	Diuretic responsive	Relative
	Diuretic resistant (with pulmonary oedema)	Absolute

Methods for dialysis therapy.
- Acute peritoneal dialysis,
- Standard intermittent (or hydrocarbon-acetate) hemodialysis;
- High intermittent hemodialysis;
- Hemodialysis with high permeability membrane and volume control;
- Intermittent hemofiltration;
- Hemodiafiltration.

Orienting map for self-training students using literature on the topic:

Main theme	Responces	Student answeres
Learn the theme	The study of main and additional literature	Reply to educational issues
Be able to make and justify the final diagnosis of the examined patients	To be able to examine the patient and make a plan of investigation	Written justification preliminary and final diagnoses, examination and treatment plan of the patient
Make the treatment plan of the patient		Control with Written test control
To know complications of diseases and their treatment		Decision situational problems

III. Materials for self-control:

• The main symptoms in nephrology
• Research Methods in Nephrology
• Glomerulonephritis and nephrotic syndrome: etiology, pathogenesis, classification , clinical manifestations, diagnostic criteria, differential diagnosis, the value of laboratory and instrumental methods of research, treatment, prognosis, complications.
• Pyelonephritis, tubulointerstitial nephritis and renal amyloidosis: etiology, pathogenesis, classification , clinical manifestations, diagnostic criteria, differential

diagnosis, the value of laboratory and instrumental methods of research, treatment, prognosis, complications.
• Chronic renal failure. Chronic kidney disease: etiology, pathogenesis, classification , clinical manifestations, diagnostic criteria, differential diagnosis, laboratory and instrumental value of research methods, methods of treatment (renal replacement therapy), the prognosis, complications.
• Acute renal failure: etiology, pathogenesis, classification , clinical manifestations, diagnostic criteria, differential diagnosis, the value of laboratory and instrumental methods of research, treatment, prognosis, complications.

Tests for self-control:

Tests for self-control. Proposes the use of tests of the base 2 KROK:

1. A 24 y.o. patient complains of nausea, vomiting, headache, shortness of breath. He had an acute nephritis being 10 y.o. Proteinuria was found out in urine. Objectively: a skin is grey-pale, the edema is not present. Accent of II tone above aorta. BP 140/100-180/100 mm Hg. Blood level of residual N_2- 6,6 mmol/L, creatinine- 406 mmol/L. Day's diuresis- 2300 ml, nocturia. Specific density of urine is 1009, albumin- 0,9 g/L, WBC- 0-2 in f/vis. RBC.- single in f/vis., hyaline casts single in specimen. Your diagnosis?
A Chronic nephritis with violation of kidney function
B Feochromocitoma
C Hypertensive illness of the II degree
D Nephrotic syndrome
E Stenosis of kidney artery
2. A 72-year-old patient after operation due to holecystectomia was prescribed gentamicin (80 mg every 8 hours) and cephalothin (2 g every 6 hours) due to fever. In 10 days there was an increase of creatinine up to 310 mu*mol/L. BP - 130/80 mm Hg, daily quantity of the urine is 1200 mL. Urine tests are without pathology. Ultrasound: the size of kidneys is normal. What is the most probable reason for renal failure?
A Nephrotoxity of gentamicin
B Acute glomerulonephritis
C Cortical necrosis of kidneys
D Unequal infusion of the liqiud
E Hepatorenal syndrome
3. A 16-year-old patient after 3 days of tonsillitis onset, antibiotic injections were prescribed. Patient’s condition was worsened: pain in lumbar region,dizzinies, nausea. BP 140/80 mmHg. CBC: Er. $3.12x10^{12}$/l, hb 120 g/l, Leuk. $10x10^{9}$/l, ESR 28 mm/h. Urine test: 1002, protein 0.99 g/l. Zimnitskiy test: daily output 3.2 l, specific gravity 1002-1005. Serum creatinine 480 mcmo/l. What diagnosis is most probable?
A Acute interstitial nephritis
B Acute pyelonephritis

C Fast progressive glomerulonephritis
D Chronic glomerulonephritis, urine syndrome
E Chronic glomerulonephritis, urine syndrome

4. A 44-year-old patient complains about difficult urination, sensation of incomplete urinary bladder emptying. Sonographic examination of the urinary bladder near the urethra entrance revealed an oval well-defined hyperechogenic formation 2x3 cm large that was changing its position during the examination. What conclusion can be made?
A Concrement
B Malignant tumour of the urinary bladder
C Urinary bladder polyp
D Prostate adenoma
E Primary ureter tumor

5. A 69-year-old female patient complains of temperature rise up to 38,3ºC, haematuria. ESR- 55 mm/h. Antibacterial therapy turned out to be ineffective. What diagnosis might be suspected?
A Renal cancer
B Polycystic renal disease
C Renal amyloidosis
D Urolithiasis
E Chronic glomerulonephritis

6. A 25-year-old man has facial edema, moderate back pains. His temperature is 37,5ºC, BP 180/100 mm Hg, hematuria [up to 100 in v/f], proteinuria [2,0 g/L], hyaline casts - 10 in v/f., specific gravity -1020. The onset of the disease is probably connected with acute tonsillitis that started 2 weeks ago. What is the most probable diagnosis?
A Acute glomerulonephritis
B Acute pyelonephritis
C Cancer of the kidney
D Urolithiasis
E Chronic glomerulonephritis

7. 2 weeks after recovering from angina a 29-year-old patient noticed face edemata, weakness, decreased work performance. There was gradual progress of dyspnea, edemata of the lower extremities, lumbar spine. Objectively: pale skin, weakening of the heart sounds, anasarca. AP- 160/100 mm Hg. In urine: the relative density - 1021, protein - 5 g/l, erythrocytes - 20-30 in the field of vision, hyaline cylinders - 4-6 in the field of vision. What is the most likely diagnosis?
A Acute glomerulonephritis
B Essential hypertension
C Acute pyelonephritis
D Infectious allergic myocarditis
E Myxedema

8. A 37-year-old patient was brought to resuscitation unit. General condition of the patient is very serious. Sopor. The skin is grey, moist. Turgor is decreased. Pulse is

rapid, intense. BP - 160/110 mm Hg, muscle tonus is increased. Hyperreflexia. There is an ammonia odor in the air.What is the presumptive diagnosis?
A Uraemic coma
B Alcoholic coma
C Hyperglycemic coma
D Hypoglycemic coma
E Cerebral coma
9. A 54-year-old patient has an over 20-year history of femoral osteomyelitis. Over the last month she has developed progressing edemata of the lower extremities. Urine test reveals: proteinuria at the rate of 6,6 g/l; in blood: dysproteinemia in form of hypoalbuminemia, increase in α_2- and γ-globulin rate, ESR - 50 mm/h. What is the most likely diagnosis?
A Secondary renal amyloidosis
B Acute glomerulonephritis
C Myelomatosis
D Chronic glomerulonephritis
E Systemic lupus erythematosus
10. A 54-year-old male patient complains of aching pain in the lumbar region, that is getting worse after standing in an upright position, physical exercise, supercooling. The patient also reports of experiencing weakness in the afternoon. Pain in the lumbar region, said about 10 years old. Objectively: pale skin, t^o- 37,2^{o}C, AP- 180/100 mm Hg, minor costovertebral angle tenderness (Pasternatsky symptom). In blood: RBCs - 3,5x10^{12}/l, WBCs - 6,5x10^9/l, ESR - 22 mm/h. In urine: the relative density - 1010, leukocytes - 12-15 in the field of vision, erythrocytes - 2-3 in the field of vision. Urine bacterial count - 100000 in 1 ml. What is the most likely diagnosis?
A Chronic pyelonephritis
B Nephrolithiasis
C Polycystic renal disease
D Chronic glomerulonephritis
E Amyloidosis
11. A 35-year-old patient has been in the intensive care unit for acute renal failure due to crush for 4 days. Objectively: the patient is inadequate. Breathing rate - 32/min. Over the last 3 hours individual moist rales can be auscultated in lungs. ECG shows high T waves, right ventricular extrasystoles. CVP - 159 mm Hg. In blood: the residual nitrogen - 62 millimole/l, K^+- 7,1 millimole/l, Cl^- - 78 millimole/l, Na^+- 120 millimole/l, Ht - 0,32, Hb - 100 g/l, blood creatinine- 0,9 millimole/l. The most appropriate method of treatment would be:
A Hemodialysis
B Plasma sorption
C Hemosorption
D Plasma filtration
E Ultrafiltration
12. A 28-year-old woman has a 12-year history of chronic glomerulonephritis with latent course. Over the past six months she has developed general weakness, loss of

appetite, low work performance, nausea. The patient complains of headache, pain in the joints. On examination: anemia, blood urea - 34,5 millimole/l, blood creatinine - 0,766 millimole/l, hyperkalemia. What complication has developed?
A Chronic renal insufficiency
B Acute renal insufficiency
C Nephrotic syndrome
D Renal amyloidosis
E Pyelonephritis
13. A 30-year-old woman with a long history of chronic pyelonephritis complains about considerable weakness, sleepiness, decrease in diuresis down to 100 ml per day. AP- 200/120 mm Hg. In blood: creatinine - 0,62 millimole/l, hypoproteinemia, albumines - 32 g/l, potassium - 6,8 millimole/l, hypochromic anemia, increased ESR. What is the first step in the patient treatment tactics?
A Haemodialysis
B Antibacterial therapy
C Enterosorption
D Haemosorption
E Blood transfusion
14. A male patient presents with swollen ankles, face, eyelids, elevated AP- 160/100 mm Hg, pulse- 54 bpm, daily loss of albumine with urine- 4g. What therapy is pathogenetic in this case?
A Corticosteroids
B Diuretics
C NSAID
D Calcium antagonists
E Antibiotics
15. A 45-year-old male patient complains of acute pain in his right side irradiating to the right thigh and crotch. The patient claims also to have frequent urination with urine which resembles a meat slops. The patient has no previous history of this condition. There is costovertebral angle tenderness on the right (positive Pasternatsky's symptom). What is the most likely diagnosis?
A Urolithiasis
B Acute appendicitis
C Acute pyelonephritis
D Acute cholecystitis. Renal colic
E Acute pancreatitis

IV. Individual assignments for students relating to theme for classes.

Selectable themes:
- independently selected topics respectively topics 10-13;
- offered by lecturer.

Form of individual work performance:
- review of the actual problem;
- thematic analysis of clinical patient with nontypical or severe disease;

- review of new methods of diagnosis and treatment in nephrology;

Presentation forms:

a report for Student conference, etc.

Recommended literature:

Basic:

1. Harrison's Manual in Medicine. 20th edition / Ed.by J. L. Jameson, A.S. Fauci, D.L. Kasper et al. / McGraw-Hill Education, 2020. 1245 p.
2. Harrison's Principles of Internal Medicine. 20th edition / Ed.by J. L. Jameson, A.S. Fauci, D.L. Kasper et al. / McGraw-Hill Education, 2020. 3528 p.
3. BMJ Best Practice. Acute kidney injury. - BMJ publishing group LTD, 2019. – 53 p.
4. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention and Treatment of Chronic Kidney Disease – Mineral and Bone Disorder (CKD-MBD). kdigo.org/wp.../2017-KDIGO-CKD-MBD-GL-Update.pdf
5. KDIGO 2020 Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation, vol. 7, № 4s
6. European Association of Urology. Guidelines on urological infections. 2020. https://uroweb.org/wp-content/uploads/EAU-Guidelines-on-Urological-infections-2020.pdf

Additional:

1. KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease, vol. 99, is.3s
2. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD), vol. 7, is.1.