4.6 Acute renal failure

Use to be defined as a **rapid impairment of renal functions leading to accumulation of nitrogenous substances in the body**. The underlying causes can be prerenal or renal, originating in parenchymal lesions, and postrenal. According to the occurence, these conditions are most frequently associated with renal hypoperfusion, with obstructive uropathy or with the renal disease per se. This situation develops in acute glomerulonephritis. The acute, reversible renal failure occurs rather frequently following surgical intervention or trauma. Renal failure is usually associated with the drug treatment of an other disease. It occurs rarely during the pregnancy. The most frequent underlying cause is renal ischaemia following a rapid haemorrhage, during a severe fall of circulating blood volume, hypotension during surgery, cardiogenic shock, during surgical intervention with interrupted renal blood flow. The duration of renal hypoperfusion is the limiting factor. The hypoperfusion can result in acute tubular necrosis.

Several **nephrotoxic substances** may be the underlying cause of acute renal failure: heavy metals and organic solvents – occuring in our milieu and many drugs. At present is the acute renal failure observed after treatment e.g. with aminoglycosidic antibiotics. Usually is the nephrotoxic effect of these antibiotics associated with concomitant application of other nephrotoxic substances and with very effective diuretics. Some anaesthetics and contrast media used in radiological investigation of kidneys and its outflow tract can lead to acute renal failure. Their effect is malignant, chiefly in patients with diabetic nephropathy or in dehydrated patients (where they are absolutely contraindicated).

The acute renal failure may be the result of **an excessive myoglobin release** in the blood. The underlying mechanism is often the rabdomyolysis following the trauma (crush syndrome). Non-traumatic rabdomyolysis may lead to acute renal failure during the heat shock, after extreme physical exertion, in hypokalaemia, hypophosphataemia, during the hyperlipidaemia, treatment by fibrates, or in genetic defects. The ischaemia in muscles results in myoglobin release. Overdosage of some drugs, infections, direct action of ethanol on muscles might be father causes of myoglobin release. The myoglobin itself is not nephrotoxic. To the development of acute renal failure contribute the myoglobin praecipitation in tubules and concomitant hypotension.

The intravascular haemolysis may result in acute renal failure. Haemoglobin is not a nephrotoxic substance. In the pathogenesis of acute renal failure have more importance substances released from the erythrocyte stroma and the concomitant hypoperfusion of kidneys.

From point of view of pathogenesis the acute renal failure can be divided into tubular and vascular type. In the **tubular type** the cylinders and the wastage are considered to be the underlying cause of urine outflow obstruction. The pressure in tubules rises, is transferred into the glomeruli and reduces or stops there the filtration process. In the **vascular form** a considerable constriction of afferent arterioles is suggested. It can be induced by stimulation of nerves, by angiotensin II, or by catecholamines. In this case the decrease of glomerular filtration would dominate. In fact such isolated disturbances do not occur. However, it is to realize, that principally two most important pathogenic factors exist, determining the course and outcome of acute renal failure: the vascular and the tubular factor.

The histological findings support the conception of two most important pathogenetic factors. The lesions observable by microscope are of various degree and considerably variable. Tubular necrosis, tubular cylinders, interstitial oedema, interstitial cellular infiltration, enlarged or narrowed tubules can be observed. The histological alterations may be of two types:

1. Diffuse necrosis of proximal tubules with intact basement membrane
2. Minor necrotic alterations occuring along the entire nephrons

Most outstanding changes are found in distal tubules on the margins between cortex and medulla renis. Disruptions of basement membrane can be observed. Between the histological alterations and impairment of renal functions do not exist almost any correlation. After healing some minute alterations in histological picture may be found.

As mentioned at the beginning, the impairment of renal functions can be induced by praerenal, re-

nal causes, or postrenal causes. The most frequent praerenal cause is the hypoperfusion and the most frequent postrenal cause is the urinary outflow tract obstruction. The glomerulonephritis and interstitial nephritis may also lead to the impairment of renal functions and to acute renal failure. The elimination of extrarenal cause leads to recovery of renal functions. **Every obstacle in urine outflow** can result in impairment of renal functions. The chronic renal failure in its terminal stage can impair to such a degree, that it can imitate the acute renal failure. Uraemic osteodystrophy, neuropathy and anaemia can be found.

Hyaline casts, epithelial cells, erythrocytes and polymorphonuclear leucocytes are found in urine. The finding can be very heterogeneous. It depends from the primary disease.

The first sign of acute renal failure is the oliguria being the cardinal symptome, nevertheless it does not occur in all patients. Azotaemia can occur also in patients without oliguria. The duration of oliguria may be 10 to 14 days, but also several hours only or some weeks. In oliguric patients the creatinine and urea plasmatic level raises. Hyponatraemia, oedema and pulmonary congestion develop. The hyponatraemia is the consequence of water retention and the oedemas are due to sodium retention.

During acute renal failure the **potassium excretion decreases**. The hyperkalaemia can occur also in other disturbances in organism e.g. as consequence of tissue destruction or by potassium shift from cells during acidaemia. When the potassium level exceeds 6,5 mmol/l electrocardiographic alterations appear: deviation of heart electrical axis to the left, pointed T waves, prolonged duration of QRS and PQ and depression of P wave. Bradycardia and cardiac arrest can occur. In acute renal failure appears hyperphosphataemia due to **decreased phosphate excretion**. It does not attain extreme values. Concomitantly with hyperphosphataemia, hypocalcaemia and hypermagnesaemia are observed. The underlying mechanism is not well understood.

In acute renal failure develops the **metabolic acidosis**. The retention of organic acids leads to decrease in plasmatic bicarbonate concentration.

Hyperuricaemia is due to decreased uric acid renal excretion. The excretion of amylase is also reduced, its plasmatic level rises only moderately, unlike in pancreatitis.

The acute renal failure leads to the **impairment of erythropoiesis** resulting in normocytic normochromic anaemia. The number of leucocytes rises owing to the tissue damage. The number of thrombocytes falls concomitantly with erythrocytes because of bone marrow depression and absence of erythropoietin. The disturbance may impair considerably and can result in haemorrhagic diathesis. Disseminated intravascular coagulation is not frequently observed.

The cardiovascular complications are outstanding. The most important are – the hypertension, arrhythmias and pericarditis. The overload of circulation is due to sodium and water retention. The hypertension is not outstanding, it appears during the 2nd week of renal failure duration and its main underlying cause is the fluid retention. Supraventricular arrhythmias occur rather frequently and may complicate the severe condition of the patient. The underlying mechanism is constituted by a complex of factors – the most important of which is congestion of circulation, changes in electrolytes, pericarditis, anaemia.

Metabolic alterations in acute renal failure lead to neurologic disorders, above all in elderly patients. Sometimes psychical disturbances are observed: lethargy, somnolence, confusions. Nearly in all cases gastrointestinal disorders are observed most frequently – anorexia, nausea, vomoting, ileus and diffuse abdominal pain. Haematological disorders and alterations in gastrointestinal tract can be complicated by gastrointestinal haemorrhage.

During acute renal failure **infections often occur** – they are very severe complications ending frequently lethally. The most common are the infections of respiratory system and of urinary tract.

In favorable conditions an **increased diuresis and glomerular filtration** can be observed after the oliguric period. **It is a sign of recovery**. Nevertheless, the complications as the gastrointestinal haemorrhage, electrolyte alterations and cardiac dysfunction may persist. The recovery can begin fallowing 1 to 2 weeks. The improvement of altered functions may last by one year following the acute renal failure. Minute renal functional alterations and hypertension can persist.

The acute renal failure may appear **at the beginning of pregnancy**, but more often during the last trimester and post partum. Following an unsterile

abortus it uses to be associated with sepsis, so with disseminated intravascular coagulation. **Acute renal failure after the delivery** occurs as consequence of acute haemorrhage. In some cases diffuse necrosis is found in renal cortex accompanied usually with disseminated intravascular coagualtion.

The impairment of renal functions can appear also **during hepatic diseases** in absence of known renal or other cause. It is manifested by oliguria associated with a modest finding in urine sediment. It occurs usually during the liver cirrhosis associated with icterus, ascites and hepatic encephalopathy.

4.7 Chronic renal failure

Renal diseases are dangerous because of destructive process progression resulting in lost of nephrones. These are: glomerulonephritis, tubulo-interstitial diseases, diabetic nephropathy, nephrosclerosis and futher renal diseases leading to an extensive reduction of renal nephrones and resulting in chronic renal failure with clinical picture termed uraemia. This term emphasizes the most important finding: the increased plasmatic level of urea. Nevertheless, it implies the deterioration of several mechanisms, causing alterations in the whole organism. The resulting condition depends on extent of nephron reduction and on the speed of its progression.

Kidneys have the capability to maintain body functions unchanged also during decreased glomerular filtration rate. This can be decreased to 35 to 55 per cent of the physiologic values and the patient will be asymptomatic. Except for glomerular filtration decrease no other changes have to be found. **However, when the glomerular filtration falls to 20 to 35 per cent of physiological values, the azotaemia appears with other pathologic signs signalizing the renal failure manifestation**. Systemic arterial hypertension and anaemia are appearing first and most frequently. Later, carbohydrate intolerance, hyperuricaemia, hypertriglyceridaemia and inability to concentrate the urine may be observed. Polyuria and nycturia appears thereafter. This condition can persist during variably long time. Later, a further decrease of nephron number occurs, anaemia and hypertension becomes more severe, renal failure becomes manifest, the metabolic acidosis, gastrointestinal, cardiovascular and nervous disturbances appear. Even in this situation are the kidneys capable to excrete potassium. Clinically important hyperkalaemia does not occur.

It has been known long ago that the serum from an uraemic patient has toxic effects on many biological systems. This fact led to searching after responsible toxins. Substances with toxic effect are protein- and aminoacid-metabolites. Lipids and carbohydrates are metabolized to CO_2 and H_2O and easily excreted by exhalation and through the skin. The waste products of protein metabolism, however, are excreted almost exclusively by kidneys. In patients with chronic renal failure urea represents about 80 per cent of nitrogen excreted by urine. The guanidine compounds are on the second place of importance among the nitrogenous substances being the end - product of protein metabolism: guanidine, methyl- and dimethyl-guanidine, creatinine and guanidine-succinic acid. Further, the metabolites of nucleic acids and derivates of aromatic aminoacids as tryptophan, tyrosine and phenylalanine exhibit toxic effects. It is not possible to decide which substance is responsible for a given symptom. The plasmatic level of urea reflects, to some degree, appearing of anorexia, malaise, nausea, vomiting and headache. Very probably not urea alone is the underlying cause of these symptomes. The guanidine-succinic acid impairs the thrombocyte functions by affecting the thrombocyte factor 3. Some metabolites are not directly toxic (e.g. creatinine), they can however influence other substance which change under their influence into the toxic ones.

In uraemia are nitrogenous substances with high molecular weight retained in the body. Analysing the plasma of uraemic patient, however, molecules of intermediate size were prevailing. The kidneys catabolise many plasmatic proteins and polypeptides. When the functional parenchyma is lost, plasmatic levels of polypeptide hormones: parathormone, insulin, glucagon, growth-hormone, luteinizing hormone and prolactin raise. Not only the renal impairment participates in this increase of proteins, but also the elevated secretion of mentioned hormones during chronic renal failure.