

molecules, including the immune complexes. The loss of electric charge may be the cause of immune complex deposition in glomeruli and vice versa – the immune complex deposition leads to the loss of basement membrane electric charge. This may be one of proteinuria causes.

In Heymann nephritis the immune complexes pass through the basement membrane and form deposits at its outer side. These immune complex deposits lead to forming the epithelial cell processes.

The circulating immune complexes are not per se the cause of pathologic process in kidneys. They occur in circulation without any renal alterations.

In some cases the antibodies against the antigens of epithelial cell pedicles may be produced. These antibodies pass through the glomerular basement membrane and can be bound to antigen. Immune complexes are formed which are situated outside the basement membrane.

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## 4.9 Glomerulopathies

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If the integrity of glomerular capillaries is structurally or functionally damaged disturbances of renal functions may appear. The renal function alterations are the underlying cause of findings occurring isolated or in combination: haematuria, proteinuria, reduction of glomerular filtration rate and hypertension. From pathophysiological point of view some disturbances of glomeruli may be distinguished relatively well: acute forms of glomerulonephritis, rapidly progressive glomerulonephritis, chronic glomerulonephritis, nephrotic syndrome and asymptomatic abnormalities. The clinical classification by itself is considerably variable. It was several times changed until the contemporary classification has been elaborated by WHO (World Health Organization) which takes into consideration mainly the clinical aspects. Thus, the effort of morphologists to adapt it to the morphologic classification is not surprising. The description of single clinical pictures and the precise classification is left to the clinicians.

### 4.9.1 Acute glomerulonephritis

Acute glomerulonephritis is characterised by an abrupt onset. Haematuria and proteinuria associated with azotaemia appear, due to reduced glomerular filtration. Retention of salt and water is present. If it is considerable, oliguria arises. The salt and water retention causes congestion of circulation, hypertension and oedemas. The fluid retention is the consequence of glomerular filtration decrease and of exaggerated water and salt absorption, mainly in the distal renal tubules. Oedema is located at sites with low oncotic pressure (e.g. periorbital oedema), but if it progresses it can lead to ascites or pleural exsudation. The congestion of circulation is manifested by elevated systemic arterial or pulmonal blood pressure associated with normal or enhanced ejection volume per minute and with shortened circulation time. If ischaemic heart disease or valvular defect are not present it is not probable that the right ventricular failure will develop. If the filling pressure in the left heart atrium rises considerably, pulmonal oedema may develop. The arterial diastolic hypertension is caused by several factors: increased volume of extracellular fluid, enhanced heart volume per minute and moderate increase in peripheral resistance. The plasmatic renin activity, aldosterone and the activity of the sympathetic nervous system are rather depressed. The systemic arterial hypertension may be, mainly in younger children associated with encephalopathy.

The most frequent and very remarkable symptom of acute glomerulonephritis is the macroscopic haematuria. The microscopic haematuria can be overlooked. In this case, the fluid retention and hypertension may be incorrectly considered to be symptoms of a different disease. Haematuria is often associated with occurrence of erythrocytic casts in urine. In the definitive urine are found frequently leucocytes and leucocytic cylinders. They are the evidence of inflammatory processes in glomeruli. The degree of proteinuria varies according the glomerular damage extent. Proteinuria may be sometimes severe. In persistent severe proteinuria the nephrotic syndrome is developing.

The course of glomerulonephritis depends on the character of glomerular lesion. In some cases the fluid retention and systemic arterial hypertension may improve. In other cases renal failure develops

rapidly. This condition is termed rapidly progressive glomerulonephritis.

#### 4.9.1.1 Acute poststreptococcal glomerulonephritis

Is observed following infections of upper airways and skin. Infections are caused most frequently by beta-haemolytic streptococci of group A. These, potentially nephritogenic streptococci possess in their superficial membrane an antigen, the M-protein.

Typical for this type of nephritis is the **latent period** between the onset of infection and appearance of first nephritic symptoms. For correct diagnosis of poststreptococcal glomerulonephritis is necessary:

1. To obtain information about the presence of beta-haemolytic streptococci of A group
2. If this is not possible, it is necessary to look for evidence of the immunity reaction to exoenzymes of streptococci. Determination of anti-streptolysine O, antistreptokinase, anti-deoxyribonuclease B, anti-nicotinamid adenin dinucleotidase and anti-hyaluronidase
3. Low plasmatic levels of C3 complement component are regularly observed; moderately decreased components C1q and C4 are also found

In advanced glomerulonephritis a transient cry-immunoglobulinaemia, positive tests demonstrating the presence of immune complexes and of fibrinogen complexes with high molecular weight are found. Sedimentation of erythrocytes used to be elevated. Moderate anaemia and hypoalbuminaemia due to fluid retention and circulating blood dilution are observed, and significant hypoalbuminaemia may be the consequence of a massive proteinuria of non-selective type. Fibrin degradation products and C3 complement component are later found in urine. In azotaemic or oliguric patients hyponatraemia, hypokalaemia and metabolic acidosis are observed. The sodium concentration in urine is usually low, due to its effective reabsorption in distal part of nephrons. Moderate pulmonary congestion and enlargement of cardiac shadow are found in radiographic examination.

**The bioptic examination** reveals diffuse endocapillary proliferative glomerulonephritis. Glomerular infiltration by polymorphonuclear leucocytes and

monocytes is commonly present. The capillary wall is thin. In some glomeruli extracapillary proliferation can be observed. Erythrocytes and erythrocytic casts are present in tubules.

In immunofluorescent microscopic examination granular deposits of IgG with C3 component of complement and properdin are found in capillary loops, at circumference of glomeruli and in mesangium. Less frequently the complement components C1q and C4 are observed. These deposits represent probably the immune complexes.

In some cases the acute poststreptococcal glomerulonephritis leads to lethal end. The underlying cause is mainly the renal failure. Commonly complete recovery occurs. The urine findings normalisation lasts long time, sometimes weeks or months, nevertheless it is not seldom, that the normalization of urine finding lasts years.

Persistent proteinuria or haematuria and slowly progressing glomerulosclerosis are an unwanted outcome of glomerulonephritis. This progression of disease used to be associated with hypertension.

#### 4.9.1.2 Acute non – streptococcal glomerulonephritis

This type of glomerulonephritis resembles to the above mentioned. It is caused by another infection (non-streptococcal). It may occur also following viral and parasitic infections. In this type of glomerulonephritis the circulating immune complexes have a determinant importance. Decrease of C1q, C4 and C3 components of complement is observed. Tests detecting the circulating immune complexes are positive.

#### 4.9.2 Rapidly progressive glomerulonephritis

It is in fact an acute glomerulonephritis without tendency to recovery. On the contrary, it leads to the renal failure in relatively short time. Extensive extracapillary glomerulonephritis with crescents dominates the histological picture. Three types of glomerulonephritis can be distinguished:

1. Renal complications of hidden, or subacute infections
2. Renal complications of systemic diseases

### 3. Primary or idiopathic disease of glomeruli

The first type has been described in the preceding section, the second type will be described in a separate section and the third type will be analysed here.

#### 4.9.2.1 Idiopathic rapidly progressive glomerulonephritis

Azotaemia develops rapidly in this type of glomerulonephritis. Therefore weakness, nausea and vomiting appear soon. In addition oliguria, abdominal pain and haemoptysis often occur. The systemic arterial blood pressure is rather moderately elevated. Haematuria occurs and erythrocyte casts are found in urine. Proteinuria is always present. It may be massive, and it is always nonselective. Products of fibrin degradation occur in urine.

An extensive extracapillary proliferation with characteristic crescents is present in glomeruli. The endocapillary proliferation may also be present, but it is rather a typical feature for the presence of immune complexes. The basement membrane is perforated. In about one third of cases linearly arranged IgG often together with C3 component of the complement occur. This finding confirms the presence of antibodies against the basement membrane. The complement level in plasma is usually unchanged. Occurrence of haemoptysis is observed (Goodpasture's syndrome). The prognosis of rapidly progressive glomerulonephritis is unfavorable. Treatment with glucocorticoids in combination with anticoagulants and cytostatic drugs might bring some hope. The haemodialysis will save the live but not the kidneys per se. Renal transplantation is not very hopeful, in these cases, because the rapidly progressive glomerulonephritis may soon affect the transplant. The antibodies against the basement membrane may circulate in the blood of recipient. The bilateral nephrectomy before the transplantation might be a solution.

#### 4.9.3 Nephrotic syndrome

The typical nephrotic syndrome is characterized by **albuminuria, hypoalbuminaemia, hyperlipidaemia and oedemas**. These alterations are the consequence of plasmatic protein losses by urine. Severe proteinuria is the main symptom of nephrotic syndrome. Protein loss can be considerable, reaching values of

3,5 g (2,5 to 10,0 g) during 24 hours/1,73 m<sup>2</sup> body surface and are considered to be the underlying cause of nephrotic syndrome. Protein loss large like this has never been observed in other renal diseases. Persistent severe proteinuria is associated with hypoalbuminaemia, stimulating the hepatic albumin synthesis. The plasmatic albumin level falls to such a degree, that it leads to changes of Starling forces involved in fluid exchange in capillaries. It results in interstitial oedema formation. It occurs in tissues with low oncotic pressure. The process of filtration at the arterial end of capillaries is not affected. Because of hypoalbuminaemia the oncotic pressure at the venous end of capillaries is low. The filtered water can not be reabsorbed into the capillaries, because the force (albumins) retracting (pulling back) the water into the capillaries is absent. These conditions accelerate or stimulate the mechanisms causing the plasma volume expansion. It is the renin-angiotensin-aldosterone system, increase in ADH secretion, stimulation of the sympathetic system and, probably, decreased secretion of natriuretic hormone. The effect of these mechanisms leads to water and sodium retention. The extent of oedemas reflects the degree of hypoalbuminaemia, respectively of the protein loss by urine. The present condition (status) of the heart and circulation participate partly in the formation of oedemas.

Decreased oncotic pressure of plasma stimulates the **synthesis of lipoproteins in the liver**. Therefore is the hyperlipidaemia often observed in nephrotic syndrome. The low density lipoproteins (LDL) and cholesterol are raised most frequently. During a very marked fall of the oncotic pressure of plasma the very low density lipoproteins (VLDL) and the triacylglycerols raise. The plasmatic protein factors regulating the system of lipoproteins are also lost by urine. This might participate in hyperlipidaemia development. The above mentioned alterations may accelerate atherosclerosis development in patients with nephrotic syndrome. Lipid casts can be found in urine.

Not only albumins but also other plasmatic proteins may be lost by urine. If, e.g. the thyroxine binding globulin (TBG) is lost the turnover of thyroxine and T<sub>3</sub> can be stimulated. Loss of cholecalciferol-binding protein may lead to vitamin D deficiency, to secondary hypoparathyroidism and to renal bone disease (renal osteodystrophy). Hypocalcaemia and hy-

percalciuria appear. The loss of transferrin can result in hypochromic microcytic anaemia resistant to iron therapy. The antithrombin III (heparin cofactor) loss can be presented by hypercoagulation of blood. This condition can be compensated by loss of coagulation factors. The haemocoagulation disorders may result in thrombosis of renal veins.

The complement components can be excreted into the urine and lost, causing so possibly a defect in opsonization of bacteria. Sometimes a severe loss of IgG is observed.

**Oedema** in nephrotic syndrome is a complicated component of the disturbance the beginning of which, respectively the main underlying cause of which - the proteinuria - is seemingly simple. The reduction of oedemas by application of drugs increasing the diuresis can reduce the circulating plasma volume. The decreased volume of plasma becomes the cause of decreased glomerular filtration, which finally may result in acute renal failure. Systemic arterial hypotension due to reduced plasma volume contributes to this process.

Owing to the increased tendency to haemocoagulation thromboembolic complications occur frequently. Thrombosis of pulmonary arteries and veins may develop. Thrombosis can attack also the renal veins manifested by massive haematuria and assymetric renal function.

#### 4.9.3.1 Idiopathic nephrotic syndrome

Comprises several forms, classification of which needs renal biopsy. This is important also from point of view of rational therapy.

**Lipoid nephrosis and minimal abnormalities of glomeruli** In this type of nephrosis any alterations should not be observed in light microscopic examination. In immunofluorescent microscopy irregular, nonspecific deposits of immunoglobulins a complement components might be visible. This type of nephrosis occurs usually in boys from 8 years of age. These patients have normal blood pressure, moderate decrease of glomerular filtration and some of them have a microscopic haematuria. IgM level is usually elevated. In some cases immunization is established in anamnesis, or the upper airways infection. Prevalence of HLA-B12 is stated, associated frequently with atopy. Disease improves spontaneously without apparent causes even for a long time.

Lipoid nephrosis is sometimes developing in patients with Hodgkin's disease. It is supposed, that the lymphocytes play the major role in the pathogenesis of this disease. Neither a rapid fall in glomerular filtration rate, nor acute renal failure occur in this condition. Since the pathogenesis is unknown, the treatment is only symptomatic. Glucocorticoids nevertheless, may induce improvement.

**Focal and segmental glomerulosclerosis** In this type of nephrotic syndrome are some, but not all glomeruli affected by sclerosing lesions and hyalinization. Rather a part of demarkated glomeruli uses to be affected, often the juxtamedullar glomeruli. Concomitant tubular and interstitial lesions occur.

On immunofluorescence deposits of IgM and C3 at sites of segmental sclerosis are found. On electron microscopy lesions of basement membrane and epithelial cells are present. Less than 80 per cent of glomeruli are affected by these alterations in glomerulosclerosis. In the segmental glomerulosclerosis are the glomeruli only partially damaged.

Systemic arterial hypertension, decreased glomerular filtration, altered tubular functions and pathological findings in urine are often observed. Nonselective proteinuria is usually present. The global condition of the patient and the degree of hypoalbuminaemia are determined by proteinuria extent. About one half of patients die in ten years. The concomitant systemic arterial hypertension and azotaemia worsen the prognosis.

**Membranous glomerulopathy** is characterized by irregular protein deposits at the outer side of basement membrane under the epithelial cells. These deposits consist mainly of IgG. In this condition are almost all glomeruli damaged rather uniformly. The progressive apposition of deposits leads to the thickening of the glomerular capillary wall. Towards the Bowman's capsule spike-shaped protrusions appear, typical features of this condition. Moderate proliferation of endothelial and mesangial cells is observed. In later stages tubulointerstitial atrophy occurs. The systemic arterial blood pressure, glomerular filtration rate and urinary sediment remain relatively long time normal.

The membranous glomerulopathy can occur during certain chronic infections, solid tumors, melanoma, pulmonary and colon carcinomas but also following penicillin application.

### Membranous proliferative glomerulonephritis

The most characteristic features in this condition are the proliferation of mesangial cells and increase in mesangial matrix, in addition, irregularly thickened walls of glomerular capillaries can be found. The basement membranes become also thicker. This type of glomerulonephritis belongs in fact to the mesangiocapillary or tubular glomerulonephritis group. Several types of proliferative membranous glomerulonephritis can be distinguished :

1. Subendothelial deposits are present; C3 component of the complement in granular form is almost regularly found
2. Lamina densa of basement membrane is extremely dense; therefore is this condition termed the dense deposit disease. The basement membrane of Bowman's capsule and of tubules are damaged, deposits of C3 component of complement and a few IgM are present.

The systemic arterial pressure is usually increased, the glomerular filtration decreases. Fibrin degradation products and the C3 component of complement are present in urine. The C3 plasmatic level falls. In the first, above mentioned type of disease, circulating immune complexes are found. Similar alterations as in type I occur in haemolytic uraemic syndrome, in transplant rejection and in chronic hepatitis. Nearly 60 per cent of patients die over a ten-years period of renal failure.

### Other forms of idiopathic nephrotic syndrome

This group may include conditions with not very clearly defined rather modest bioptic findings as the mesangial proliferative glomerulonephritis, or the crescentic glomerulonephritis, or finally the segmental proliferative glomerulonephritis. Deposits of IgA and IgM may be present and haematuria with proteinuria use to occur.

Nephrotic syndrome can develop also during or following treatment with some sort of drugs. Drug-induced nephropathy occurs frequently after the therapy of patients with rheumatic arthritis with gold containing drugs. Idiopathic nephrotic syndrome may be induced also by application of antiserum during infection diseases.

## 4.9.4 Isolated asymptomatic renal disorders

In these conditions proteinuria of non-nephrotic character associated with haematuria is found, or isolated haematuria without oedemas, hypertension and decreased glomerular filtration. These alterations can be persistent or intermittent, interrupted by asymptomatic intervals.

### 4.9.4.1 Idiopathic renal haematuria (Berger's IgA nephropathy)

Characteristic of the disease is recurrent micro- or macrohaematuria. The microscopic examination reveals large deposits of IgA in mesangium and in glomeruli. Haematuria is often associated with rather moderate proteinuria. The level of IgA in serum is increased. In skin examination the IgA, C3 component of the complement and fibrin deposits are often observed in skin capillaries. Similar skin alterations occur in Henoch-Schönlein purpura. The Berger's IgA nephropathy might be in fact a form of this purpura. The biopsy shows a wide range of changes in glomeruli. The most frequently are such alterations present which are typical of the segmental proliferative glomerulonephritis. The progression of disease is slow. It results about in a half of cases in renal failure.

Histological changes in kidneys are sometimes not observed, apart from IgM and IgG deposits. In this case is the prognosis of disease favorable.

### 4.9.4.2 Isolated glomerular proteinuria of non-nephrotic type

Proteinuria does not exceed 3,5 g of proteins / 1,73 m<sup>2</sup> of body surface per day. It is usually not associated with renal alterations and the urinary sediment use to be normal. The orthostatic proteinuria is the most common type of this proteinuria.

### 4.9.4.3 Chronic glomerulonephritis

Chronic glomerulonephritis presents persistent proteinuria and/or haematuria and progressive deterioration of renal functions. The condition leads to the hypertension of shrunken kidneys and renal failure. The terminal stage is preceded by changes which could form three groups of typical processes:

1. Proliferative processes: as in endo and extracapillary proliferative glomerulonephritis, focal and segmental proliferative glomerulonephritis
2. Sclerosing processes; focal and diffuse glomerulosclerosis
3. Membranous processes; are the most frequently occurring

The so-called chronic nonspecific glomerulonephritis may exceptionally be included. Chronic glomerulonephritis is not a specific nosologic unit. It represents, in fact, a group of diseases with various etiology, pathogenesis, course, morphological and clinical pictures. The chronic glomerulonephritis is not presented by typical strictly defined clinical features, thus it is diagnosed usually by different ways:

1. by appearance of pathologic urinary finding, impaired renal functions and systemic arterial hypertension in subjects with moderate clinical symptomatology
2. by statement of renal disease progression and impairment with appearance of hypertension and anaemia
3. by determination of glomerulonephritis exacerbation during viral or bacterial diseases

Some symptoms dominate the clinical picture of chronic glomerulonephritis. The most important are: symmetric shrinkage of kidneys, severe proteinuria and pathologic finding in urine sediment. In sediment prevail the erythrocyte casts.

The chronic glomerulonephritis could be virtually limited in time. It can be, in fact, any type of severe glomerulonephritis in the period before the renal failure.

#### 4.9.5 Glomerulopathies in other diseases

Glomerular damage is observed in several systemic diseases. It may be the dominant finding in metabolic disturbances (diabetes mellitus), neoplastic processes, genetic disorders, in diseases where different immune processes are the underlying cause.

##### 4.9.5.1 Systemic lupus erythematosus

The underlying cause of lupus erythematosus is till now unknown. The serum of patients suffering from systemic lupus erythematosus contains large amount of antibodies against DNA, nucleoproteins, and several components of nuclei. These antibodies are termed in common: antibodies against nuclear antigens (ANA antibodies to nuclear antigens). The antibodies per se do not damage living cells providing they do not penetrate the cell membranes. ANA form complexes with their specific antigens. DNA and the antibodies to DNA, nuclear proteins, antibodies to nuclear proteins and the components of the complement are observed in the basement membrane of glomerular capillaries, but also in basement membrane of other capillaries.

The pathological process in glomeruli leads to massive haematuria and proteinuria associated with fulminant inflammatory alterations. Impairment results in renal failure. Of the large number of variable glomerulonephritis forms associated with lupus erythematosus some clinical pictures may be defined on the basis of glomerular morphologic changes.

**Mesangial lupus glomerulonephritis** is presented by proliferation of mesangial cells or by mesangial sclerosis. Immunofluorescent examination reveals IgG, IgM, IgA immunoglobulins and C1q, C4 and C3 components of the complement forming outstanding electron-dense deposits. Glomerular filtration rate is usually normal at the beginning. Occurrence of hypertension is not constant. The development of disease depends on disturbances of other organs.

**Focal lupus glomerulonephritis** In this condition focal and segmental distribution of cell proliferation is observed, often associated with necrosis and diffuse mesangial hypercellularity. The glomerular deposits of immunoglobulins and complement components are larger than in mesangial form. The mesangium and glomerular capillary loops are involved. Subendothelial deposits are observed. Impairment can lead to nephrotic syndrome. The glomerular filtration rate is usually not changed. The disease may progress like diffuse proliferative glomerulonephritis.

**Diffuse proliferative lupus glomerulonephritis** Diffuse proliferation of mesangial and endothelial cells is typical of this disease. In addition focal cellular necrosis is found. Subendothelial and subepithelial deposits and extracapillary proliferation are present. Nearly in all glomerular loops granular deposits of

immunoglobulins and complement components are observed. In this type of glomerulonephritis the patients have severe proteinuria and progressively impairing renal functions.

**Membranous lupus glomerulonephritis** is similar or rather identical with the idiopathic membranous glomerulopathy. In addition mesangial deposits and proliferation of mesangium are observed. The walls of glomerular capillaries are thickened in subepithelial region by deposits of immunoglobulins and complement components. Nearly in all patients a massive proteinuria with signs of nephrotic syndrome is present. The glomerular filtration rate progressively diminishes. Disease results in renal failure. Rapid obliteration of capillaries occurs in some nephrons. Owing to this glomeruli undergo sclerosis. This is usually the last stage of disease.

#### 4.9.5.2 Goodpasture's syndrome

The characteristic features are pulmonary haemorrhage, glomerulonephritis and presence of antibodies to basement membrane antigens. The pulmonary haemorrhage may be of various severity. During the cough might the haemoptysis become very dramatic. Otherwise it can be mild but longlasting, leading to sideropenic anaemia. The haemoptysis can be associated also with renal failure, systemic lupus erythematosus, Henoch-Schönlein purpura, cryoglobulinaemia, pulmonary embolia Legionnaires' disease and further conditions. The extracapillary proliferation is often present. Renal failure might develop rapidly. The histologic examination shows typical linear deposits of antibodies to basement membrane, associated sometimes, with C3 deposits.

In peripheral blood of 90 per cent of patients, presence of circulating antibodies against the glomerular basement membrane, alveoli and tubules is stated. The levels of these antibodies do not provide a precise information on the severity of the condition and on the degree of the damage.

#### 4.9.5.3 Henoch-Schönlein purpura

Presence of nonthrombotic purpura, arthralgia, abdominal pain and glomerulonephritis are the characteristic features of this condition. The underlying cause of purpura is the vasculitis in the skin, dominantly in the vicinity of low extremity joints. Arthralgia and abdominal pain may be of various inten-

sity. Even gastrointestinal haemorrhage with perforation may occur. The renal damage is manifested by haematuria and proteinuria. The disturbance may progress rapidly in form of nephritis or nephrotic syndrome. The beginning of disease may be presented as postinfectious glomerulonephritis. About in one half of patients is the IgA level in serum increased. Renal biopsy reveals a wide range of alterations. Diffuse proliferation of mesangial cells or focal segmental proliferative glomerulonephritis can occur. The picture of diffuse proliferative glomerulonephritis may also occur, associated sometimes with extracapillary proliferation. Granular deposits of IgA, IgG, C3, properdin and fibrinogen are usually present. It is supposed, that the Henoch-Schönlein purpura may be very probably caused by immune complexes containing IgA. The origin of antigen is not known. The IgA nephropathy (m. Berger) could be considered to be a form of Henoch-Schönlein purpura.

The course of disease may be benign, in some patients however, it can result in renal failure.

#### 4.9.5.4 Renal lesions in various types of systemic vasculitis

Glomerular disturbances used to be associated with diseases manifested by inflammatory vascular lesions. The most typical are: the macroscopic and microscopic polyarteritis nodosa and the Wegener's disease.

**Macroscopic polyarteritis** – typical features in this condition are the inflammatory lesions of large vessels. Occlusions of renal vessels and renal infarctions may occur. Deposits of immune complexes are found in vessels. These immune complexes are in some cases in connection with hepatitis B in anamnesis of the patient. The level of circulating immune complexes used to be increased, hypertension associated with microangiopathic haemolytic anaemia is often present. Fever, abdominal pain, skin alterations and disorders of nervous system and coronary vessels occur occasionally.

**Microscopic polyarteritis** affects small vessels of kidneys and other organs. The pulmonary vessels are often involved. Antibodies to basement membrane are often present. During the pulmonary vessels involvement eosinophilia appears. The picture of segmental or diffuse capillary necrosis is observed in kidneys. In affected glomeruli deposits of IgG and IgM

are found. Some patients with macroscopic or microscopic polyarteritis may have rheumatoid arthritis. The prognosis depends on glomerulonephritis progression.

**Wegener's granulomatosis** is a vasculitis disseminated in upper airways and kidneys. In lungs, kidneys and other organs sclerosing vasculitis can be seen due to the deposition of immune complexes. The origin of the antigen is unknown.

#### 4.9.5.5 Cryoglobulinaemia

This disturbance is associated with the presence of circulating immuno-globulins praecipitating reversibly when exposed to cold. They consists usually of IgG and IgM. Purpura, necrosing cutaneous lesions, arthralgia, fever and hepatosplenomegaly may occur. The condition can be due to hepatitis B, bacterial, viral mycotic and other diseases. Cryoimmunoglobulins may be found in serum also during several further diseases. The cryoimmunoglobulins praecipitate in glomerular capillaries, thus the clinical picture of acute renal failure or of rapidly progressing glomerulonephritis, or of nephrotic syndrome can develop. The complement level in serum is often reduced and circulating immune complexes are regularly present. The picture of diffuse proliferative glomerulonephritis with circulating cryoimmunoglobulins may develop.

#### 4.9.5.6 Plasmacytoma (multiple myeloma)

The most frequent renal damage in plasmacytoma is the amyloidosis. Amyloidosis however, may occur in several pathologic conditions. The cellularity in glomeruli is reduced and glomeruli are progressively infiltrated by amorphous amyloid deposits. Amyloid is a protein with typical ultrastructure. The renal amyloidosis is a persistently progressing disease.

#### 4.9.5.7 Neoplastic diseases

Glomerular lesions may appear in various neoplastic conditions. Adenocarcinoma of lung, colon, stomach and breast, especially, can lead to the development of idiopathic membranous glomerulonephritis. The focal or segmental proliferative glomerulonephritis or amyloidosis dominates the histological picture. The disturbance is clinically presented by nephrotic syndrome. The underlying cause of glomerular lesion

is the deposition of circulating immune complexes composed of tumor antigens and antitumor antibodies. Lymphomas and leukaemias are also associated with glomerulopathies. Proliferative and sclerosing glomerulopathy is dominant in the histological picture.

#### 4.9.5.8 Renal disorders in rheumatoid arthritis

can develop as consequence of gold therapy or penicillamine treatment. The clinical picture may be similar to the amyloidosis, or to the disturbance described in systemic lupus erythematosus. During rheumatic fever proliferative glomerulonephritis may occur. Chronic hepatic diseases are often connected with renal disturbances. In chronic active hepatitis membranous proliferative glomerulonephritis with deposits of immune complexes occur. Hepatic cirrhosis use to be accompanied with glomerulosclerosis. In alcoholic cirrhosis deposits of IgA can be found in mesangium.

#### 4.9.5.9 Diabetic nephropathy

All renal disturbances appearing in diabetic patients are termed diabetic nephropathy. Glomerulosclerosis, arterionephrosclerosis, chronic interstitial nephritis, papillary necrosis and various tubular disorders are observed most commonly. The diabetic nephropathy use to be associated with several clinical syndromes, mainly with asymptomatic proteinuria, nephrotic syndrome, renal failure and hypertension.

The diffuse diabetic glomerulosclerosis is the most frequent type of renal damage in diabetics. Moderate enlargement of mesangial matrix and thickening of glomerular capillary basement membrane are observed. Degenerative process in form of hyaline arteriosclerosis affects vasa afferentia. In diabetes where the antibodies to the Langerhans' islet cells are present, intercapillary nodes are formed in kidneys (intercapillary glomerulosclerosis) and enlargement of mesangial matrix occurs. The nodes do not contain cells. In other cases may occur, on the contrary, the picture of membranous proliferative glomerulonephritis. Pathogenesis of diabetic nephropathy is not well understood, nevertheless it depends, in a considerable degree, on metabolic compensation of diabetes.

Diabetic nephropathy is clinically presented by

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.

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## 4.10 Infections of the urinary tract

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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-