**PATHOPHYSIOLOGY OF KIDNEY**

All the factors causing disturbances in the urogenous function of kidneys are divided into 2 groups:

1. **Extrarenal factors.**
2. **Renal factors.**

The extrarenal factors disturbing urine secretion are the following:

1. Disturbances in neuroendocrine regulation of urine secretion. Disturbances in uropoiesis may be provoked by dysfunction of the central nervous system ( particularly the medulla oblongata and tuber cinereum). A needle puncture in the medulla oblongata or tuber cinereum causes increased excretion of urine. Uropoiesis is frequently increased in cases of tumors of the diencephalon. Excretion of water, electrolytes and urea is decreased from denervated kidneys.

The renal function may be changed under the influence of the cerebral cortex (psychical excitation, inhibition in the cerebral cortex, fright, hypnotic suggestion of drinking, effects of conditioned stimuli).

Frequently disturbances in renal function arise by reflex way. Intense pain stimulation may cause decrease in uropoiesis (oliguria) or its complete cessation (anuria). For instance, damage to one kidney may cause temporary cessation of activity of other kidney. The nervous system and humoral factors take part in the mechanism of the reflex anuria connected with pain. Pain causes excitation of the sympathetic nervous system, and large amounts of adrenalin and antidiuretic hormone are secreted into the blood.

Thyroxin and hydrocortisone increase urine excretion. It is influenced also by aldosterone (sodium retaining hormone).

2. Changes in the chemical composition and physicochemical properties of the blood. These are connected, in the first place, with metabolic disturbances. The amount of substances that have to be excreted in the urine may increase, or substances may appear which are normally absent in urine: hyperglycemia and glucosuria in diabetes mellitius, increase in bilirubin and bile acids in jaundice, appearance of hemoglobin in the plasma in cases of hemolysis of erythrocytes, increased concentration of sodium chloride and other salts in disturbances in mineral metabolism.

Drop in the osmotic and oncotic pressures of the plasma leads to increased production of urine of low specitic gravity (for instance, as a result of intravenous infusion of hypotonic solutions).

3. Disturbanes in the general circulation. Circulatory disorders (changes in the circulation rate and blood presure) may cause increase, decrease or even cessation of the excretion of urine.

Decreased circulation rate and arterial pressure lead to decreased excretion of urine. This is connected with decrease in blood flow into the kidneys and lowering of the filtration pressure. At an arterial pressure below 50-40 mm Hg uropoiesis ceases completely. Besides, secretion of renin is accelerated which causes hypersecretion of aldosterone; reabsorption of sodium and water is increased, excretion of urine is still more decreased.

Decompencation of heart activity causes decreased excretion of urine, in the pathogenesis of which venous congestion takes part. As a result of venous congestion edema is developed in renal parenchyma, and intrarenal pressure increases. These changes impede the filtration.

The renal factors disturbing urine secretion are the following:

1. infectious- allergic lesions of kidneys(diffuse glomerulonephritis);
2. inflammation of kidneys of infectious character (pyelonephritis, focal nephritis);
3. dystrophic changes in renal tubules (nephrosis);
4. factors preventing excretion of urine (urinary calculi, pression of ureters);
5. damaging action on kidneys of infectious diseases and intoxications of other localizations(abdominal typhoid, sepsis ,tuberculosis);
6. toxic substances (heavy metal salts );
7. disturbances in renal blood circulation ;
8. congenital defects of fermental systems in renal tubules (Fanconi’s syndrome);
9. congenital anomalies ( hypoplasia, polycystosis) of kidneys.

According to the predominant involvement of corresponding morphological components the following renal diseases are distinguished: glomerular diseases (mainly of immune character), tubular diseases (caused mainly by toxic or infectious agents), interstitial diseases (frequently involve also tubules); vascular diseases (changes in the nephron as a consequence of increased intraglomerular pressure), obstructive uropathy (including urolithiasis), congenital anomalies and tumors of the kidneys.

Glomerulonephritis is bilateral diffuse inflammation of kidneys with primary lesion of glomeruli. There is a triad of symptoms in nephritis: hypertension, edema, hematuria.

Pyelonephritis is inflammation of mainly renal interstitial tissue and renal pelvis. It may be acute and chronic, and gradually results in lesion of renal blood vessels and destruction of renal parenchyma. Pathogenic microorganisms (staphylococcus, streptococcus, colibacillus, proteus ) may get into renal pelvis by hematogenic and urogenous (ascending )ways; lymphogenous way is disputable.

Dystrophic (from slight dystrophy to necrosis) lesion of renal tubules epithelium forms the basis of nephrosis .Nephrosis develops as a result of prolonged diseases (osteomyelitis, pneumonia), chronic infections (tuberculosis,syphilis) and intoxications. Nephrotic syndrome is characterized by massive proteinuria, hypoalbuminemia, edema, hyperlipidemia and lipiduria.

The renal diseases may be reproduced in experiment .Glomerulonephritis is caused by the way of administration of the heterogeneous nephrotoxic serum to a rabbit .Overfeeding of animals with proteins during several weeks causes amyloid nephrosis. After ligation of the efferent renal lymphatic vessels lymphogenic nephrosis develops. Degenerative-dystrophical changes in renal tubules are discovered in animals with experimental radiation sickness. Necronephrosis develops as a result of administration to animals of mercuric salts (sublimate kidney ), preparations of bismuth, salts of uranium, chrome, phosphorus, arsenic,some antibiotics. To produce uremia in experiment, both ureters of a dog are ligated. Polyuria in dog may be produced by conditioned reflex way.

Nephrosclerosis is pathological process connected with sclerotic changes in the small renal arteries. The changes in the vascular system lead to impairment of nutrition of renal tissue and destruction of specific elements; the renal parenchyma is replaced by connective tissue. The proliferated connective tissue shrivels and alters the size and shape of the kidneys. This is called contracted kidney 2 types of which are distinguished:

1. Primary contracted kidney- frequently develops as a result of protracted hypertensive disease. Renal arteries are sclerosed, glomeruli are atrophied and replaced by cicatricial tissue.
2. Secondary contracted kidney- is one of the complications of chronic diffuse glomerulonephritis and pyelonephritis.It is characterized by sclerosis of the blood vessels , induration and contraction of the kidneys, atrophy of a considerable number of nephrons.

In both forms of contracted kidney arterial pressure may be increased, the processes of filtration and reabsorption are disturbed, gradually azotemia and uremia develops.

# In order to judge of renal function a number of tests are used which are divided into 4 groups

# Concentration and dilution tests;

# hemorenal (renal clearance) tests;

3) blood chemistry;

4) urine analysis;

Concentration and dilution tests are designed to evaluate functional capacity of the renal tubules. By the way of changing specific gravity of the urine according to amount of fluid entering the organism, kidneys participate in maintenance of constant amount and osmotic pressure of fluids in the organism. Normally specific gravity of the urine ranges from 1.002 to 1.030; kidneys can excrete urine with osmotic pressure 4 times more or 6 times less than that of the blood plasma.

The ability of nephron to concentrate and dilute urine depends both on the functional activity of the tubular cells and presence of ADH (antidiuretic hormone). Failure to achieve adequate urinary concentration can be due either to defects within the renal medulla (nephrogenic diabetes insipidus), or to the lack of ADH (central diabetes insipidus). The following phenomena arise when the ability of kidneys to concentrate urine is disturbed:

1. Hyposthenuria - the specific gravity of the urine (1.006—1.012) is lower than that of glomerular filtrate (primary urine). In acute pyelonephritis and in initial stage of chronic pyelonephritis hyposthenuria is observed together with polyuria. Because tubular reabsorption is disturbed , whereas glomerular filtration is not changed much. If the glomeruli are also damaged, hyposthenuria is accompanied by oliguria.

2. Isosthenuria – the specific gravity of the urine (1.010—1.012) is equal to that of glomerular filtrate and practically is not changed regardless of changing levels of plasma hydration. Such monotonous diuresis shows complete disturbance of reabsorption of water and salts in kidneys, the ability of nephron to concentrate and dilute urine. As a result of destruction of the epithelial cells tubules lose their resorption and secretion functions and the glomerular filtrate passes into renal pelvis without any changes. In more severe disturbances of the renal function isosthenuria is accompanied by oliguria.

To study the concentrating and diluting functions of kidneys the following tests are applied:

1. Concentration test. Artificial fluid deprivation is induced in the patient for 36 hours. 12 hours after cessation of water intake, every 3 hours (in all—8 times) the urine is collected, volume and specific gravity of each portion is determined. If the nephron is normal, water is selectively rearbsorbed resulting in excretion of urine of high concentration (specific gravity - 1.025 or more). If the tubular cells are nonfunctional, the concentration of the urine will remain constant regardless of water deprivation.

Acute inflamatory diseases of kidneys, renal failure, cardiovascular insufficiency and hypertensive disease are contraindications for employment of the concentration test.

2. Dilution test. An excess of fluid (1.5 litres of water during 30—45 minutes) is given to the patient on an empty stomach. Then during 4 hours every 30 minutes (in all – 8 times) the urine is collected. Normally renal compensation should result in excretion of urine of lower concentration (specific gravity -1.003 or less). During 4 hours 75% of the accepted water is excreted. If the renal tubules are diseased, the concentration of different portions will remain constant (no lower than 1.006) irrespective of the excess water intake. During 4 hours no more than 70% of the water is excreted.

Chronic renal failure, edema and hypertensive diseaseare contraindications for employment of the dilution test.

3. Zimnitsky’s test – has no contraindications.In patient’s ordinary way of life during 24 hours volume and specific gravity of portions of the urine excreted every 3 hours (in all-8 times) are determined.Normally, volume of different portions ranges from 1.005 to 1.028; diurnal diuresis is almost twice more than nocturnal diuresis. In functional insufficiency of kidneys specific gravity of different portions is almost the same and no more than 1.012 (hypostenuria); volume of the nocturnal diuresis prevails (nycturia).

Clearance tests are employed to assess the rate of glomerular filtration and renal blood flow. The rate of this filtration is measured by determining the excretion rate of a substance which is filtered through the glomerulus but subsequently is neither reabsorbed nor secreted by the tubules . The glomerular filtration rate (normally 120 ml/minute in an average adult) is usually equal to clearance of that substance and is calculated from the following equation :

## C=UV/P

C- clearance of the substance in ml/minute; U- concentration of the substance in the urine;P- concentration of the substance in the plasma; V- volume of urine passed per minute.

Inulin (a mixture of fructose polymers) is considered the ideal substance for the clearance test since it is filtered from the glomerulus and is excreted unchanged in the urine. Its clearance coefficient is equal to the volume of the primary urine formed per minute, 120 ml/minute. Decrease of this coefficient points to disturbed filtration function of kidneys.

In creatinine clearanse test, there is no need for its intravenous infusion since creatinine is normally released into plasma by muscle metabolism and its very small fraction is secreted by the tubules.

In urea clearance test the sensitivity is much less than the creatinine or inulin clearance because plasma concentration of urea is affected by a number of factors (dietary protein, fluid intake,infection) and is partly reabsorbed by the tubules.

So, clearance coefficients of different substances differ depending on the mechanism of their excretion by kidneys – 70 ml/minute for urea, 100 ml/minute for creatinine, 400 ml/minute for phenol red, 550- 650 ml/minute for para- aminohippuric acid(PAH).

As distinct from inulin and creatinine tests which measure glomerular filtration, PAH clearance test is employed to measure renal blood flow. Because PAH, when infused intravenously, is both filtered at the glomerulus and secreted by the tubules. Normally, renal blood flow is about 1200 ml per minute in an average adult. This index increases in hypertensive form of glomerulonephritis and decreases in hypertensive disease.

Disorders of the renal function are reflected in blood chemistry, causing changes in the quantity as well as composition of the blood. Impairement of renal function results in elevation of end- products of protein metabolism. This includes increased accumulation of certain substances in the blood, chiefly urea (normally 20- 40 mg/dl), blood urea nitrogen (normally - 10-20 mg/dl) and creatinine (normally 0.5- 1.5 mg/dl). The total amount of nitrogen containing in the low- molecular substances of the plasma is called residual nitrogen (normally 0.2 - 0.4 g/l or 20-40 mg%). Increase of the residual nitrogen, that is, of these end- products in the blood, is called azotemia. Damage to more than 1/3- 1/2 of the total number of nephrons cause azotemia. But azotemia may be observed also in some diseases that are not connected with kidneys- severe diseases of liver and pancreas, sepsis, pneumonia, malignant tumors, disturbances in blood circulation, protracted diarrhea and vomiting, etc.

Ratio of urea nitrogen to residual nitrogen is important for diagnosis. This ratio is normally no more than 48%, whereas in renal failure increases up to 90%.

In renal failure the electrolyte content of the blood is disturbed, osmotic pressure increases, alkaline reserve decreases. Hypoalbuminuria in some renal diseases results in hypoalbuminemia.

The simplest diagnostic tests for renal function are the physical, chemical, bacteriological and microscopic examination of the urine.

The physical examination includes 24-hour urinary output (diuresis), colour, specific gravity, smell, etc. For instance, in hematuria, hemoglobinuria, uroporphyrinuria urine becomes red or pink; in inflammation of urinary bladder it smells of rotten egg (characteristic of hydrogendisulphide).

The chemical tests permit to detect the presence of protein, glucose, erythrocytes and hemoglobin to assess the permeability of glomerular membrane.

Various components of urinary sediment observed on microscopic examination of urine in renal diseases are divided into two groups:

1) organized elements- epithelial cells, erythrocytes, leukocytes, cylinders (casts), mucus, etc.

2) non- organized elements- uric acid crystals, urates, oxalic acid salts, amorphous phosphates, ammonium salts of uric acid, hippuric acid, etc. Some of non- organized elements are found only in a pathological states: leucine , tyrosine, cystine, fat and fatty acid crystals, cholesterol, bilirubin, xanthine, etc.

Pathological changes in urine may be caused not only by diseases of kidneys and urinary tracts, but also by pathology of other organs and systems. In diseases connected with obstruction of biliary ducts and damage to liver bilirubin, in acute hemolysis – hemoglobin, in diabetes mellitus-glucose are found in urine.

The following pathological components of urine are characteristic of renal diseases:

1.Erythrocyturia (excretion of erythrocytes in urine) - is one of the main symptoms of glomerulonephritis; it is observed also in pyelonephritis, renal amyloidosis, renal anomalies.Erythrocytes may pass into urine from damaged urinary bladder and urinary tracts (tumor and stone in the bladder, calculus in the ureter). Excretion of blood in urine is called hematuria.

2. Leukocyturia (excretion of leukocytes in urine)- is observed in pyelonephritis,glomerulonephritis,tuberculosis, diabetic glomerulosclerosis, inflammation of urinary tracts and urinary bladder.Excretion of turbid urine containing a large amount of leukocytes and purulent bodies is called pyuria.

3. Proteinuria- excretion of proteins in urine.

4. Cylindruria- excretion of different cylinders (casts) in urine: hyaline casts (transparent particles formed as a result of clotting of blood serum proteins- in all renal diseases accompanied by proteinuria), epithelial casts (result from degenerative changes in renal tubules), granular casts (clotted proteins and particles of cells), waxy casts (in severe renal diseases), leukocyte cylinders, erythrocyte cylinders.

5. Saline sediments- result from renal diseases (oxalates, phosphates and urates in nephrolithiasis) or disturbances in metabilism (urates in gout).

Urolithiasis is formation of urinary calculi (stones) at any level of the urinary tract. Formation of stones in the renal parenchyma, calyces renales and renal pelvis is called nephrolithiasis.The following factors may cause formation of urinary calculi:

1. disturbances in mineral metabolism ;
2. hereditary disturbances in metabolism ;
3. stagnation of urine;
4. infectious diseases of urinary tracts ;
5. injury to kidneys;
6. vitamin A and vitamin D deficiency .

The chemical composition and structure of the urinary calculi depend on etilogic factors : urate stones in disturbances of purine metabolism, cystine stones in hereditary cystinuria, sulfanilamide stones in persons who intake sulfa drugs, etc.

There are four main types of urinary calculi-calcium stones ( 75% of the urinary calculi ), mixed stones , uric acid stones, cystine stones and a small number of rare types (xanthine stones). Mixed stones consist of magnesium- ammonium- calcium phosphate, often called struvite. That is why they are also called struvite stones or triple phosphate stones.

There are different theories about formation of the urinary stones:

1. Crystallization theory- when the amount of substances, inclined to crystallization, is increased in urine, they are settled. Slowed down movement of urine in ureters and inflammatory processes promote formation of stones.

There are different theories about formation of urinary stones:

1. Template theory- salts which are part of urine , are settled on the frame consisting of proteins and carbohydrates. The role of frame promoting formation of urinary stones is played by plasma proteins that pass into the composition of the primary urine by the way of gromerular filtration and uromucoid that go out of the damaged epithelial cells of renal tubules.

 The main mechanisms of the disturbanses in renal activity are the following:

1. disturbances in the glomerular filtration;
2. disturbances in the tubular reabsorption;
3. disturbanes in the tubular secretion.

 In the following cases the filtration is decreased:

1. Decrease of the number of functioning nephrons and diminution of filtration surface of the kidneys- in chronic glomerulonephritis , nephrosclerosis, pyelonephritis part of nephrons perish and are replaced by connective tissue elements (contracted kidney). Disturbance in activity of 80-90 % of nephrons cause development of severe renal failure.

2. The factors impeding outflow of urine from kidneys – nephrolithiasis, hypertrophy and tumors of prostate, narrowing and squeezing of ureters and urethra. Impeded outflow of urine from kidneys results in increased intrarenal pressure. Increase of intrarenal pressure higher than 40 mm Hg causes anuria (complete cessation of filtration).

1. Decreased pressure in the general blood circulation –shock, collapse, heart failure. This causes decrease of filtration pressure in glomeruli.
2. Narrowing of the renal artery and arterioles- stenosis of renal artery and arterioles, reflex pain anuria, hypersecretion of renin, hypertensive disease. Decreased blood flow into glomeruli causes delay of filtration.
3. Increased oncotic pressure of the blood dehydration, administration of a large amount of albuminous preparations into the blood. These cause decreased filtration pressure.

 In the following cases the filtration is increased:

 1. Decreased tension of the afferent artery and accelerated renal blood circulation.

 2. Increased tension of the efferent artery (for instance, under the influence of small dose of adrenalin).

 3. Decreased oncotic pressure of the blood.

The small doses of adrenalin as well as the weak stimulation of the sympathetic fibers of kidneys increase filtration, whereas adrenalin's large doses and the strong sympathetic stimulation decrease or even stop it. Because in the first cases, though both afferent and efferent vessels are constricted, but the lumen of the afferent vessel (with a greater than the efferent vessel's diameter) is preserved, however, in the second cases it is also closed, and no blood enters the kidney.

 The following factors cause disturbance in the tubular reabsorption:

 1) changes in he structure of tubules (dystrophy and necrosis)- inflammatory processes in kidneys, disturbances in blood circulation, intoxications;

 2) decreased activity of enzyme systems in tubules- hereditary disturbances in enzyme systems participating in reabsorption (Fanconi’s syndrome) or poisoning with inhibitors of these enzymes;

 3) excessive intensity of process of reabsorption and decompenstion of mechanisms increasing activity of enzyme systems (as a result of excess of substanses in the primary urine which must be reabsorbed).

 Disturbed reabsorption of proteins causes proteinuria (albuminuria). Proteinuria may be observed in some physiological states (in newborns, in persons during intensive physial work or long working). But constant proteinuria is one of the main symptoms of renal diseases.2types of proteinuria are distinguished:

 1. Glomerular proteinuria –is oberved in glomerulonephritis., disturbance of renal blood supply, congestive hyperemia(cardiac decompensation). When membrane permeability in glomeruli is increased, a large amount of proteins pass into primary urine, all of which cannot be reabsorbed in tubules, and part of proteins remains in the final urine. In severe lesion of kidneys high- molecular proteins (globulins) also appear in the urine.

2.Tubular proteinuria- is connected with disturbed reabsorption of proteins . It results from lesion of epithelial cells of proximal tubules (amyloidosis, sublimate necronephrosis), hereditary fermental deficiency, disturbance in flow of lymph in kidneys.

Since in nephrotic syndrome glomeruli and tubules are damaged at the same time , more protein appears in urine.

Loss of a large amount of proteins in urine causes decrease of albumen – globulin ratio ,as well as oncotic pressure of the blood ; renal edema develops.

Disturbed reabsorption of amino acids causes aminoaciduria which is observed in hereditary deficiency of enzyme systems participating in reabsorption and diseases that are accompanied by lesion of renal tubules.

One of the severe hereditary defects of the enzyme systems regulating process of reabsorption is Fanconi’s syndrome (familial idiopathic nephronophthisis). In the first month of life gradually hyalinosis of renal tubules develops, renal function is disturbed. In the first years of life polyuria is observed (specific gravity of the urine-1.008-1.010), reabsorption of amino acids, glucose, phosphates is disturbed, metabolic acidosis comes into being. Loss of a large amount of phosphates in urine results in changes in bones , and walk of the person is disturbed . Severe renal failure develops.

Disturbed reabsoption of glucose is observed when its blood content is higher than 150-180 mg %; this causes glucosuria. In protracted diabetes mellitus renal glomeruli are damaged (diabetic glomerulosclerosis), this limits the process of filtration, and glucosuria is not observed, in spite of hyperglycemia.

 Glucosuria connected with inactivation of enzyme systems participating in reabsorption of glucose goes without hyperglycemia (renal diabetes). This type of glucosuria may be reproduced in experiment by the way of administration of phloridzin.

 Hereditary renal glucosuria is resulted from deficiency of hexokinase or glucose-6- phosphatase in epithelial cells of the proximal part of tubules.

 Disturbed reabsorption of sodium may be caused by hyposecretion of aldosterone: a large amount of sodium and water is lost in urine.

 Hyposecretion of antidiuretic hormone results in disturbance in reabsorption of water; a large amount of hypotonic urine is excreted (diabetes insipidus).

 Since tubular secretion is active process requiring expenditure of energy, disturbed synthesis of ATP (poisoning with cyanides and dinitrophenol) causes sharp weakening of secretion. Renal failure is accompanied by disturbance in secretion. The substances, that must be excreted from the organism by the way of secretion (for instance, antibiotics) are accumulated in the blood. Therefore, antibiotics must be prescribed to such patients with caution.

 The chronic diseases resulting in lesion and atrophy of renal tubules , hereditary defects of enzyme systems ensuring secretion of hydrogen ions, intake of drugs decreasing activity of carbonic anhydrase cause disturbance in the processes of acidogenesis and ammoniogenesis.

 Regardless of cause, renal disease usually results in the evolution of one of the two major pathological syndromes: acute renal failure and chronic renal failure. The term azotemia is used for biochemical abnormality characterized by evolution of the blood urea nitrogen and creatinine levels, while uremia is defined as association of these biochemical abnormalities with clinical signs and symptoms,

 Renal failure is weakened ability of kidneys to excrete the metabolites which are formed in the organism and to ensure constancy of the plasma composition.

 Acute renal failure is a syndrome characterized by rapid onset of renal dysfunction , chiefly oliguria or anuria , and sudden increase in metabolic waste – products (urea , creatinine) in the blood with consequent development of uremia.

 The causes of acute renal failure may be classified as the following:

1. pre- renal causes – sharp decrease of the circulating blood volume and arterial pressure (shock, loss of blood), loss of large amount of electrolytes and water (intense diarrhea and vomiting, burns, poisoning with diuretics);
2. intrarenal causes –vascular disease of the arteries and arterioles within the kidney, rapidly progressive glomerulonephritis , acute tubular necrosis due to ischemia or the effect of nephrotoxin, acute tubulointerstitial nephritis and pyelonephritis;
3. post-renal causes- obstruction to the flow of urine anywhere along the renal tract distal to the opening of the collecting ducts which may result from a mass within the lumen (urinary stones) or from wall of the tract , or from external compression (tumor or hematoma in surrounding tissues).

In the initial period of the acute renal failure oliguria and anuria are observed, then they are replaced by polyuria. In favourable conditions renal activity is recorvered during several months.

Chronic renal failure is a syndrome characterized by progressive and irreversible deterioration of renal function due to slow destruction of renal parenchyma , accompanied by contracted kidney and eventually terminating in death when sufficient number ( 90- 95%) of nephrons have been damaged .Acidosis is the major problem in chronic renal failure with development of biochemical azotemia and clinical uremic syndrome. All chronic nephropathies (chronic glomerulonephritis, chronic pyelonephritis, diabetic glomerulosclerosis) can lead to chronic renal failure.

The diseases leading to chronic renal failure can be classified into two major groups (those causing glomerular pathology and those causing tubulointerstitial pathology) though disease rarely remains confined to either glomeruli alone or tubulointerstitial tissue alone. In the final stage of chronic renal failure all parts of the nephron are involved.

The main signs of the functional insufficiency of kidneys are the following:

1. oliguria or anuria;
2. hyposthenuria or isosthenuria;
3. decreased clearance index;
4. azotemia;
5. changed plasma content of electrolytes ( hyper - or hypokalemia, hyponatremia, hypocalcemia, hyperphosphatemia);
6. acidosis.

Besides , edema , arterial hypertension and anemia may be observed.

Uremia must be considered one of the most clearly pronounced manifestations of renal insufficiency . Uremia is a symptom complex showing autointoxication of the organism by nitrogenous products which should be eliminated with the urine but are retained in the blood. Azotemic uremia develops at the terminal stage of renal insufficiency, and nitrogeneous metabolites accumulate in the blood and tissues. A large amount of sulfur, phosphorus, magnesium compounds is accumulated in the organism. Electrolytic balance is disturbed, acidosis develops. These changes cause disturbance in metabolism and hormonal balance, dystrophy in tissue, dysfunction in organs and systems .All of these changes are important in the development of uremic syndrome.

Some of clinical signs of uremia come into being as a result of compensation of weakened renal function by activity of skin, mucous membranes, digestive glands. Excretion of nitrogen- containing metabolites by skin causes excruciating itch. Enzyme systems of bacteria break down urea which is excreted by mucous membrane of the respiratory tracts and oral cavity; ammonia is formed and causes characteristic odour from the mouth. This “uremic odour “ may be felt when concentration of residual nitrogen is 1 g/l (100 mg%). In the mucous membrane of the oral cavity inflammation (stomatitis, gingivitis) and necrosis develop. Ammonia and its salts that are formed in intestines irritate mucous membrane of gastrointestinal tract, causing uremic gastritis and colitis.

Action of excreted metabolites on the respiratory tract results in laryngitis, tracheitis, bronchitis. Nitrogen- containing organic substances are excreted also by serous membranes causing pericarditis, pleuritis and peritonitis.

Since in uremia blood content of calcium is decreased, involuntary muscle contractions occur. Hypocalcemia stimulates activity of the parathyroid glands and causes secondary hyperparathyroidism which results in disturbances in phosphoric and calcic metabolism in bones, osteoporosis and spontaneous fracture of bones.

Uremia causes severe changes in activity of the central nervous system: sleep and memory are disturbed, general malaise, headache, fatigue are observed, vision is weakened.

The function of bone marrow is disturbed, anemia develops which is accompanied by leukocytosis and trombocytopenia; subcutaneous hemorrhages and hemorrheas are frequent. Uremic gastritis, colitis, diarrhea, disturbances in digestion and loss of electrolytes result in cachexia. At the terminal stage of uremic intoxication loss of consciousness and coma occur .At intervals psychical excitement, hallucinations, delirium are observed. Activity of the respiratory center is disturbed, Kussmaul's respiration and sometimes Cheyne- Stokes respiration are observed.

Unlike azotemic uremia, uremic eclampsia, i.e., another complication of renal insufficiency, arises suddenly. It is frequently observed in acute diffuse glomerulonephritis, but may be caused also by acute attack of chronic glomerulonephritis. Since the uremic eclampsia does not involve appreciable azotemia, it is called also pseudouremia. The main factors in the pathogenesis of uremic eclampsia are edema of brain tissue, increased intracranial pressure , spasm of cerebral vessels and resultant cerebral anemia.

Frequently the uremic eclampsia begins with general malaise and somnolence, then violent headache , amaurosis, speech disturbance, temporary paralysis, mental disorder , rapid increase of arterial pressure are observed. Suddenly epileptiform convulsions begin. Cyanosis in the face, dilatation of the veins of the neck, pupil dilatation are observed . Pupils do not react to the light . After the seizure the state of sopor or coma develops . To take the patient out of the state of uremic eclampsia, the intracranial pressure must be decreased .

In order to extend the life of uremic patients "artificial kidney" is applied. In these apparatuses the principle is that of hemodialysis - the property of substances in the blood to pass selectively through semi- permeable membrane. In uremic patients hemodialysis is applied 1- 4 times per week ( each time 8- 10 hours ).

Artificial kidney makes it possible to remove from the blood 6- 16g and more urea per hour.