

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.

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## 4.11 Tubulointerstitial renal diseases

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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.

In analgesic nephropathy is the patients condition impaired by repeated renal colics caused by fragments of necrotic tissue. The colic is usually accompanied with haematuria. Proteinuria is rather moderate. Kidneys of patients with analgesic nephropathy lose the capability to concentrate maximally the urine. Anaemia and systemic arterial hypertension are developing proportionally with azotaemia. Disease may progress rapidly resulting in renal failure. Even when the progression is slow the disease leads to renal failure.

#### 4.11.1.2 Nephropathy due to lead intoxication

Chronic lead intoxication is always associated with renal tubulointerstitial damage. The lead accumulates in cells of proximal tubules and induces degeneration of these cells. The tubular degenerative alterations are accompanied with ischemic alterations of glomeruli and fibrosis of small arteries in cortical region. Azotaemia develops and tubular functions impair. The renal glycosuria and aminoaciduria may appear. In patients with this type of nephropathy the hyperuricaemia is always present due to enhanced uric acid reabsorption. Hypertension, peripheral neuropathy and encephalopathy appear later.

Further toxic substances like heavy metals, radiographic contrast media and antibiotics may induce similar clinical picture of nephropathy.

#### 4.11.1.3 Hyperuricaemic nephropathy

During overproduction of uric acid may the hyperuricaemia cause acute renal failure termed sometimes – the hyperuricaemic nephropathy. This condition does not develop during classic hyperuricaemia. The acute hyperuricaemic nephropathy may arise during treatment of lymphoproliferative or myeloproliferative diseases by cytotoxic substances. In hyperuricaemic nephropathy the deposits of uric acid crystals are formed in collecting ducts, renal pelves and ureters. They may cause obliteration and acute renal failure characterized by oliguria and rapid increase of creatinine concentration. Crystals of uric acid can be found in urine. Haematuria occurs frequently.

During long lasting hyperuricaemia the nephropathy can develop. Uric acid and monosodium urate deposits are formed in renal parenchyma, inducing

an inflammatory process with lymphocytic infiltration. Fibrosis develops in medullar and papillary regions. Systemic arterial hypertension, hyperlipidaemia and degenerative alterations of renal arterioles are commonly observed in patients. Owing to the renal interstitium lesions the capability of urine concentration is diminished. The interstitial fibrosis progresses and leads usually to renal failure.

#### 4.11.1.4 Hypercalcaemic nephropathy

The cause of nephropathy is the chronic hypercalcaemia. Persistent, chronic hypercalcaemia appears during primary hyperparathyroidism, sarcoidosis, multiple myeloma, vitamin D intoxication and metastatic skeletal processes. The tubulointerstitial damage arises first, resulting in renal failure.

The persistent hypercalcaemia causes at the beginning damage of cells of Henle's loop, distal tubules and collecting ducts. The cell damage is very severe and leads to necrosis. The cell necrosis may be the underlying cause of tubular system obstruction resulting in intrarenal urine stasis and calcium precipitation. During this disturbance are the kidneys usually affected by infection.

The tubular cell necrosis and destruction of nephrons due to their obstruction, leads to interstitial fibrosis, mononuclear leucocytic infiltration and interstitial calcium deposition. This condition has been termed in past nephrocalcinosis. Calcium deposits may occur in glomeruli and in blood vessels. Kidneys lose the ability to concentrate the urine. Collecting ducts lose partly the capability to response to ADH. The glomerular filtration rate falls. In long lasting hypercalcaemia nephrolithiasis arises.

#### 4.11.1.5 Hypokalaemic nephropathy

Potassium depletion leads in relatively short time to severe morphologic and functional alterations in kidneys. Alterations of tubular epithelial cells with typical excessive vacuolization may appear. The glomerular cells are usually not affected. Clinical symptoms of hypokalaemic nephropathy appear before the morphologic changes become apparent. Polydipsia, polyuria and nycturia are typical signs of longstanding potassium depletion. Enhanced intrarenal prostaglandin production contributes to the renal alterations. Prostaglandins antagonize the osmotic effects of ADH in collecting ducts. It is how-

ever not well understood to which extend the manifested pyelonephritis might participate in these alterations. Therapeutic management of hypokalaemia and the best adjustment of potassium levels in serum leads within several months to functional and morphologic renal improvement.

#### 4.11.1.6 Neoplastic processes

In malignant processes renal alterations with various manifestation are observed. Postmortal studies revealed histological renal alterations in about 50 per cent of patients. Not only the metastatic process by itself, but also metabolic disturbances due to the basic primary disease cause renal damage.

#### 4.11.1.7 Tubulointerstitial reaction due to drugs

Many drugs may be the cause of tubulointerstitial renal damage. In addition to sulphonamides, the antibiotics and diuretics may be nephrotoxic. The renal lesions are observed interstitium. Oedema and polymorphonuclear leucocytic infiltration of interstitium is frequently found. In extensive damage the necrosis of tubular cells is observed.

In addition the drugs attach to the basement membrane whereby it becomes antigenic. If this occurs the disturbance will present clinically two weeks after the drug administration in form of acute glomerulonephritis.

#### 4.11.1.8 Sjögren's syndrome

Dry keratoconjunctivitis and lesions of mucous membranes of salivary and lacrimal glands are due to immunological disturbance, accompanied sometimes with rheumatic arthritis. Renal impairment may be found. Histologic examination shows lymphocytic infiltration in tubulointerstitial region of kidneys.

#### 4.11.1.9 Irradiation nephropathy

Nephropathy due to irradiation is developing several weeks following exposition to radiation. Glomerular hyalinization, tubular atrophy, interstitial fibrosis and hyalinization of media of renal arteries are found. The underlying cause of these alterations is ischaemia due to irradiation damage. Azotaemia, systemic arterial hypertension, anaemia and proteinuria are rapidly developing.

#### 4.11.1.10 Balkan nephropathy

This condition occurs in the watershed of Danube. Its occurrence is endemic and the underlying cause unknown. The histological examination shows tubular atrophy, interstitial oedema and diffuse interstitial fibrosis. Disease can result in renal failure.

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## 4.12 Renovascular diseases

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This group of diseases comprises renal disturbances related to renal blood supply. The primary disorder is in fact of non-renal origin. Disturbances occurring during stenosis and occlusion of renal arteries, nephrosclerosis, polyarteritis nodosa, haemolytic uraemic syndrome, scleroderma, and prae-eclampsia may be included. Renal damage depends on the speed of occlusion development determining the extent of ischaemia.

As already mentioned, the renal blood flow through kidney, calculated per gram of tissue is the highest in the whole organism. It exceeds many times the heart, liver and brain blood flow. The purpose of this arrangement is not only the oxygen supply but, above all, the glomerular plasma filtration. Kidneys have at disposal several mechanisms to ensure appropriate filtration of plasma and a proper sodium economy. Nevertheless, these mechanisms may influence other systems, mainly the circulation and act at their expense. Extremely reduced glomerular filtration can result in renal failure.

### 4.12.1 Diseases related to the blood supply

#### 4.12.1.1 Acute renal artery occlusion

This term includes acute occlusion of the renal artery, or occlusion of its main intrarenal branch. The acute occlusion may be caused by trauma or embolia. Embolus can occur in stenosis of mitral valve, in bacterial endocarditis, myocardial infarction or atherosclerosis of aorta. The embolus might be, of course, of various size and according to it, it can occlude small or larger branches of renal artery. The