

moderate and asymptomatic proteinuria. Even before proteinuria appears carbohydrate intolerance is almost in all cases present. The glomerular filtration rate is normal or increased.

When the proteinuria appears during the diabetes, glomerular filtration begins to decrease. Very exact regulation of glucose level in peripheral blood can significantly delay the appearance of diabetic nephropathy.

4.9.6 Hereditary glomerulopathies

4.9.6.1 Alport's syndrome (hereditary nephritis with deafness)

Pathogenesis of this condition is not known exactly. There is a disorder of glycoprotein, non-collagenous components of glomerular and tubular capillary basement membrane synthesis. The clinical manifestation is haematuria and proteinuria. The microscopic picture shows commonly focal and diffuse glomerular proliferation with segmental sclerosis.

4.9.6.2 Fabry's disease (hereditary dystopic lipidosis)

is an inherited disorder of glycosphingolipid metabolism with accumulation of trihexosylceramide in the tissues of eye, skin, cardiovascular system and kidneys. In glomeruli, tubules and in renal interstitium typical foam cells are found with lipid vacuoles and excentric location of nucleus. Clinical manifestation of disease are: haematuria and proteinuria with progressive development, resulting in renal failure.

4.9.6.3 Congenital nephrotic syndrome

is a fatal hereditary disease, inherited as an autosomal recessive trait, manifested by nephrotic syndrome in first weeks of life. The synthesis of glomerular and tubular basement membrane components is pathologically altered. Large amount of proteins cross the impaired basement membrane. The proteinuria of non-selective type is very massive. The disease leads to renal failure. Concomitant infection is commonly fatal.

4.10 Infections of the urinary tract

In most cases of urinary system infections is bacteriuria present. Bacteriuria is a condition where in the midstream urine more than 10^5 bacteria are found. Less amount of bacteria may also indicate infection if the urine was obtained by catheterization or by suprapubic aspiration. Bacteriuria however, might be absent in some cases, though the urinary system infection is evident. This situation may occur following or during the antibiotic treatment, during high urea concentration in urine and when the pH of urine is low.

4.10.1 Cystitis, acute pyelonephritis, urethritis

Various types of microbes might be the underlying cause of these diseases. Ninety per cent of acute urinary tract infections are caused by *Escherichia coli*. Further Gram-negative microbes, as *Proteus*, *Klebsiella*, *Enterobacter* and *Pseudomonas* may be responsible for urinary infections. They participate in nosocomial infections. Among the Gram-positive cocci the enterococci and *Staphylococcus saprophyticus* occur most commonly. The viral infections may be the cause of cystitis and pyelonephritis.

Under physiological circumstances the urinary tract cannot be settled by micro-organisms. The urine dispose of direct antibacterial effects. The high urea content and the high osmolarity of urine kill directly the pathogenic germs. The prostatic secretion has also antibacterial activity. The polymorphonuclear leucocytes in the urinary bladder wall also have a protective function.

Favorable conditions for infection arise if obstruction occurs. Tumors of urinary tract, urinary calculosis and hypertrophy of prostata may lead to hydronephrosis and urinary tract infections. In these cases the concomitant infection accelerates the renal tissue destruction.

Vesicoureteral reflux facilitates sometimes the development of infection. The reflux of urine may at-

tain ureters or even renal pelvis. Reflux occurs most commonly in anatomic aberrations.

Renal disturbances raise the possibility of infections appearance. It is not known if renal hypertension accelerates the infection occurrence. The diabetic nephropathy has, however, a very close relation to the urinary tract infections. During the diabetic nephropathy the chronic pyelonephritis occurs most frequently and necrosing papillitis is easily developing. Renal papillae and medulla are very receptive to pathogenic microorganisms.

Infections of urinary tract can clinically occur as strictly defined diseases. Bacteriuria per se occurs also in completely asymptomatic patients. Cystitis has a rather strict clinical symptomatology. Acute pyelonephritis may include the symptoms of the cystitis and further signs as fever attacks, nausea, vomiting, diarrhea and tachycardia. Leucocyte casts and purulent matter are found in urine. Bacteriuria and pyuria may persist longtime. Haematuria is present only at the beginning of disease. During urethral syndrome dysuric troubles are dominant. Infections of urinary tract in hospitalized patients occur namely in connection with catheterization.

4.10.2 Prostatitis

Prostatitis includes various types of inflammatory processes comprising acute and chronic inflammations caused by specific bacteria. Clinical manifestations are: sacralgia, and peritoneal pains. Sometimes testicular discomfort and moderate dysuria are experienced. In additions, microscopic pyuria and haematuria are occasionally observed.

The underlying cause of acute prostatitis use to be the Gram-negative bacterial flora or *Staphylococcus pyogenes aureus*. It is difficult to diagnose the chronic bacterial prostatitis, because the symptoms are often inapparent. In uric sediment excessive leucocyte number may be found. The bacteriologic examination however, might be negative. Dysuric disorders appear when infection reaches urinary bladder.

4.10.3 Chronic pyelonephritis

This term indicates the condition developing following renal infections. It can occur under the influence of predisposing factors as obstructions, vesicoureteral reflux and disorders of urinary bladder

function. Patients with chronic pyelonephritis have a history of frequent, repeated urinary outflow tract infections with impaired renal functions. Their urine contains pus, leucocyte casts and bacteria. Alterations of renal pelvis can be detected by excretion urography. In other cases this finding can be absent in spite of chronic pyelonephritis presence.

Kidneys are of uneven magnitude, with irregular, rugged surface. The pathologic process begins usually in renal interstitium, in medullar region and in renal papillae. Fibrous tissue, lymphocytes and plasma cells replace completely the interstitium and the tubules. In the interstitium, mainly in the medulla renalis are foci of inflammation. In some tubules leucocyte casts occur, in others large amount of eosinophilic material and colloid casts are found. These tubules are dilated. Proliferative arteritis may be present. None of these alterations is pathognomonic for chronic pyelonephritis. The finding in kidneys described above may appear during diabetic nephropathy and many different nephropathies.

The chronic pyelonephritis does not have any typical clinical manifestation. Systemic arterial hypertension is commonly found stimulating the search for the underlying cause. Patient usually visits the doctor only when the first signs of renal failure appear: fatigue, malaise, nausea, tendency to suffusion formation, anorexia, body weight loss, polyuria and nycturia. The progression of pyelonephritis is accompanied with decreased glomerular filtration rate and reduced renal blood flow. The picture of uraemia is developing. Proteinuria raises to 2 g/day. The renal ability to concentrate urine decreases. Presence of bacteria, leucocytes, leucocyte casts in urine may be only intermittent. Renal biopsy can be completely normal.

Chronic pyelonephritis need not cause discomfort and troubles to patients until the renal functions do not impair substantially. Hypertension makes the prognosis of patient worse. During acute infection or dehydration the renal functions may become essentially impaired. The impairment can result even in uraemia. At the beginning is the impairment usually reversible.

4.10.4 Papillary necrosis

Renal papillae play a very important role in the pathogenesis of chronic interstitial nephritis. Renal papillae have high affinity to bacterial infection. It is

very probable that first occurs the papillary damage and the chronic interstitial nephritis develops later. Papillae may be damaged during arthritis urica, and diabetes mellitus. Relatively frequently the papillary lesions occur during treatment with various drugs. Some substances attain just in papillae high concentrations affecting with toxic action papillae and the surrounding area. The effect of phenacetin – a component of analgesic tablets is well known. It is not understood exactly which substances can damage renal papillae. It is suggested however, that the urinary tract infections might cause papillary lesions.

Papillary necrosis appears when the infection is retained in renal pyramids. Participation of a further factor is necessary to give rise to the papillary necrosis. These factors are often: diabetes mellitus, chronic alcoholism and blood vessel diseases.

Clinical manifestations of papillary necrosis are: back pains, abdominal pains, and fever. Acute renal failure with oliguria or anuria can occur occasionally. A sudden impairment of renal functions in patients with diabetes mellitus or with obstruction of ureters signalizes almost in every case the papillary necrosis. If so, fever or pains are not present.

4.11 Tubulointerstitial renal diseases

A large group of diseases exists affecting both kidneys simultaneously, in which morphologic alterations in interstitium and in tubules are present. Also the functional disturbances are limited rather exclusively to the tubules and interstitium.

Glomeruli and the renal vessel system are usually not involved. Interstitial edema prevails in acute form of these diseases, associated often with cortical and medullar infiltration by polymorphonuclear leucocytes. Here are the foci of cellular necrosis. In chronic forms more outstanding interstitial fibrosis, mononuclear inflammatory infiltration with signs of atrophy are observed. The tubular lumen is dilated and the basement membranes are thickened. In past was this morphologic finding considered to be the picture of chronic pyelonephritis. We are aware now,

that only some of these alterations might be caused by infection. In tubulointerstitial disturbances are non-bacterial factors involved, as: exogenous toxins, immunologic and metabolic disorders.

Tubular disturbance is manifested by impaired capability of concentration of the urine, by decreased reabsorption of filtered solutes, especially of aminoacids, phosphates, sodium, chlorides and potassium. Tubular alterations appear at the beginning separatly, later they become concomitant. The structural alterations lead to the progressively reduced glomerular filtration rate. Tubulointerstitial damage causes secondary glomerular disturbances of glomeruli and their involution.

Kidneys have to excrete unnecessary substances, toxins or drugs from the body. This is why these substances cummulate in urine. Various medicaments, the antibiotics above all, can damage the renal interstitium.

4.11.1 Nephropathies

4.11.1.1 Phenacetin nephropathy (Analgesic nephropathy)

It is known that in persons taking large amounts of analgesics lesions of renal interstitium and papillar necrosis frequently are developing. Especially phenacetin and acetylosalicylic acid can cause papillary necrosis.

Analgesic nephropathy is characterized by papillary necrosis and tubulointerstitial inflammation. The papillary necrosis occurs usually following the tubulointerstitial inflammation which causes glomerular filtration rate decrease.

Papillary damage following phenacetin intake is due to its metabolite acetaminophen. Its concentration in papillae is ten times higher than in renal cortex. High water intake reduces papillary acetaminophen concentration and protects the papillae from necrosis. Acetylosalicylic acid inhibits the synthesis of renal prostaglandins which are important vasodilating factors. Thus, the acetylosalicylic acids acts simultaneously by its toxic and by indirect vasoconstrictive effects increasing so the possibility of renal damage appearing.

Analgesic nephropathy is developing usually if the daily intake of phenacetin, lasting 1 to 3 years, is 1 to 2 g.