Kidney diseases

Morphology and general pathology
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Classification of kidney diseases

- Currently, there is no single classification of kidney disease.
- According to the structural and functional principle, the following groups of kidney diseases are distinguished:
  - With predominant glomerular lesions (glomerular, or glomerulopathies),
  - With predominant involvement of tubules (tubular, or tubulopathies),
  - With a predominant lesion of stroma and vessels (stromal, or interstitial).

Glomerulopathies

- A group of kidney diseases with a predominant lesion of the glomerular apparatus.

- On the etiology of glomerulopathy:
  - Hereditary,
  - Acquired.

- By the nature of the pathological process of glomerulopathy are:
  - Inflammatory,
  - Non-inflammatory.

Glomerulopathies

- Hereditary glomerulopathies:
  - Alport syndrome (nephritis with hearing loss and blindness),
  - Hereditary amyloidosis of the kidneys,
  - Lipid nephrosis.

- Acquired glomerulopathies:
  - Glomerulonerphitis,
  - Membranous nephropathy,
  - Focal segmental glomerulosclerosis,
  - Diabetic nephropathy,
  - Acquired amyloidosis of the kidneys,
  - Others.

Morphology of glomeruli damage

- Lesions of glomeruli in terms of scale and location can be:
  - Global - involves the glomerulus entirely,
  - Segmental - only a part of the glomerulus is affected;
  - Diffuse - all the glomeruli of the kidney are captured,
  - Focal (focal) - a part of the glomeruli of the kidney is damaged.

- These terms are used in the histological classification of glomerulonephritis.

Morphology of glomeruli damage

- Changes in glomeruli are characterized by one (or more) of 4 main types of tissue reactions:
  - Hyper-cellularity,
  - An increase in the extracellular matrix,
  - Sclerosis and hyalinosis,
  - Additional damage.

Morphology of glomeruli damage

- Hyper-cellularity (multicellularity) can be caused by:
  - Proliferation (increase in the number) of the cells of the glomerulus (mesangial, endothelial),
  - Accumulation (infiltration) of leukocytes (neutrophils, monocytes, rarely lymphocytes) in the lumens of the glomerular capillaries, under endothelial cells or in mesangium.

Morphology of glomeruli damage

- The accumulation of cells in the urinary space is called a semi-moon.
- Semi-moons occurs as a result of severe damage to the walls of the glomerular capillaries with a violation of their integrity and "spillage" of fibrin from damaged capillaries into the urinary space.
- This leads to the proliferation of cells of the parietal and, possibly, visceral epithelium and the accumulation of monocytes and other cells in the urinary space.

Morphology of glomeruli damage

- An increase in the extracellular matrix means an expansion of the mesangial matrix or thickening of the glomerular basement membrane (GBM).

- The expansion of the mesangial matrix can be diffuse - approximately equally in all lobules of the glomerulus, or in the form of nodules.

- Thickening of the GBM under a light microscope is manifested in the form of a thickening of the walls of capillaries, which is clearly visible in sections stained with the help of a PAS-reaction.

- However, the thickening of GBM is better assessed by electron microscopy.

Morphology of glomeruli damage

- Gialinosis of glomeruli is associated with the accumulation of a substance that under the light microscope looks homogeneous and eosinophilic; Electron microscopy shows that this substance is located outside the cells and consists of precipitated plasma proteins.

- There is also an increase in the basal membrane proper and mesangial matrix; These changes lead to the obliteration of the capillary loops of the glomerulus (sclerosis).

- Additional damage is caused by precipitation of fibrin, intraglomerular thrombosis, precipitation of abnormal substances (amyloid, lipids, so-called dense deposits).

Inflammatory glomerulopathies

- Presented by various forms of glomerulonephritis.

Glomerulonephritis (GN)

- Glomerulonephritis is a disease of an infectious-allergic or unknown nature, is characterized by bilateral purulent inflammation of the kidney glomeruli with the development of both renal and extrarenal symptoms.

- The renal symptoms include proteinuria, hematuria, cylindruria and oliguria.

- The extrarenal symptoms - edema, arterial hypertension, hypertrophy of the left heart, dysproteinemia, hyperazotemia, uremia.

- The listed symptoms with glomerulonephritis can have a different combination.

Classification of GN

- Primary glomerulonephritis, in which the kidney is the only or predominantly affected organ,

- Secondary glomerulonephritis, in which the kidney is damaged as a result of some disease (for example, with SLE).

Classification of GN

- By the nature of the current:
  - Acute,
  - Rapidly progressive (subacute),
  - Chronic;

- By localization of the process in the glomerulus:
  - Intracapillary,
  - Extracapillary;

- By the nature of inflammation:
  - Exudative,
  - Proliferative,
  - Mixed.

Etiology of GN

- The causative agents of glomerulonephritis are most often nephritogenic strains of hemolytic streptococcus.
- However, it can also be caused by staphylococcus, pneumococcus, a number of viruses (for example, hepatitis B), pale treponema, malarial plasmodium.
- Infectious glomerulonephritis, which develops after infectious diseases (angina, scarlet fever, acute respiratory infections, pneumonia, meningococcal infection, malaria, bacterial endocarditis, syphilis), is an allergic reaction of the organism to the pathogen.
- Among the non-bacterial causes of primary glomerulonephritis may be some drugs, alcohol.

Pathogenesis of GN

- In the overwhelming majority of cases, the immunologically conditioned glomerulonephritis primarily develops.

- There are two mechanisms of damage to the renal glomeruli:
  1) damage associated with precipitation of the CIC (immunocomplex glomerulonephritis);
  2) damage caused by antibodies binding in situ with insoluble antigens of the renal glomerulus, or with antigens embedded in the glomerulus (antibody glomerulonephritis).

- The provoking factor in the development of glomerulonephritis in a body that is sensitized to a particular causative agent is hypothermia.

Pathogenesis of GN

- 1. Damage associated with precipitation of the CIC: CECs penetrate the glomerular basement membrane (GBM) and settle in the basal membrane or on its outer side in the form of deposits.
- At the same time, complement is activated, C3 is deposited along with immune complexes.
- Chemotaxis of neutrophilic leukocytes, which destroy the GBM with proteolytic enzymes.
- At the same time, the hemocoagulation system is activated locally, mediators of inflammation are released.
- The immunocomplex mechanism of glomerular lesions was confirmed by granular luminescence of the glomerular capillary walls with immunofluorescence microscopy.

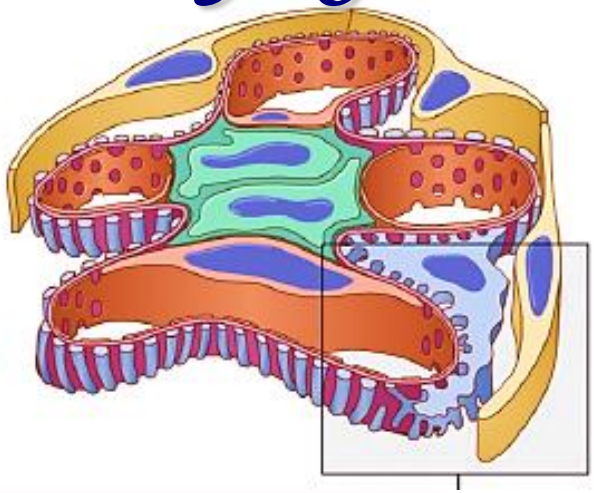
Pathogenesis of GN

- 2. Precipitation of immune complexes in situ:

- With this form of damage, the antibodies react directly with the constant components of the glomerulus (for example, type IV collagen in the GBM, visceral epithelium) or antigens implanted in the glomerulus.

- The linear luminescence of immunoglobulins along the basal membrane in immunofluorescence microscopy indicates the in situ binding of antibodies to GBM with its components.

Pathogenesis of GN



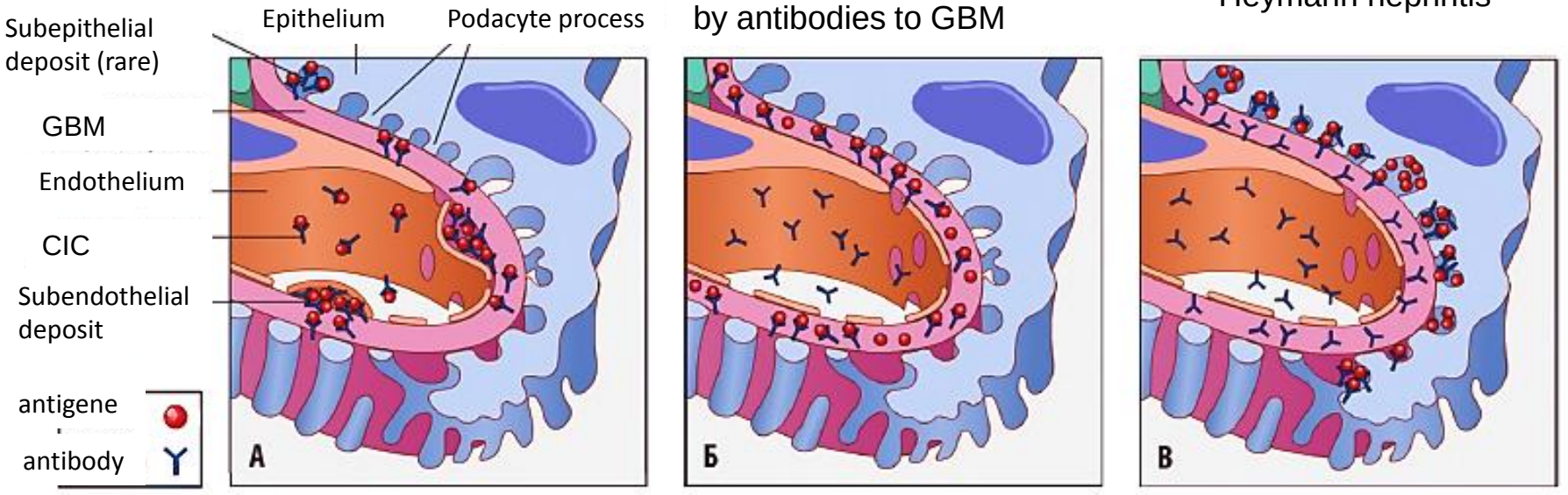
circulating immune complexes

immune complexes in situ

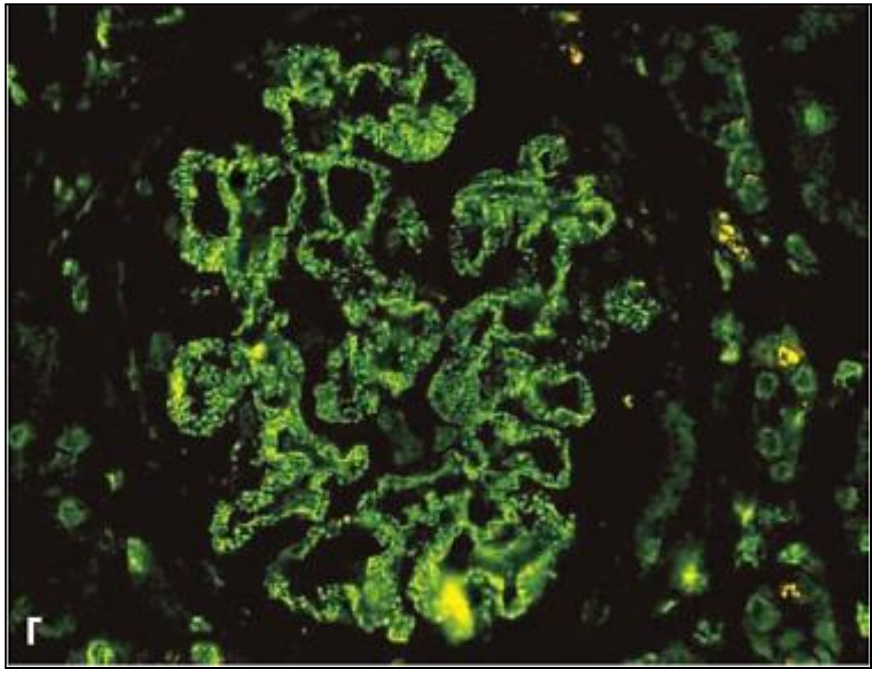
Deposits of CIC

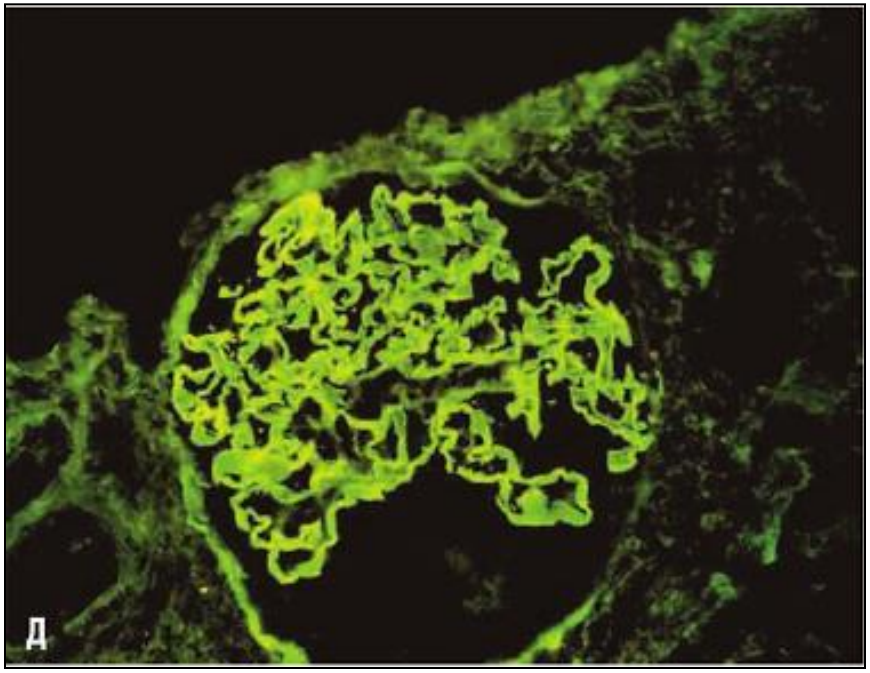
Glomerulonephritis induced by antibodies to GBM

Heymann nephritis



Granular and linear glow with GN (Immunofluorescence microscopy)





Acute GN

- Synonyms: acute post-infection glomerulonephritis, acute post-streptococcal glomerulonephritis, diffuse intracapillary proliferative glomerulonephritis.
- It is characterized by a diffuse global lesion of the renal glomeruli.
- Usually it develops 1 to 4 weeks after a streptococcal, or other infection, is more common in children, but adults of any age can also be ill.
- It is caused by β-hemolytic streptococcus of group A (other strains than in rheumatism).

Acute GN

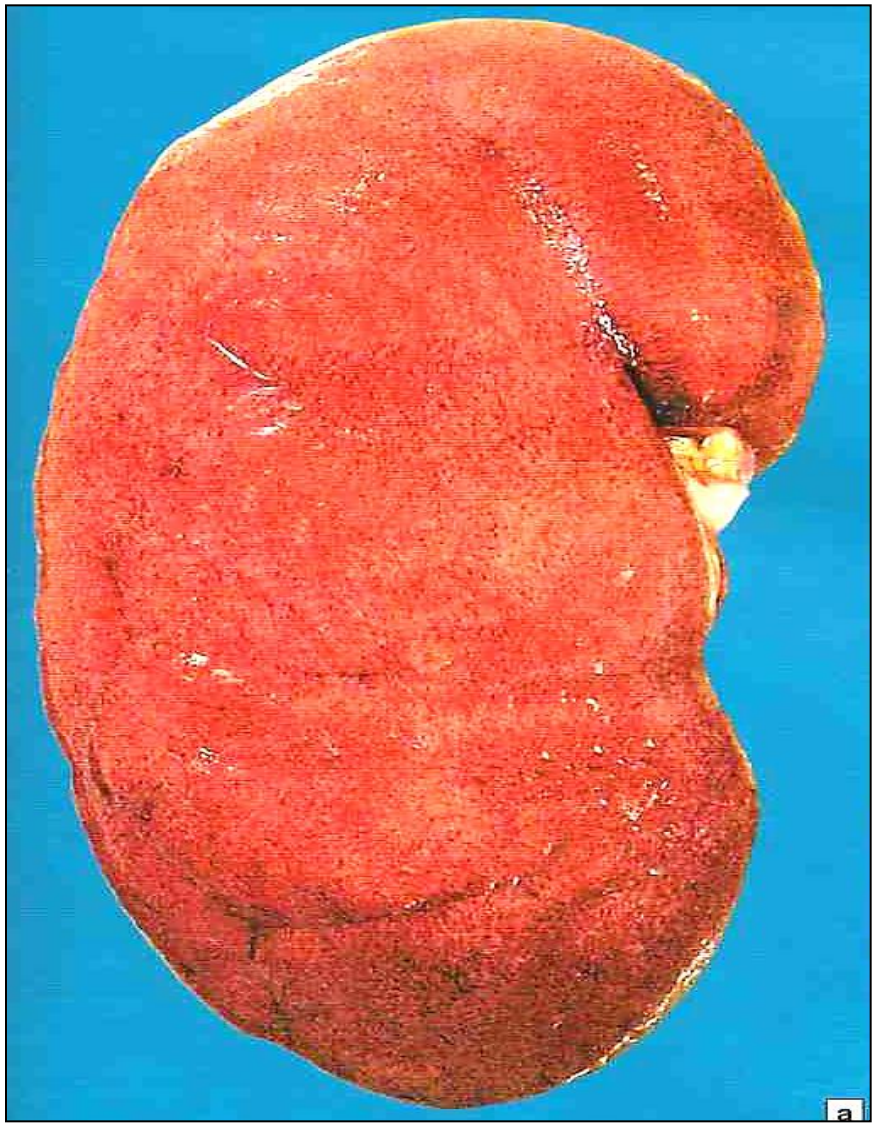
- Pathogenetically, this is an immunologically conditioned disease that has an immune complex mechanism of damage.
- Clinically characterized by acute nephritic syndrome.
- Acute glomerulonephritis usually ends in recovery, but in a number of cases it acquires a prolonged course with the formation of a second-wrinkled kidney and the development of chronic renal failure.

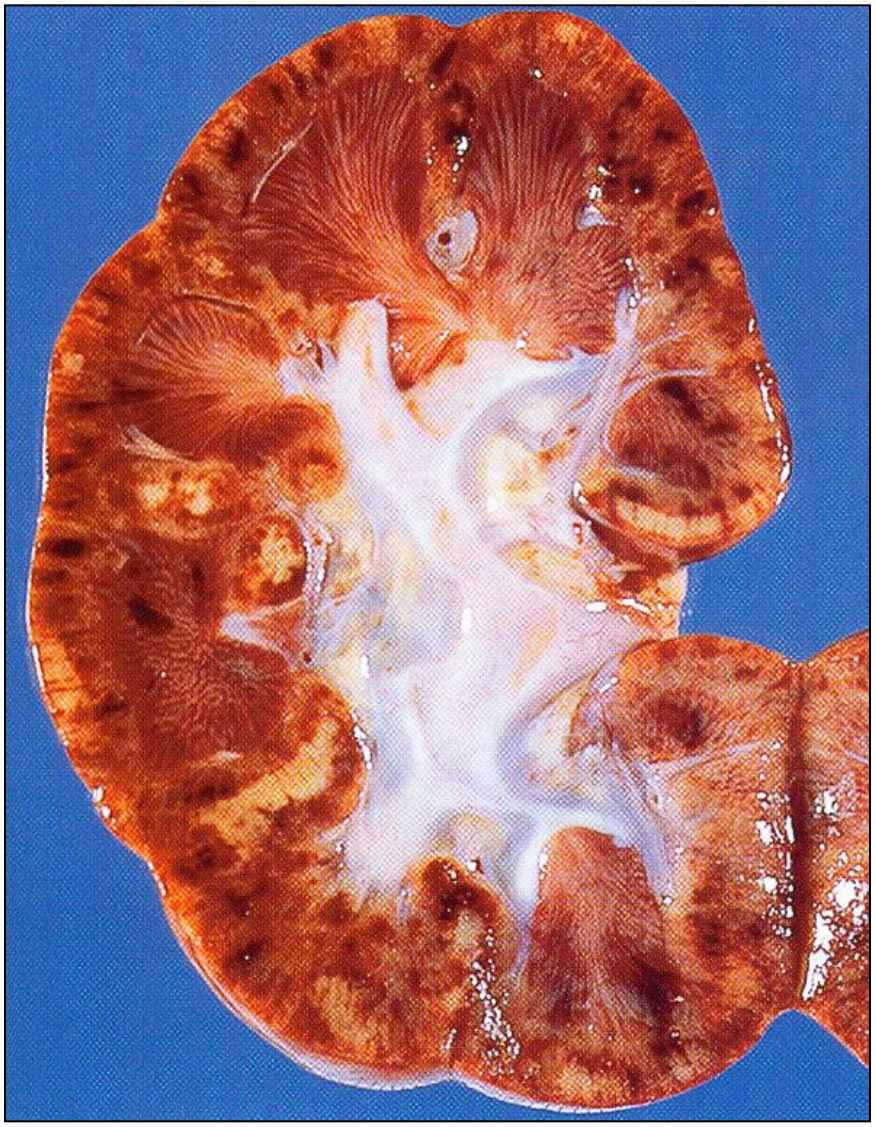
Morphology of acute GN

- Macroscopic picture:
  - The kidney is enlarged in size,
  - Flabby consistency,
  - The layer of the cortical substance is expanded, full-blooded, in it under the capsule red patch ("large variegated kidney") can be seen.

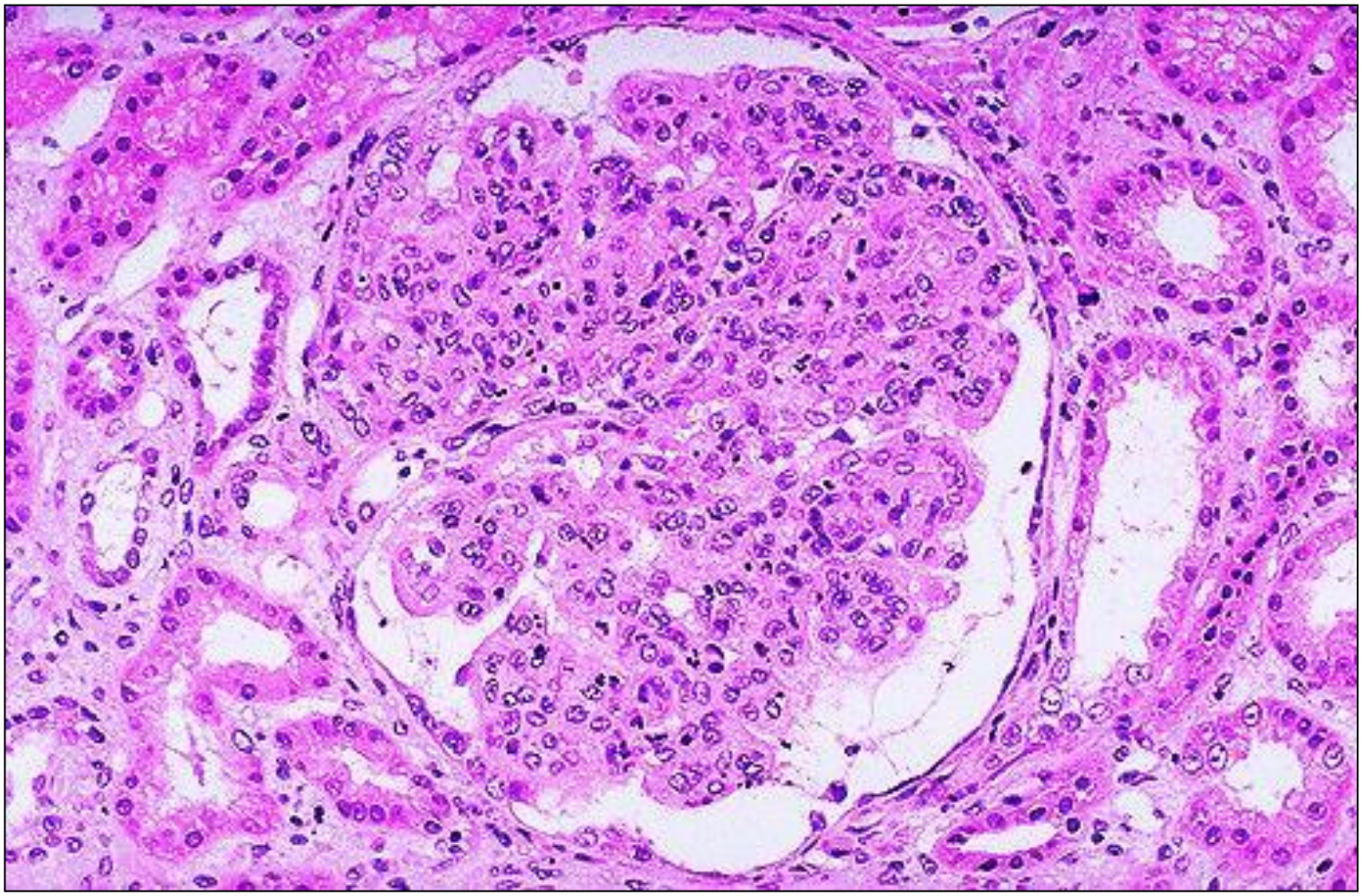
- Microscopic picture:
  - Hypercellularity of the renal glomerulus due to neutrophilic leukocyte infiltration and proliferation of endothelial and mesangial cells (intracapillary proliferative glomerulonephritis),
  - The contours of the glomerular capillary loops are poorly expressed.

"Large variegated kidney"





Hypercellularity of the glomerulus with acute GN

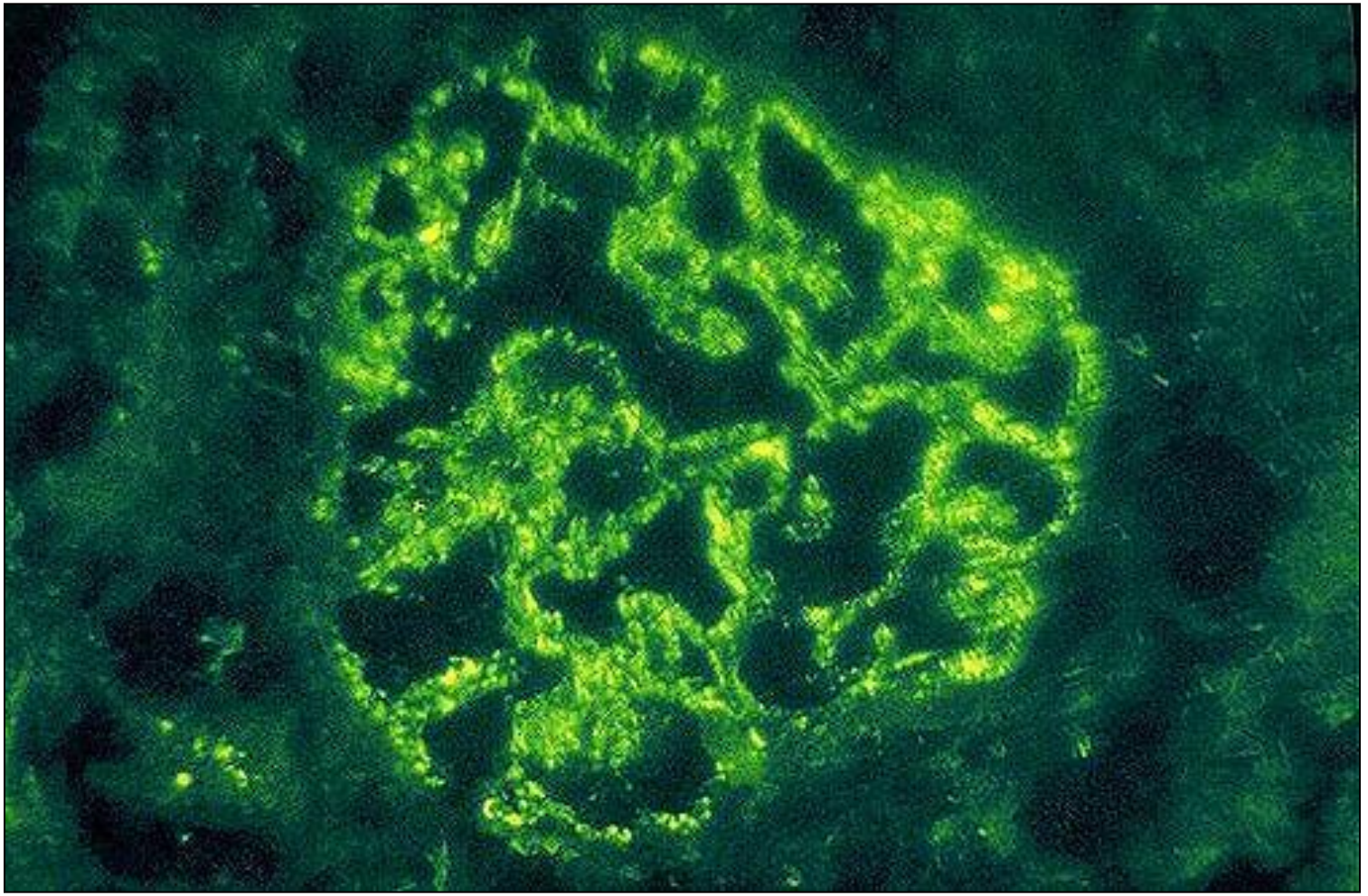


Morphology of acute GN

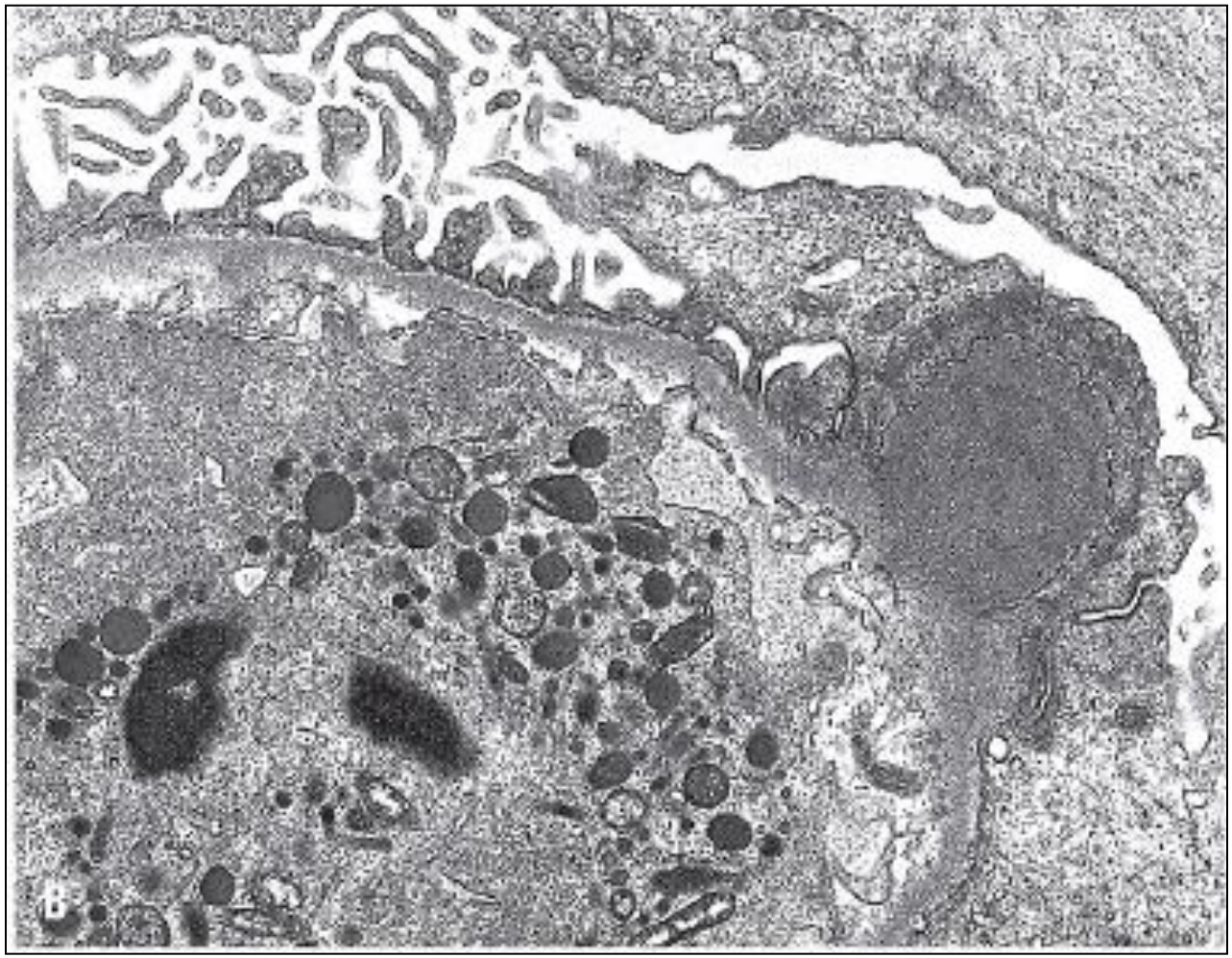
- In immunofluorescence microscopy, granular deposits from the IgG, IgM and C3 components of the compliment are detected in the mesangium and along the GBM.

- With electron microscopy - electronically dense subepithelial deposits that look like "humps."

Granular deposits C3 with acute GN (IFM)



Subepithelial deposit in the form of a "hump" with acute GN (EM)



Rapidly progressive GN (RPGN)

- Synonyms: malignant glomerulonephritis with semilunium, diffuse extracapillary proliferative glomerulonephritis, subacute glomerulonephritis.

- It occurs more often in the elderly, but can also occur in adolescence, with the same frequency among men and women.

- The RPGN is divided into 3 groups:
  - Postinfection (poststreptococcal);
  - With systemic diseases (systemic lupus erythematosus, Goodpasture syndromes, Wegener syndromes),
  - Idiopathic (unclear etiology).

Rapidly progressive GN

- There is no single pathogenetic mechanism that could explain all the cases of the RPGN.
- With systemic lupus erythematosus and with post-streptococcal forms, the RPGN is associated with immune complexes.
- The RPGN with Goodpasture syndrome (pneumo-renal syndrome) is a classic example of an antibody nephritis.
- Idiopathic RPGN can be associated with various pathogenetic mechanisms: immune complexes, antibodies to GBM.
- The RPGN usually ends with the development of acute or chronic renal failure.

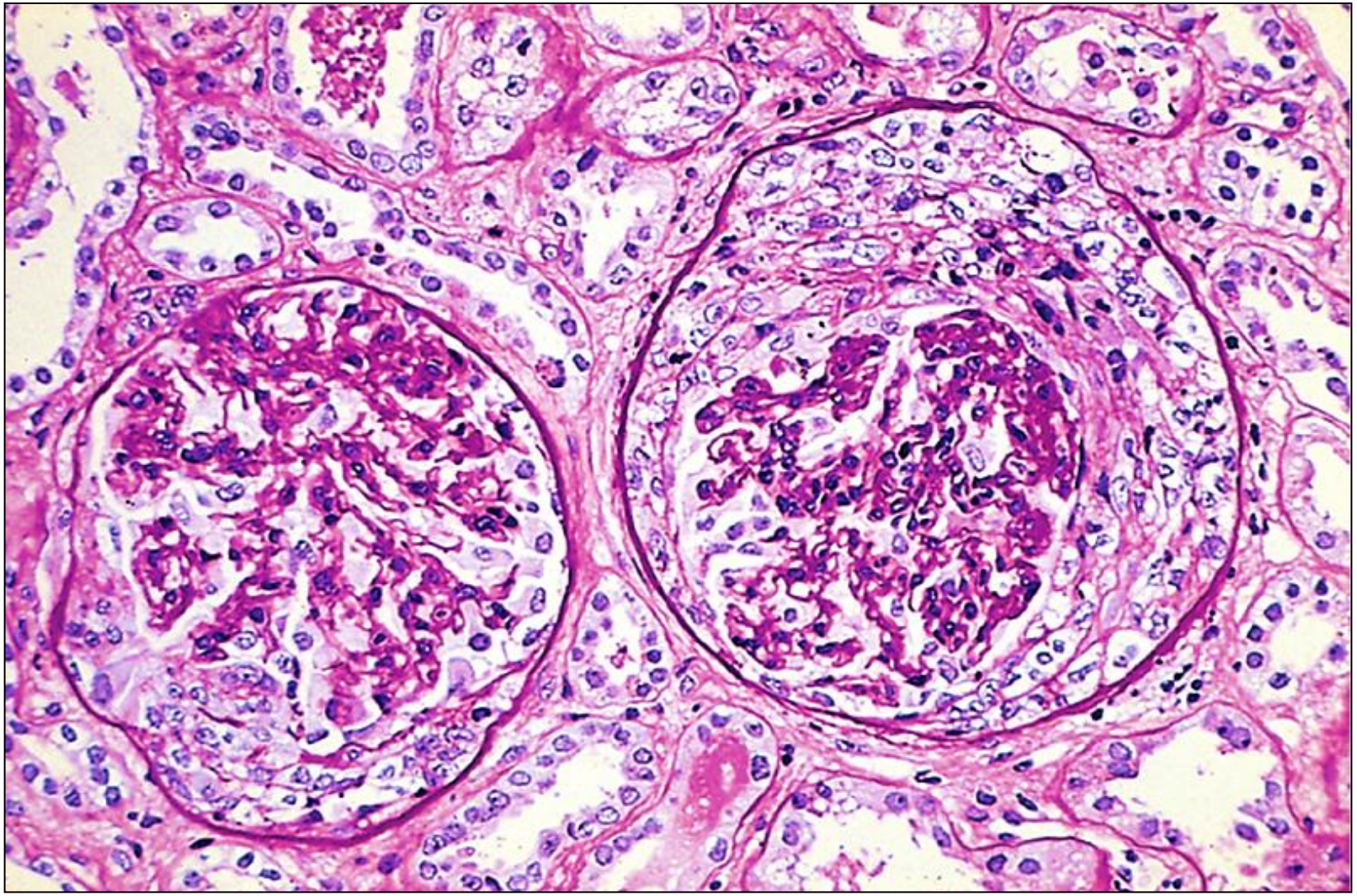
Morphology of RPGN

- Macroscopic picture:
  - The kidneys are enlarged,
  - Flabby consistency,
  - A layer of cortical substance is wide, pale brown with a red mottle, the pyramids are sharply full-blooded ("large variegated kidney"),
  - Sometimes the cortical layer is sharply full-blooded and merges in color with the red pyramids ("big red kidney").

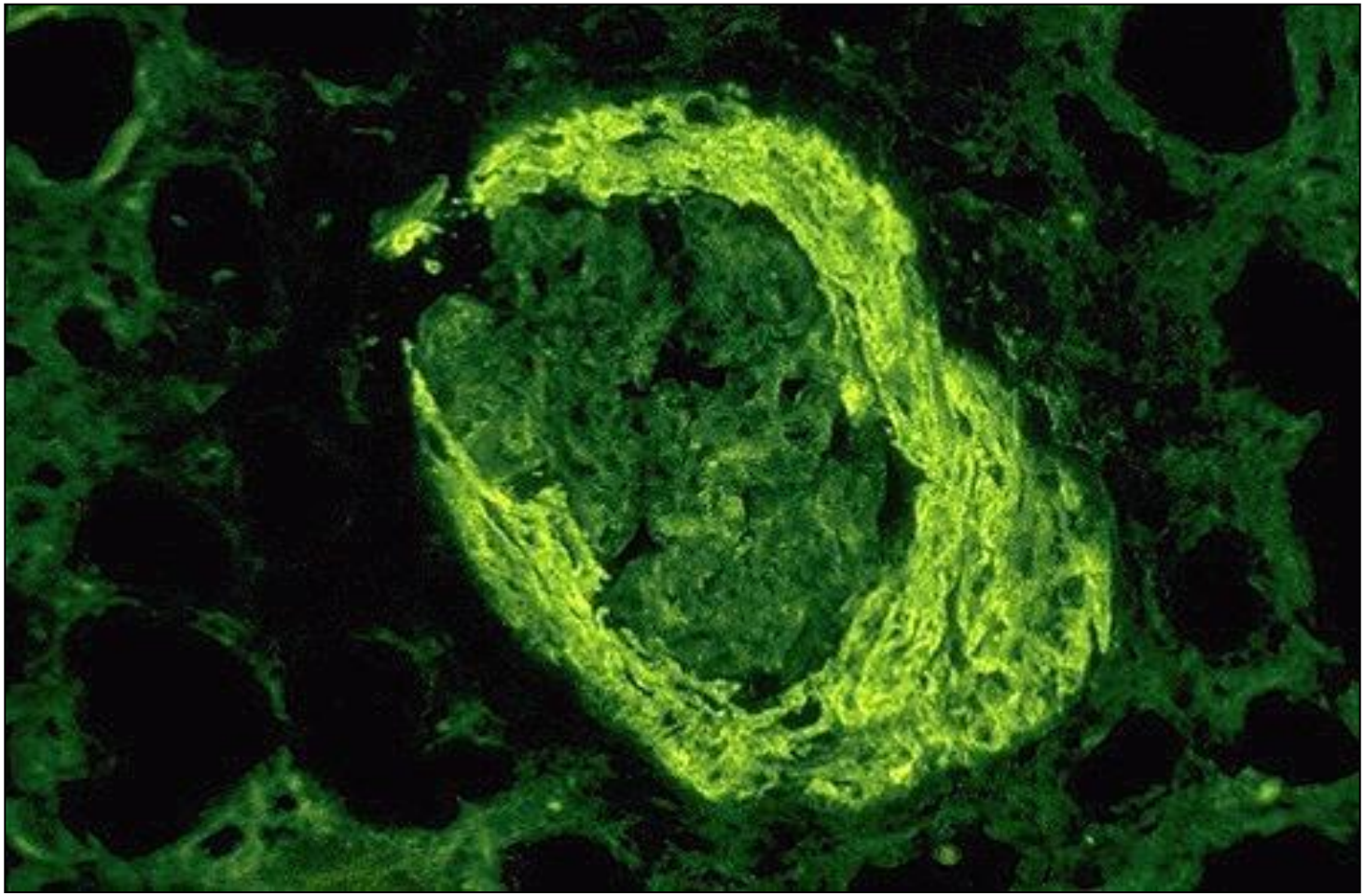
Morphology of RPGN

- Microscopic picture:
  - In the lumen of the capsules of the renal glomeruli, characteristic semi-moon are found, consisting of proliferating epithelium, fibrin and monocytes (extracapillary proliferative glomerulonephritis);
  - The semi-moon obliterate the Bowman space and squeeze the glomerulus, quickly undergo sclerosis.

Semi-moon with RPGN



The deposition of fibrinogen in the semi-moon with RPGN (IFM)



Chronic GN

- Characterized by the duration of the disease for more than 12 months, occurs latently or recursively, has a variety of clinical manifestations.
- The etiology is unknown.
- The main mechanism of occurrence is immunocomplex.
- Histologically, chronic glomerulonephritis is represented by two types:
  - Mesangial,
  - Sclerosing (fibroplastic).

Mesangial GN

- It develops in connection with the reaction of mesangiocytes to fixing the deposits of immune complexes and antibodies on the subepithelial, subendothelial sides of the GBM, intramembrane and paramesangially.

- Mesangiocyte proliferation occurs, mesangium expands due to matrix accumulation, mesangial cell outgrowths are evicted to the periphery of the vascular loops, causing splitting of GBM (mesangium interposition).

- Individual vascular loops are emptied and sclerosed.

Mesangial GN

- Depending on the degree of complexity of the proposals and sclerotic changes in the glomerulus, which include the following types of mesangial glomerulonephritis:
  - Mesangioproliferative,
  - Membrane-proliferative.

Mesangioproliferative GN

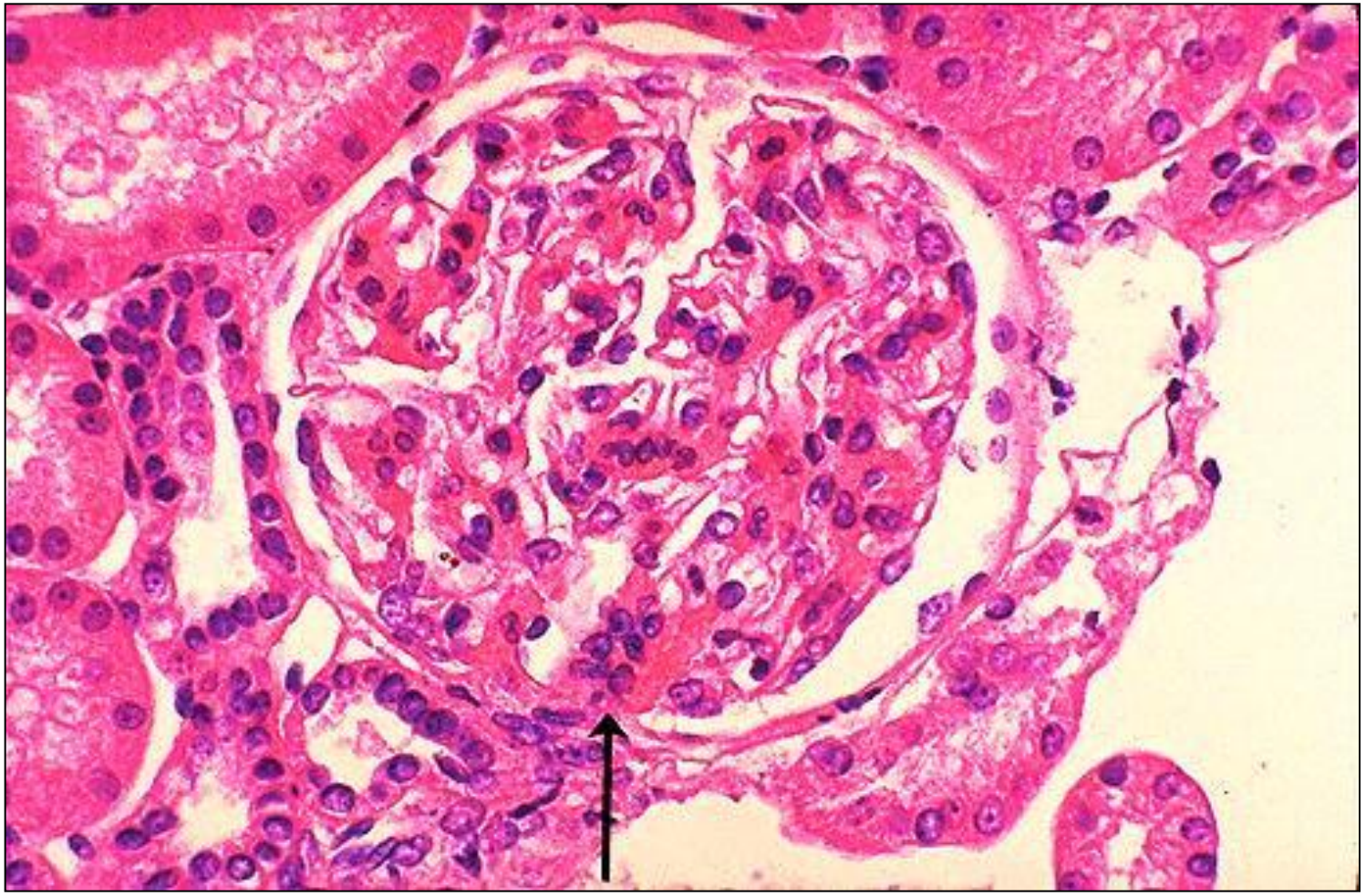
- Clinically it proceeds with hematuria, latent.
- The duration of the disease is stretched for decades.
- The etiology is unknown.
- Histologically it is characterized by:
  - Expansion of mesangium due to pronounced proliferation of mesangiocytes,
  - Focal cleavage of GBM, on which immune deposits containing IgG, IgA, IgM, C3 - complement component are determined (mesangium interposition is poorly expressed).

IgA-nephropathy

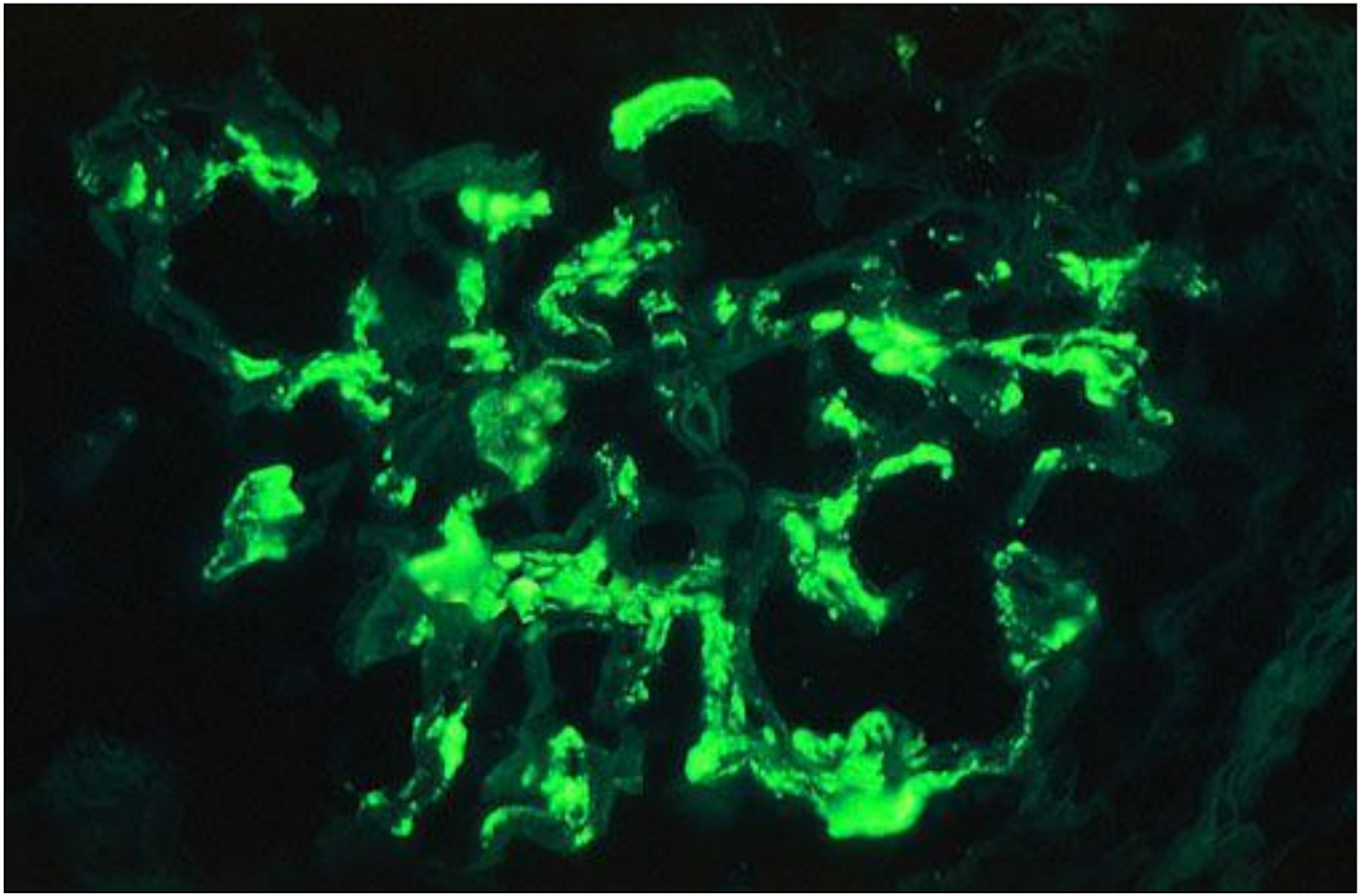
- A special form of mesangioproliferative glomerulonephritis is nephritis with IgA deposits (IgA-nephropathy, Berger's disease), which is currently considered as an independent disease.

- It is characterized by recurrent hematuria and an unfavorable clinical course.

Increase in the number of mesangium cells with IgA nephropathy



Deposits of IgA in mesangium with IgA-nephropathy (IFM)



Membrane-proliferative GN (MPGN)

- Synonym: mesangiocapillary glomerulonephritis, membranous-proliferative glomerulonephritis.

- This is the most severe type of glomerulonephritis, characterized by a progressive course and the least favorable prognosis.

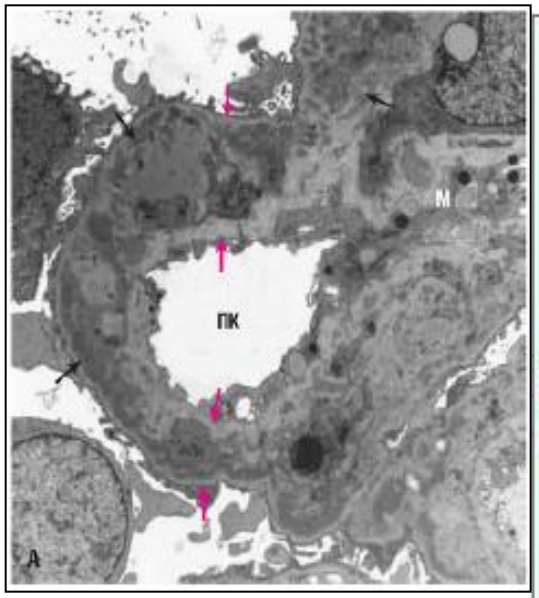
- Clinical manifestations are very variable, beginning with minimal asymptomatic urinary syndrome, ending with severe nephrotic syndrome or rapid development of CRF.

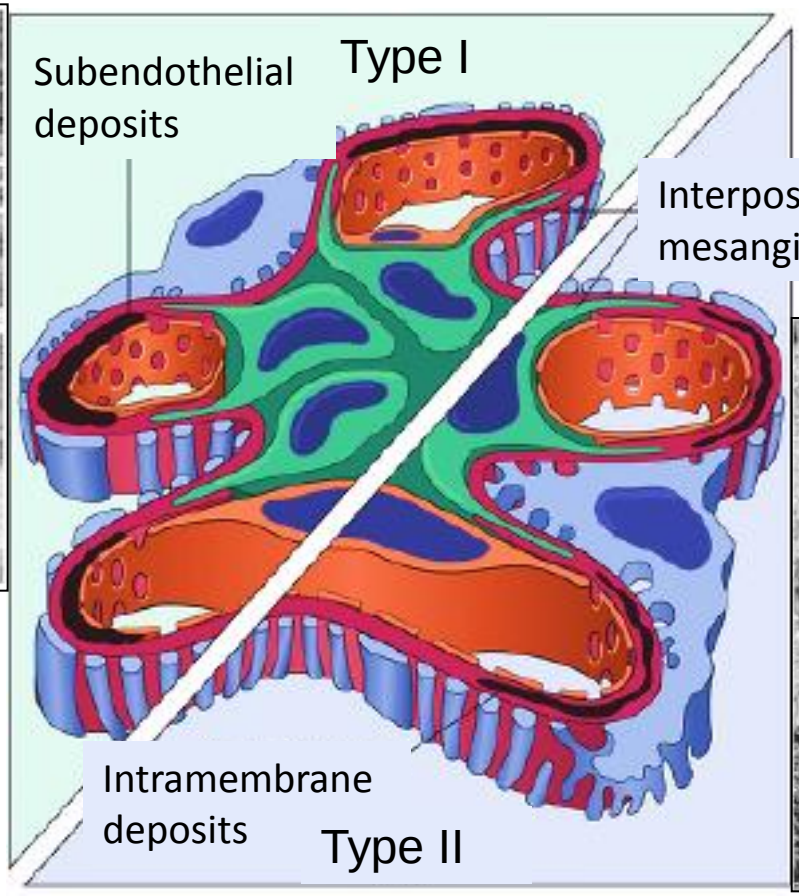
- The disease occurs at any age, more often in children and young women, especially after suffering toxicosis during pregnancy.

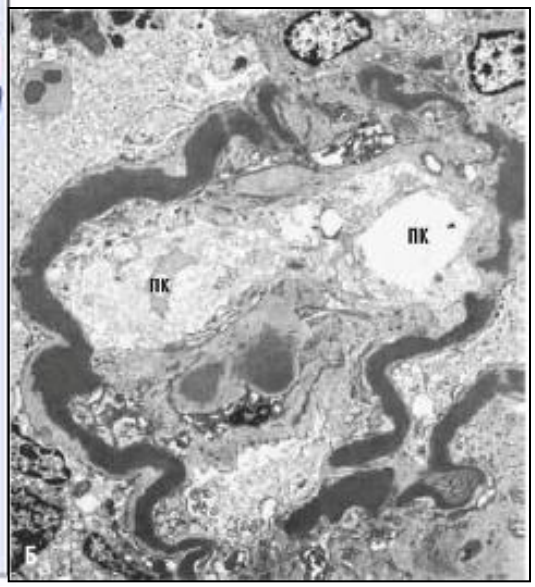
MPGN

- There are two types of membrane-proliferative glomerulonephritis, distinguished on the basis of distinct ultrastructural, immunofluorescent and pathogenetic features:
  - Type I - with subendothelial deposits;
  - Type II - with dense deposits inside the basal glomerular membrane ("disease of dense deposits").

Types of MPGN



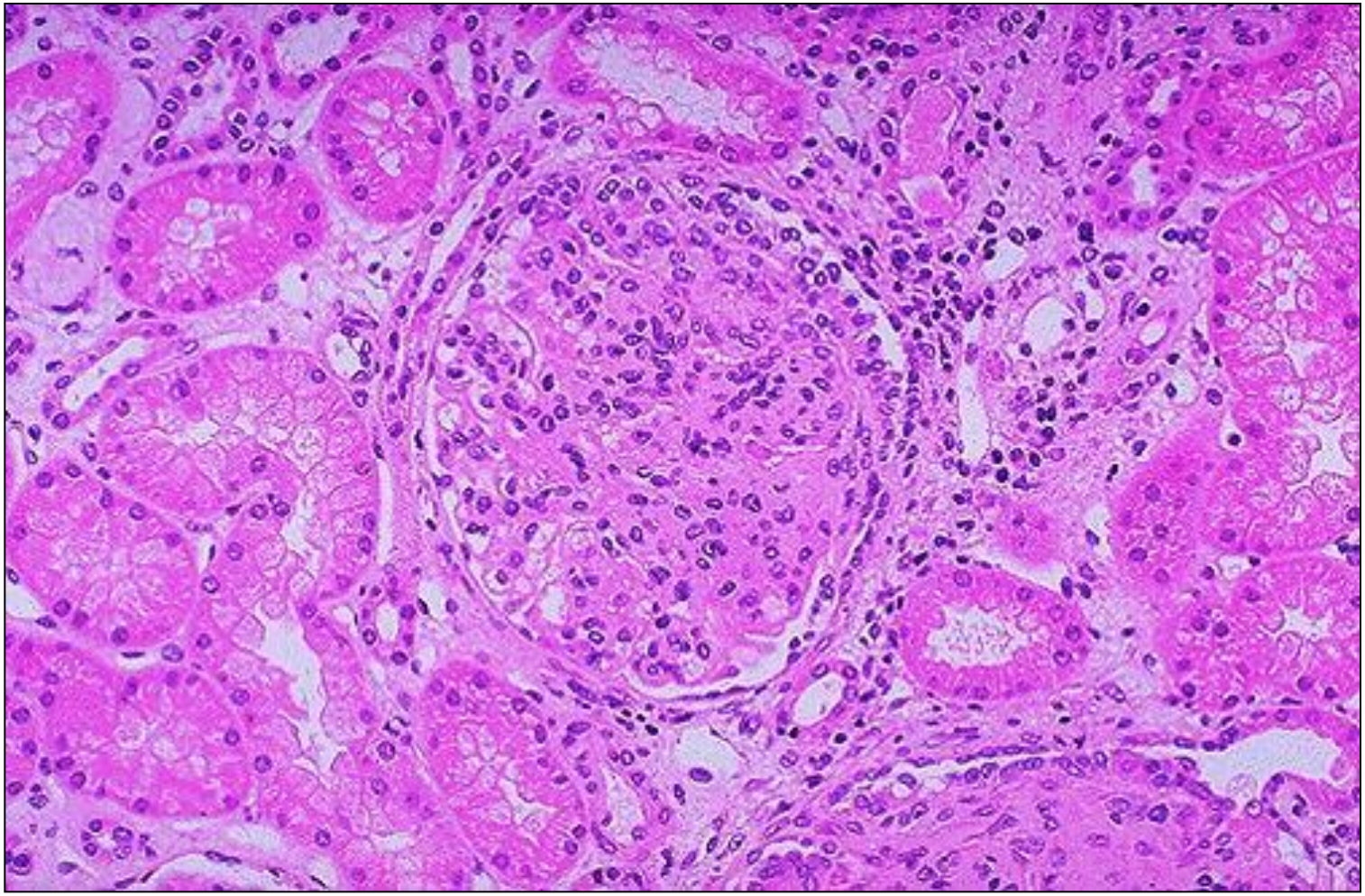




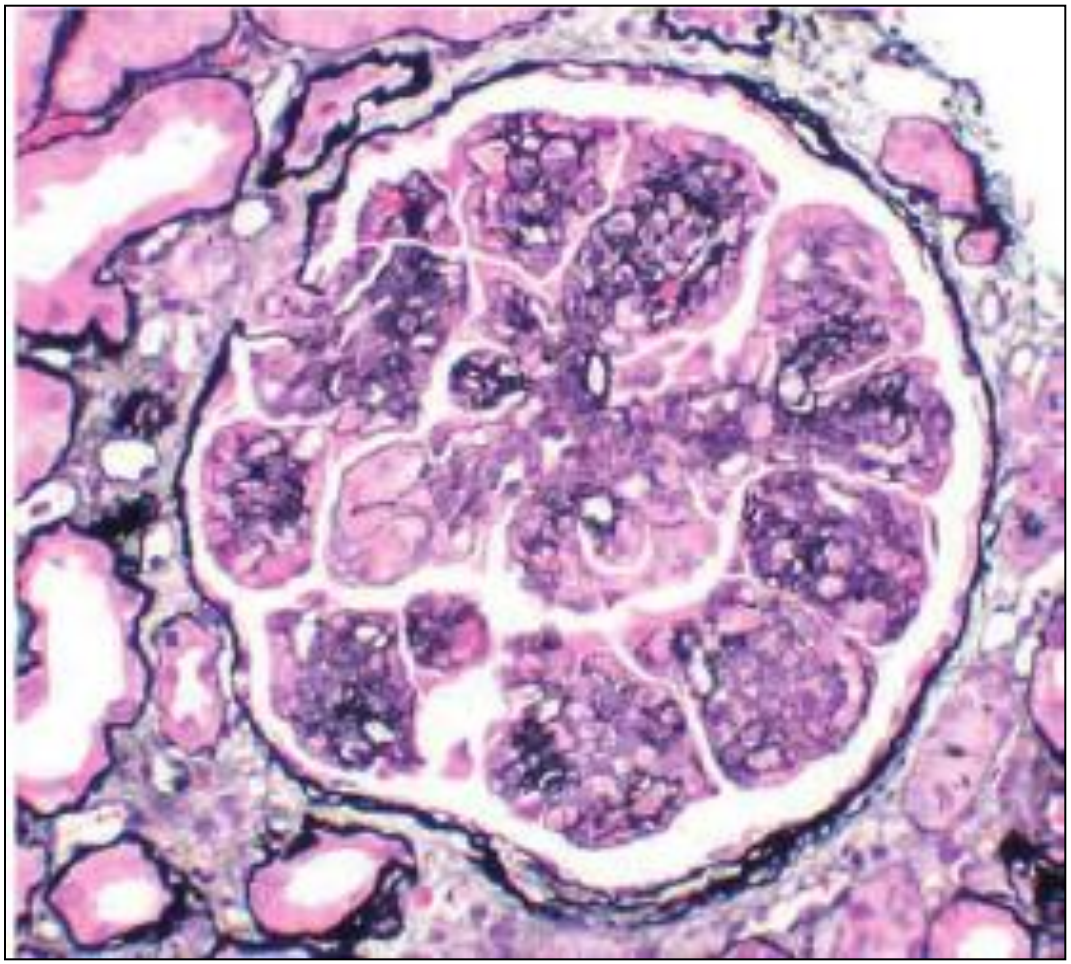
MPGN

- With light microscopy, both types are similar:
  - Renal glomeruli large and hypercellular due to the pronounced proliferation of mesangiocytes;
  - Expansion of the mesangial matrix;
  - Uneven diffuse thickening of the GBM and its "doubling", the so-called. "Rail-like" basal membrane, which is due to the interposition of mesangium;
  - Underlined lobulation of the glomerulus ("lobularity") due to proliferative and sclerotic changes in the center of the lobules.

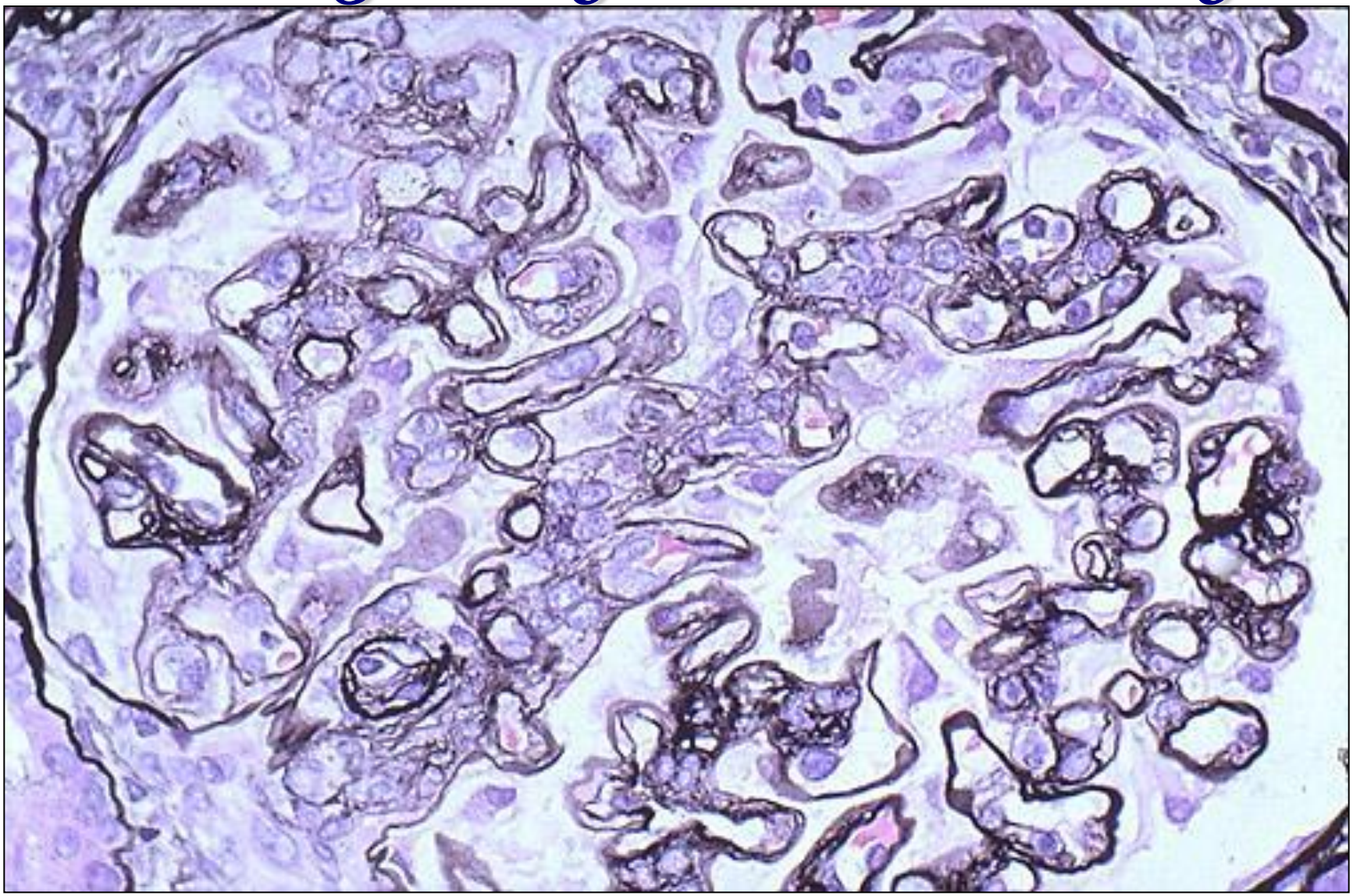
Hypercellularity of the glomerulus with MPGN



Lobularity of the glomerulus with MPGN



Doubling the GBM with MPGN



Fibroplastic GN

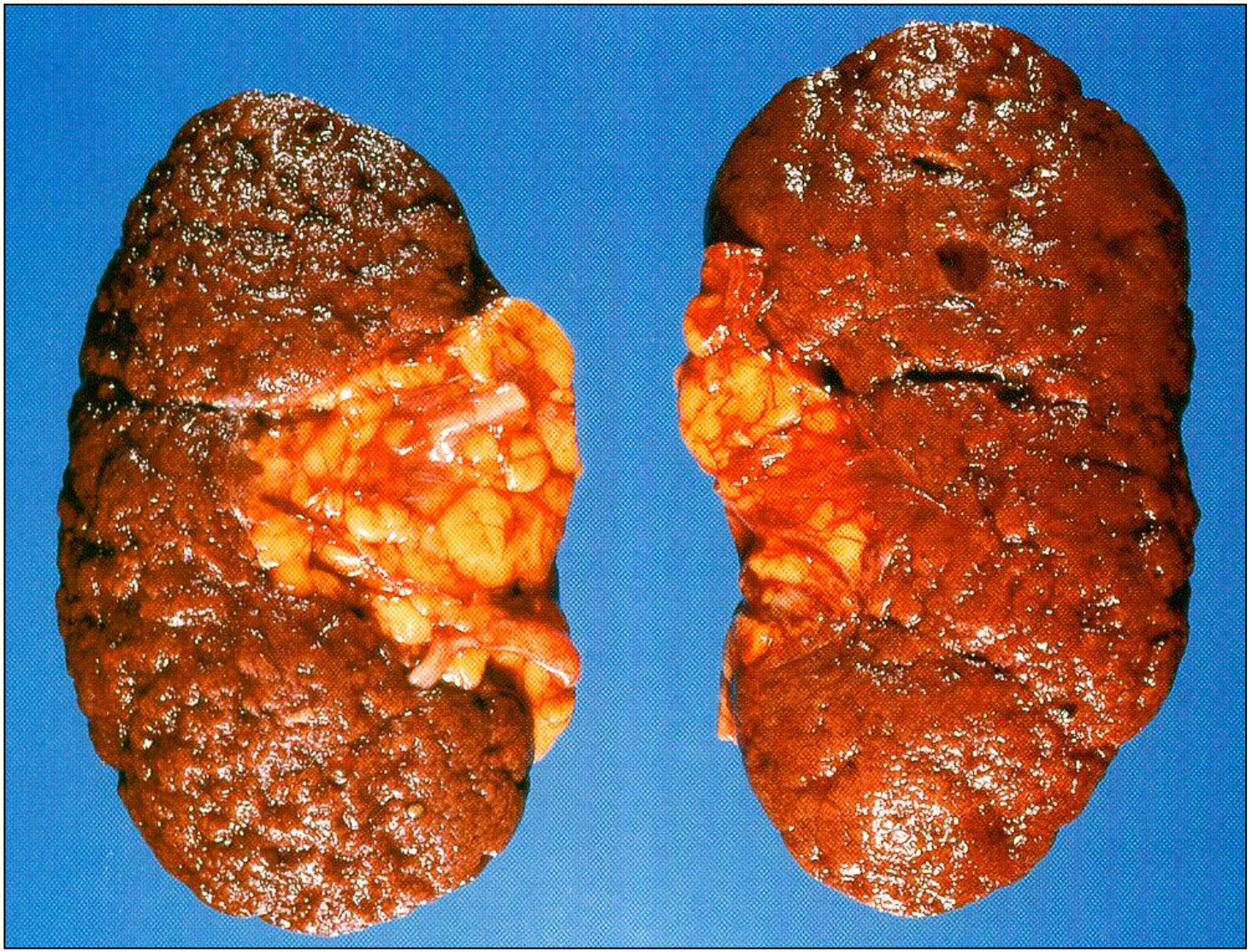
- Synonym: sclerosing glomerulonephritis.
- In fact, this type of glomerulonephritis represents the final stages of all other nephropathies.
- The growth rate of nephrosclerosis depends on the etiological factor and the activity of immunological reactions.
- This disease is more common in adults, usually elderly with equal frequency in men and women, but also in young people.

Fibroplastic GN

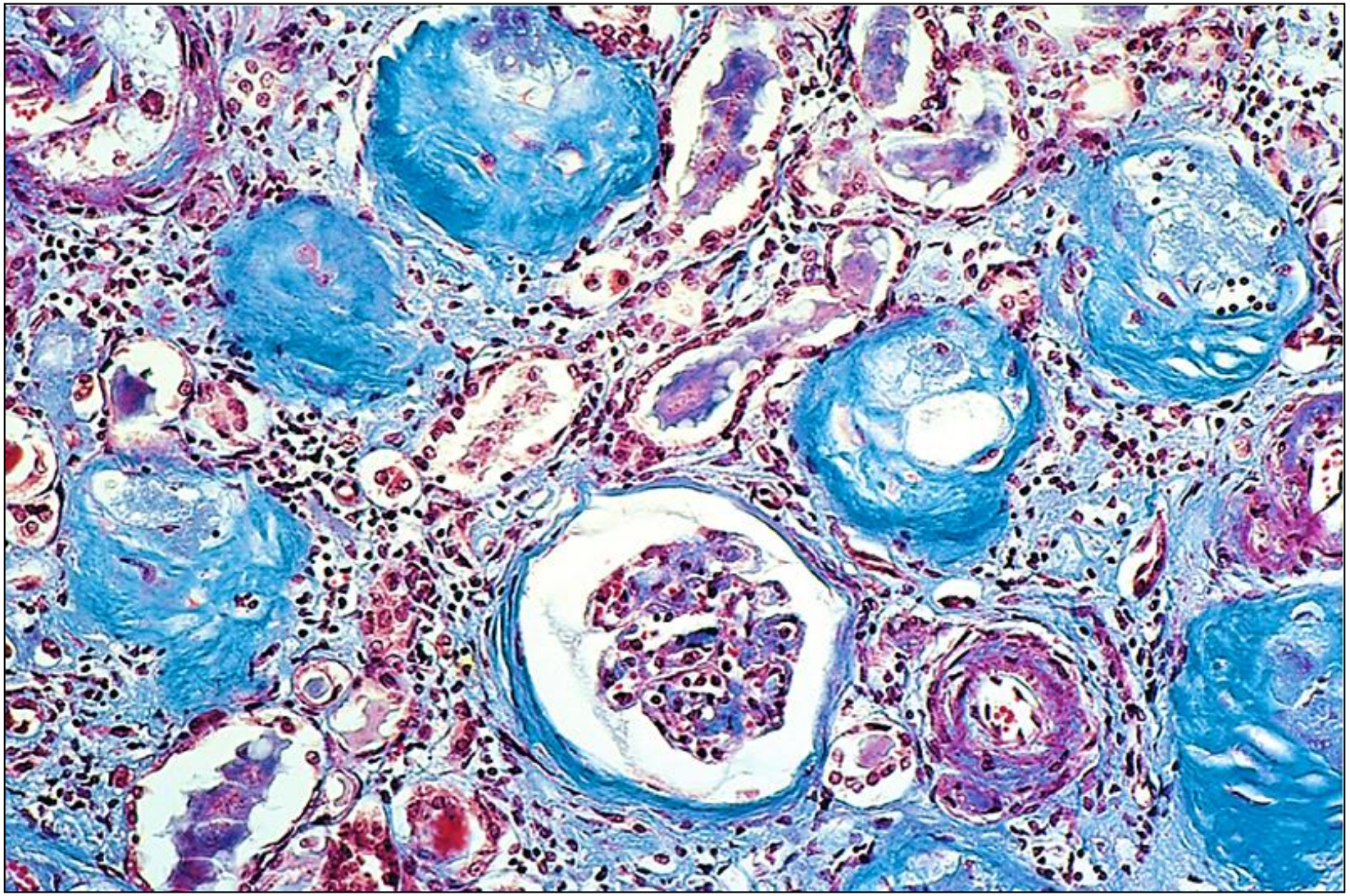
- Macroscopic picture:
  - Kidneys are reduced in size,
  - Consistence dense,
  - The surface is fine-grained.

- Microscopic picture:
  - Varying degrees of sclerosis and hyalinosis of the glomeruli with obliteration of the lumen of the glomerulus capsule,
  - In interstitium - lymphomacrofagal infiltration, thickening of the walls of the arteries,
  - The tubules are enlarged and contain protein impressions.

Fibroplastic GN



Fibroplastic GN



Non-inflammatory glomerulopathies

- Non-inflammatory glomerulopathies include:
  - Amyloidosis of the kidneys (amyloid nephrosis),
  - Lipoid nephrosis (nephropathy with minimal changes),
  - Membranous nephropathy,
  - Focal segmental glomerulosclerosis / hyalinosis.

Kidney amyloidosis

- Synonym: chronic amyloid nephrosis.
- It develops as a manifestation of acquired (secondary) amyloidosis in chronic purulent diseases, rheumatoid arthritis, myeloma.
- There is amyloid nephrosis in several stages:
  - Latent,
  - Proteinuric,
  - Nephrotic,
  - Uremic.
- Can be accompanied by the development of nephrogenic arterial hypertension.
- Patients die from chronic renal failure and complications associated with elevated blood pressure.

Latent stage

- Macroscopic picture:
  - The kidneys are not changed.
- Microscopic picture:
  - Deposition of amyloid masses in the papillae of the pyramids of the medulla, along the collecting tubules and in the walls of the blood vessels.

Proteinuric stage

- Macroscopic picture:
  - The kidneys are enlarged,
  - Dense consistency,
  - On a cut the cortical layer is matte, the medullar substance is a sebaceous species ("large greasy kidney").
- Microscopic picture:
  - Amyloid deposited on the basal membranes of the tubules and appears in the glomeruli.

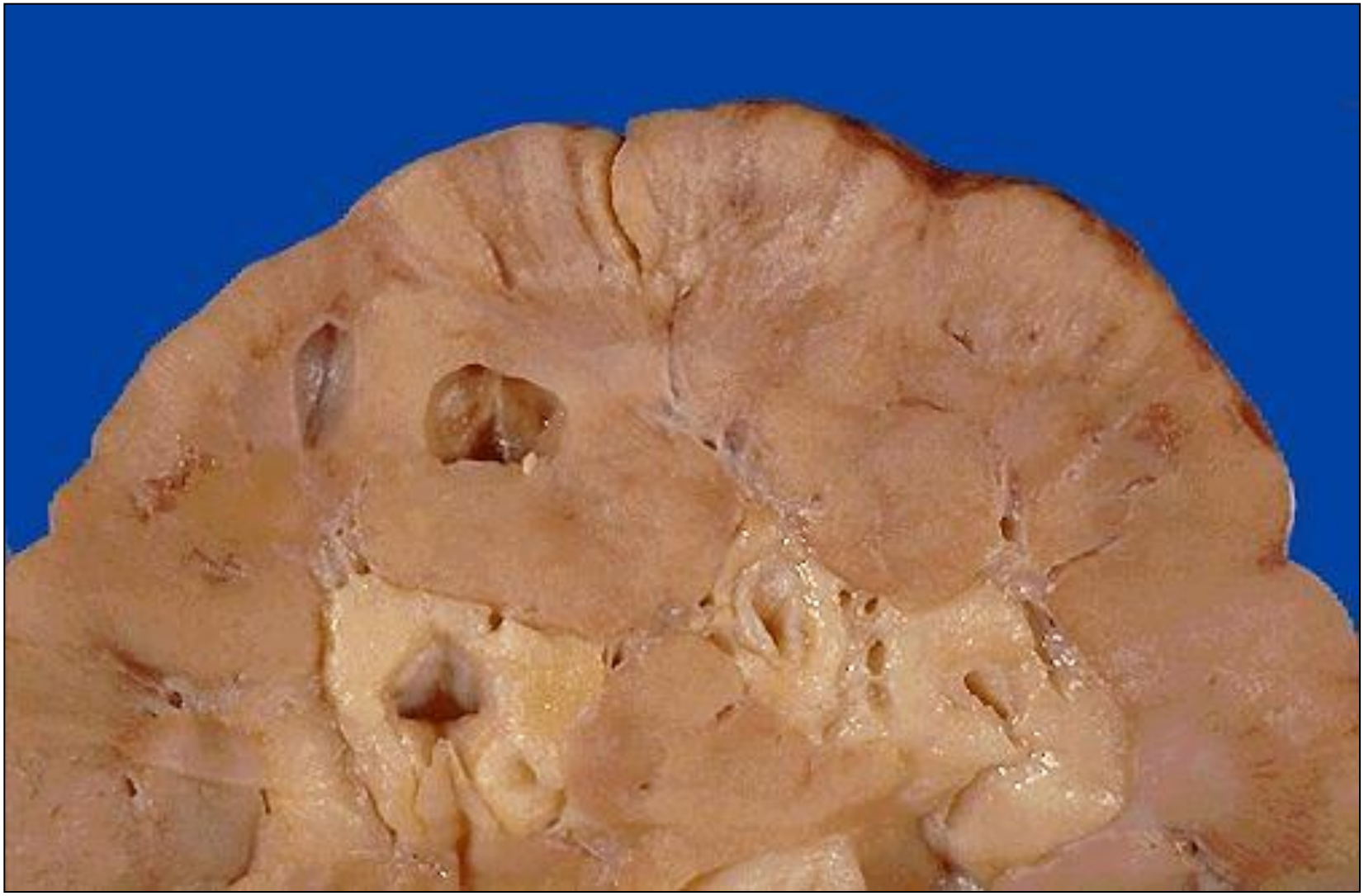
Nephrotic stage

- Macroscopic picture:
  - The kidneys are enlarged,
  - Dense consistency,
  - Become waxy ("large white kidney").
- Microscopic picture:
  - Deposition of amyloid masses in the mesangium of capillary glomeruli loops.

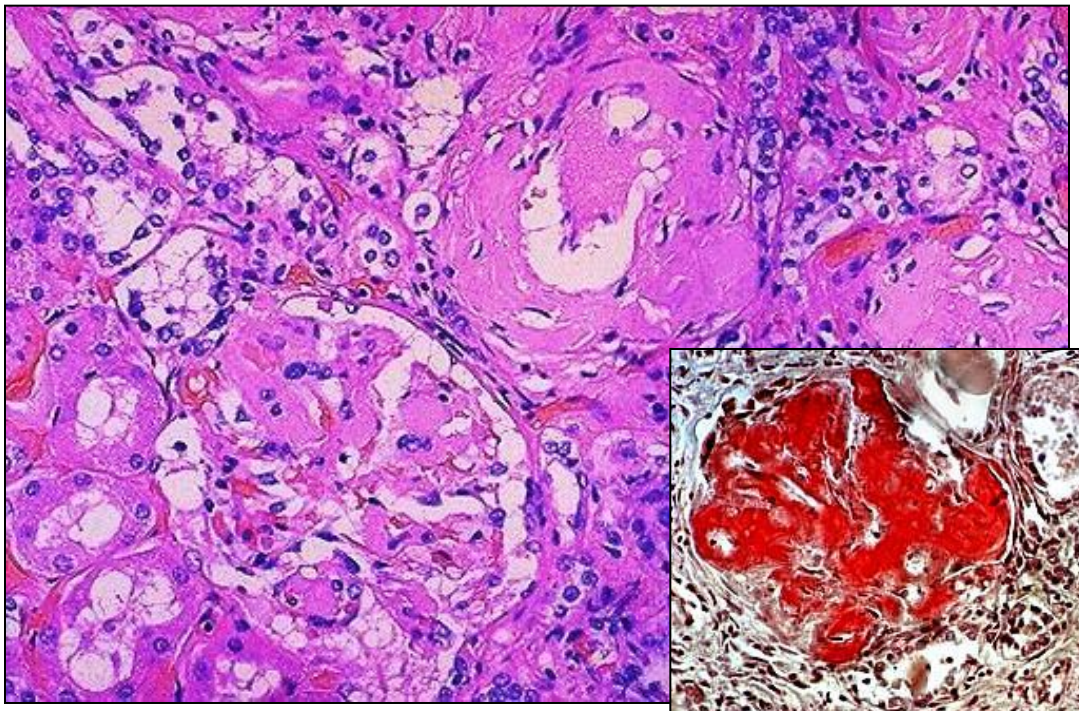
Uremic stage

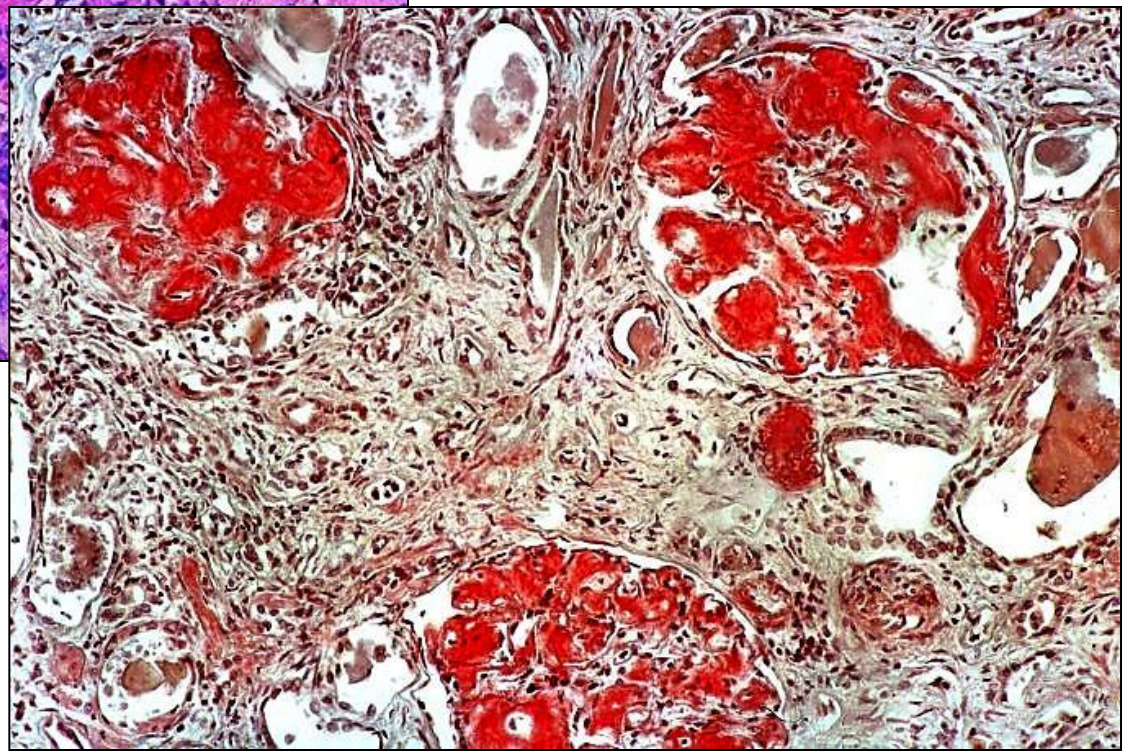
- Macroscopic picture:
  - Kidneys are reduced in size,
  - Dense consistency,
  - With cicatricial retraction ("amyloid-shriveled kidneys").
- Microscopic picture:
  - Sclerosis of the glomeruli.

"Large white kidney"



Kidney amyloidosis





Lipoid nephrosis

- Synonyms: nephropathy with minimal changes, the disease of minimal changes, nephrotic syndrome with minimal changes, disease of small legs of podocytes.

- This relatively benign disease is characterized by a diffuse disappearance of the legs of the processes of podocytes, which look normal with light microscopy.

- It occurs mainly in boys aged 3 to 10 years, but can be in adults of any age.

- The etiology is unknown. A congenital defect of the podocytes is recognized - shortening or absence of small legs

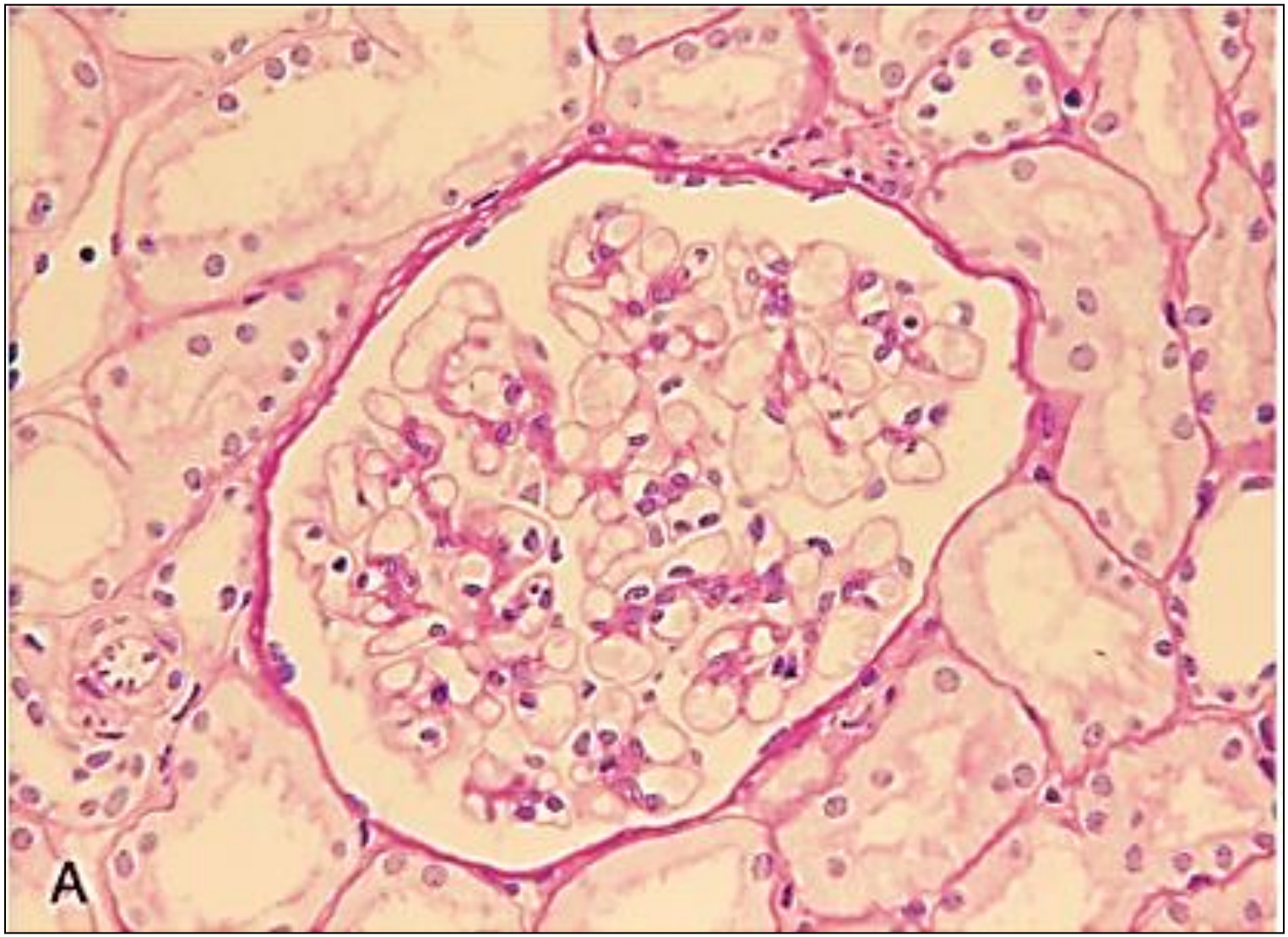
Lipoid nephrosis

- It is combined with lymphoproliferative (Hodgkin's disease), atopic (rhinitis, eczema) diseases.
- Among patients, the number of persons with HLA-B12 and HLA-DR7 was increased.
- The disease sometimes develops after a respiratory infection or routine prophylactic immunization.
- Clinically characterized by nephrotic syndrome.
- Despite massive proteinuria, the kidney function remains intact.
- It Is treated well with steroid therapy.

Lipoid nephrosis

- With light microscopy:
  - The glomeruli are not changed.
  - Rarely there is a non-uniform increase in epithelial cells (podocytes) and a slight thickening of mesangium, or a slight increase in cellularity.
  - The response to immunoglobulins and complement in epithelial cells is negative.

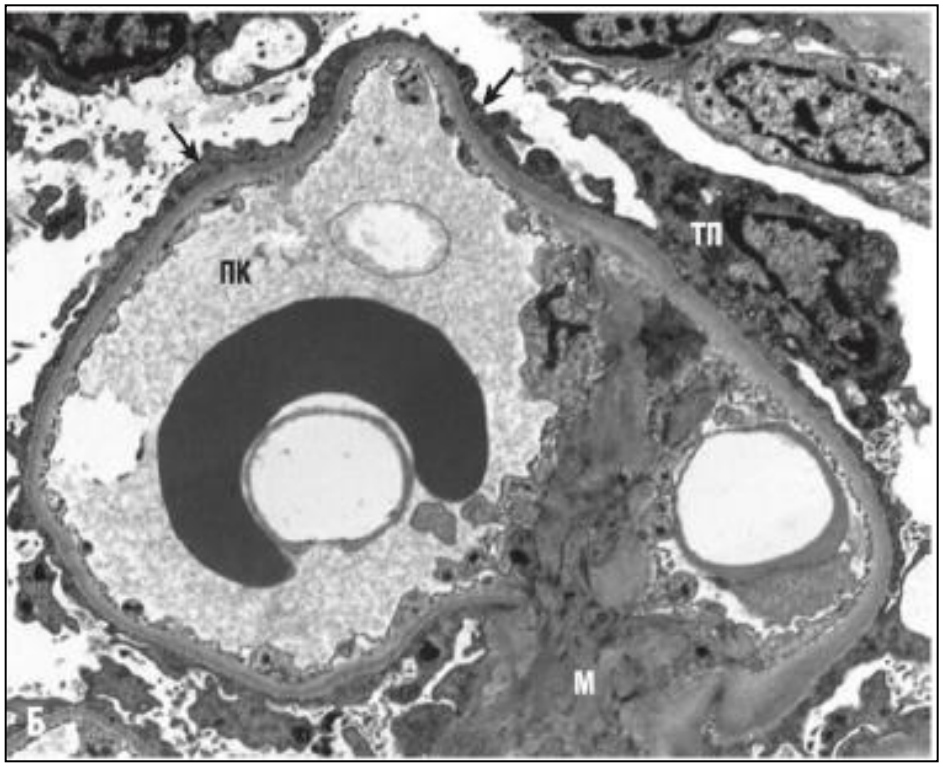
Lipoid nephrosis

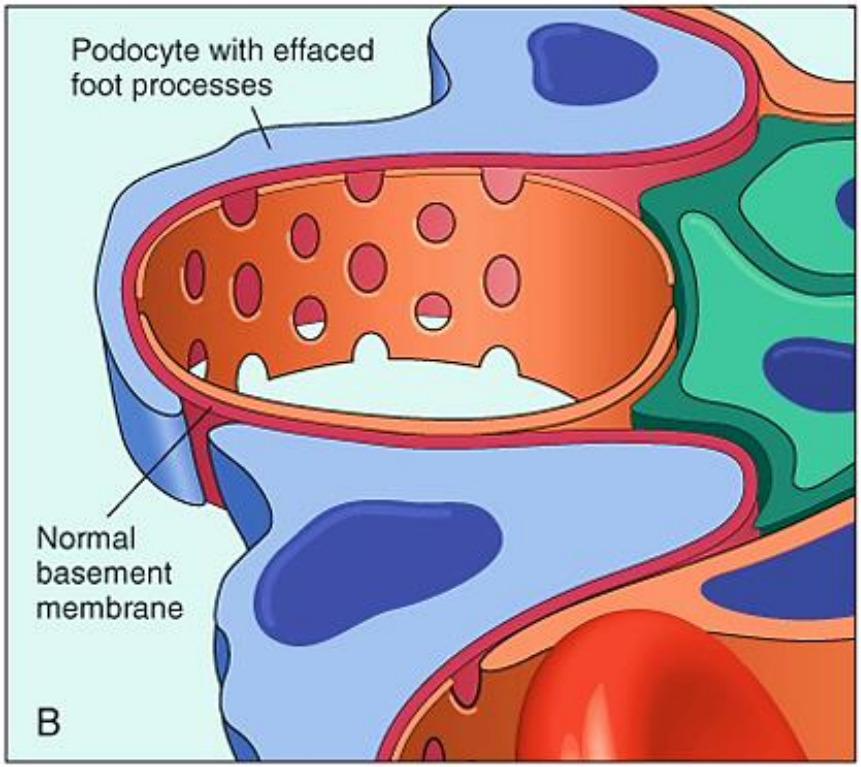


Lipoid nephrosis

- Electron microscopy makes it possible to more clearly verify the diagnosis:
  - The basal membranes of the glomeruli are formed correctly, of uniform thickness.
  - Absence of small processes of podocytes.
  - The cells of the proximal tubules are loaded with lipids (reabsorption by tubules of lipoproteins that pass through the damaged glomeruli).
  - In the interstitial tissue of the kidney, foam cells are determined.

Lipoid nephrosis





Membranous nephropathy

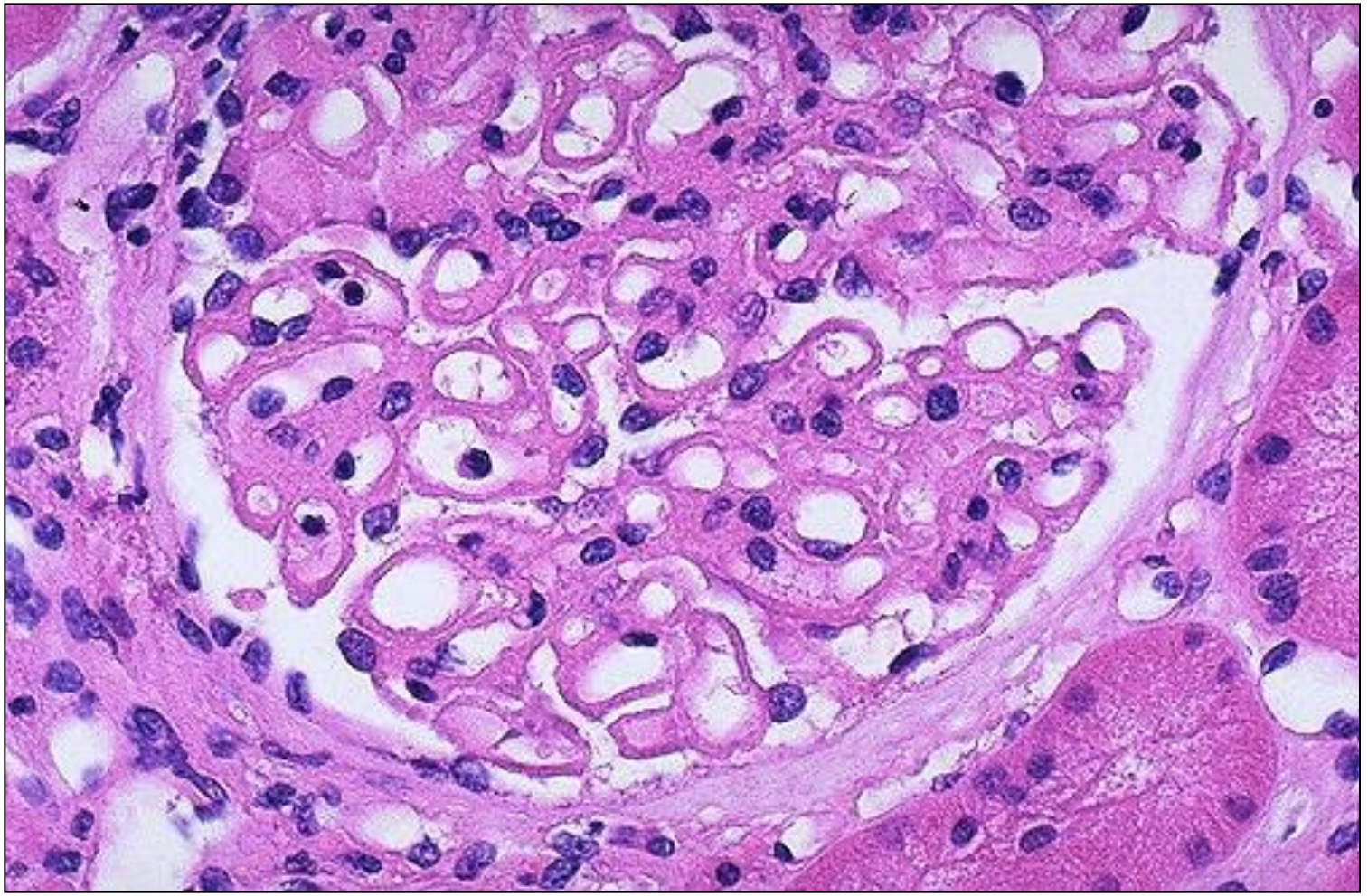
- Synonym: membranous glomerulonephritis.
- Most cases are primary, idiopathic, but may be secondary due to the action of endogenous (tumor, SLE) or exogenous (hepatitis B, malaria, syphilis, LS) antigens.
- A classic clinical manifestation is nephrotic syndrome, often in combination with microhematuria.
- The disease occurs at any age, but often occurs in adults. It is characterized by chronic course with high frequency of remission and great variability in progression.
- Does not treated with corticosteroid therapy.

Membranous nephropathy

- Macroscopic picture:
  - The kidneys are enlarged,
  - Flabby,
  - Cortical layer wide, white, less often yellow ("large white kidneys").

- With light microscopy:
  - The glomeruli slightly enlarged,
  - Hypercellularity, as a rule, is absent.
  - Capillary wall thickened.

Thickening of capillary walls with membranous nephropathy

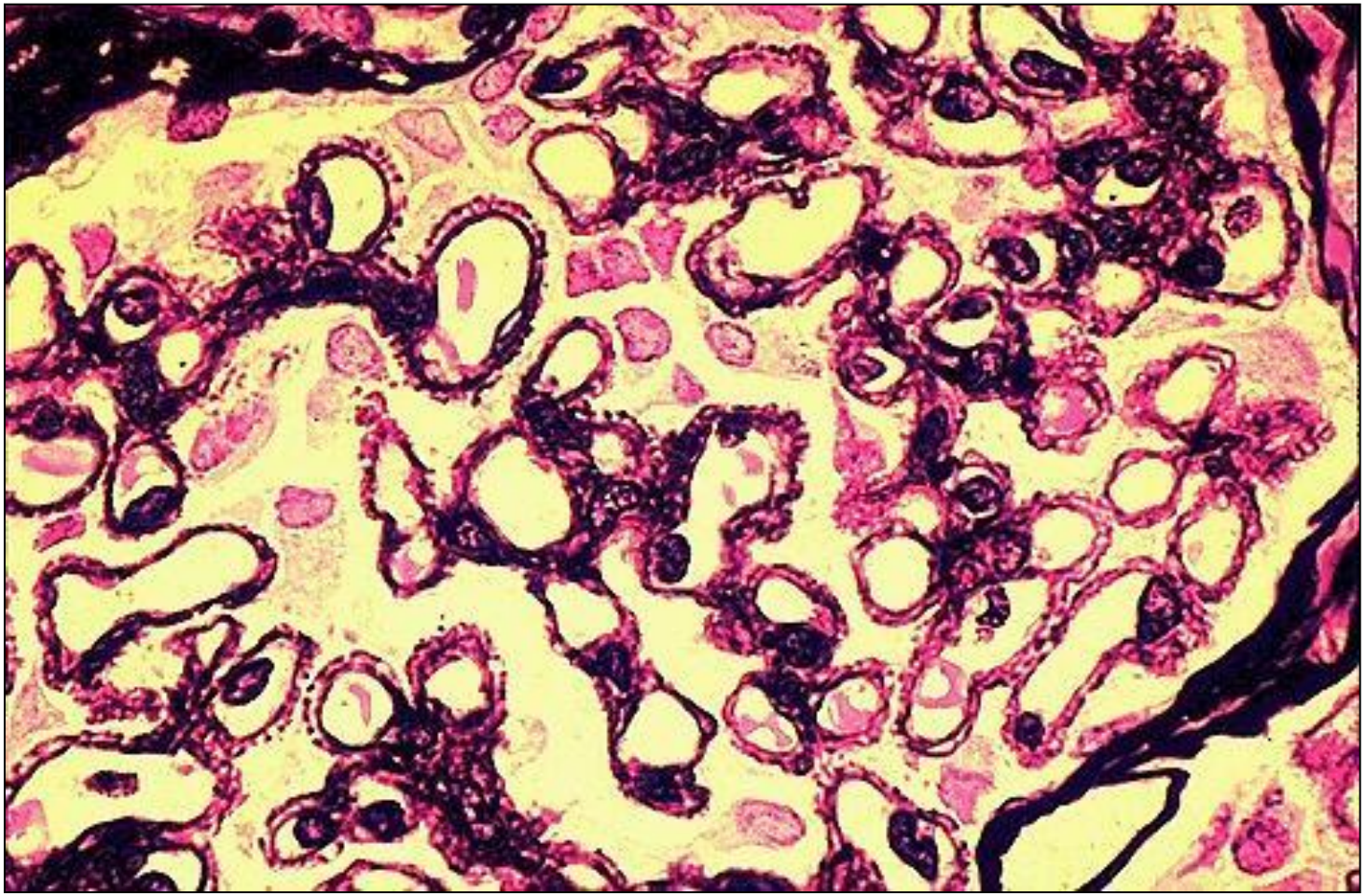


Membranous nephropathy

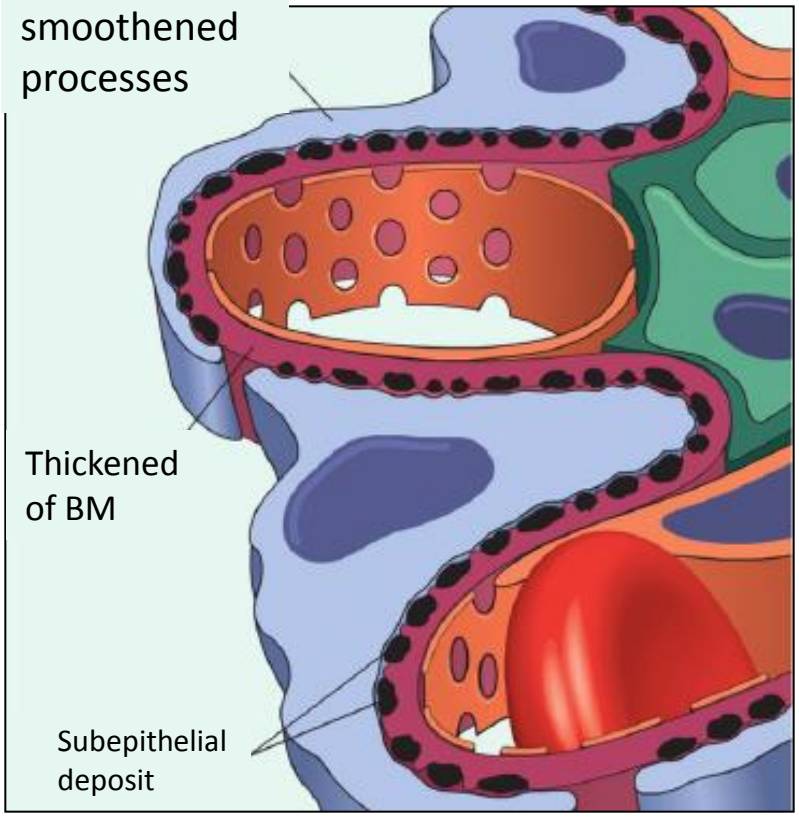
- In the early stages of the disease, when using silvering methods in combination with the PAS- reaction, the following are revealed:
  - Numerous outgrowths ("spinules") on the GBM (membrane-like substance surrounding the immune complexes), which are not stained with silver.
  - With the progression of the wall of the capillaries thicken even more, narrowing the lumen of the capillary until its complete obliteration and sclerosis of the glomerulus.

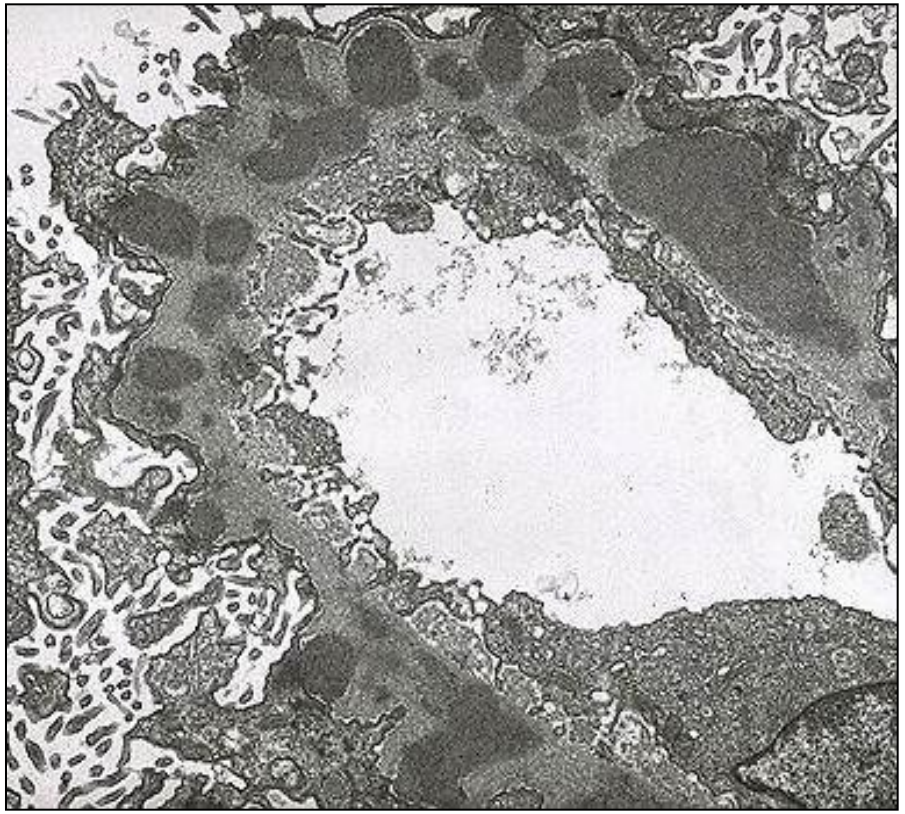
- Immunofluorescence investigation reveals a typical for this pathology focal-spread luminescence of the IgG and C3-complement components on the basal membrane of the glomerular capillaries.

"Spinules " on GBM with membranous nephropathy

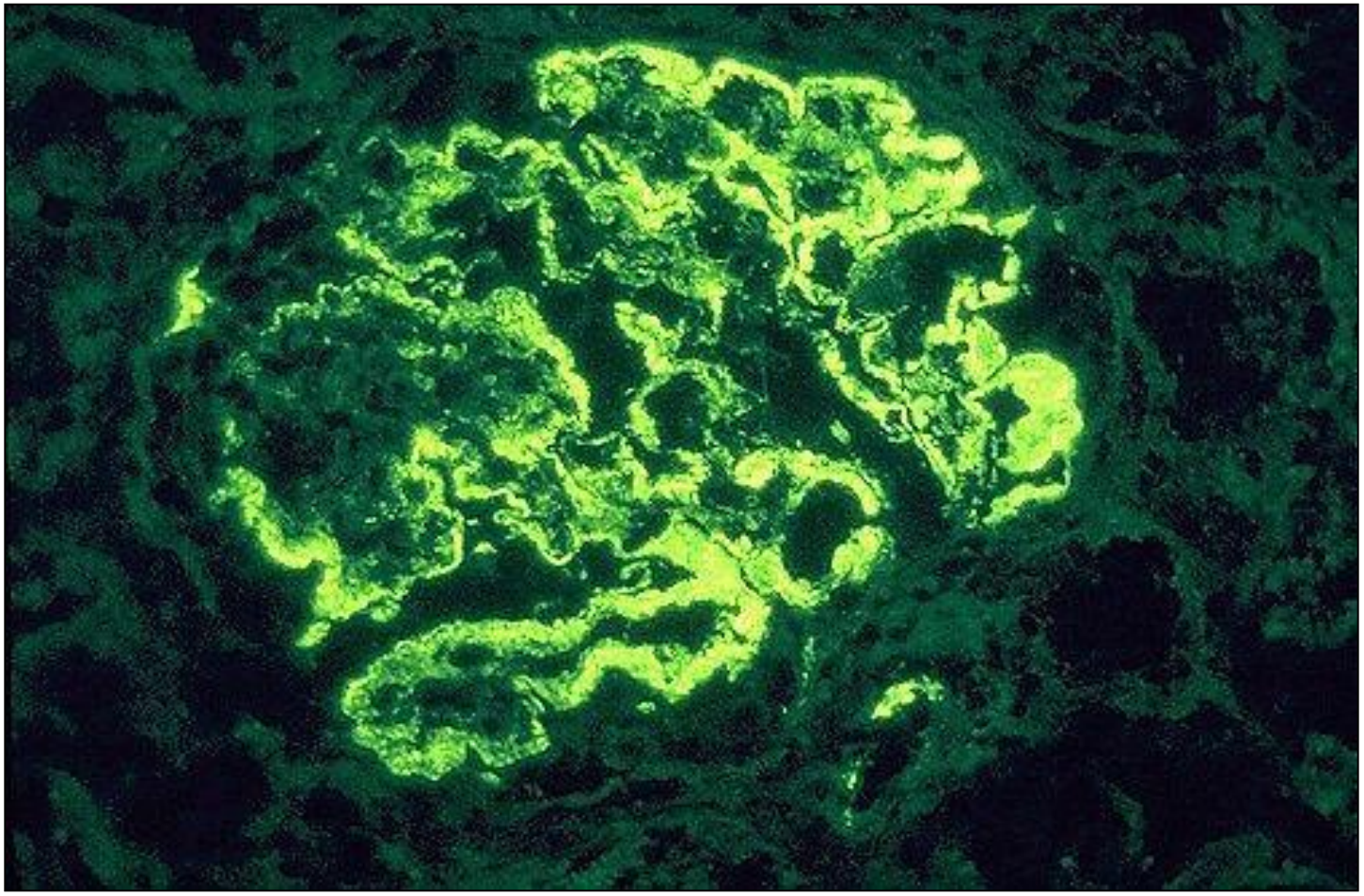


Spinules " on GBM with membranous nephropathy





Deposits of IgG with membranous nephropathy (IFM)



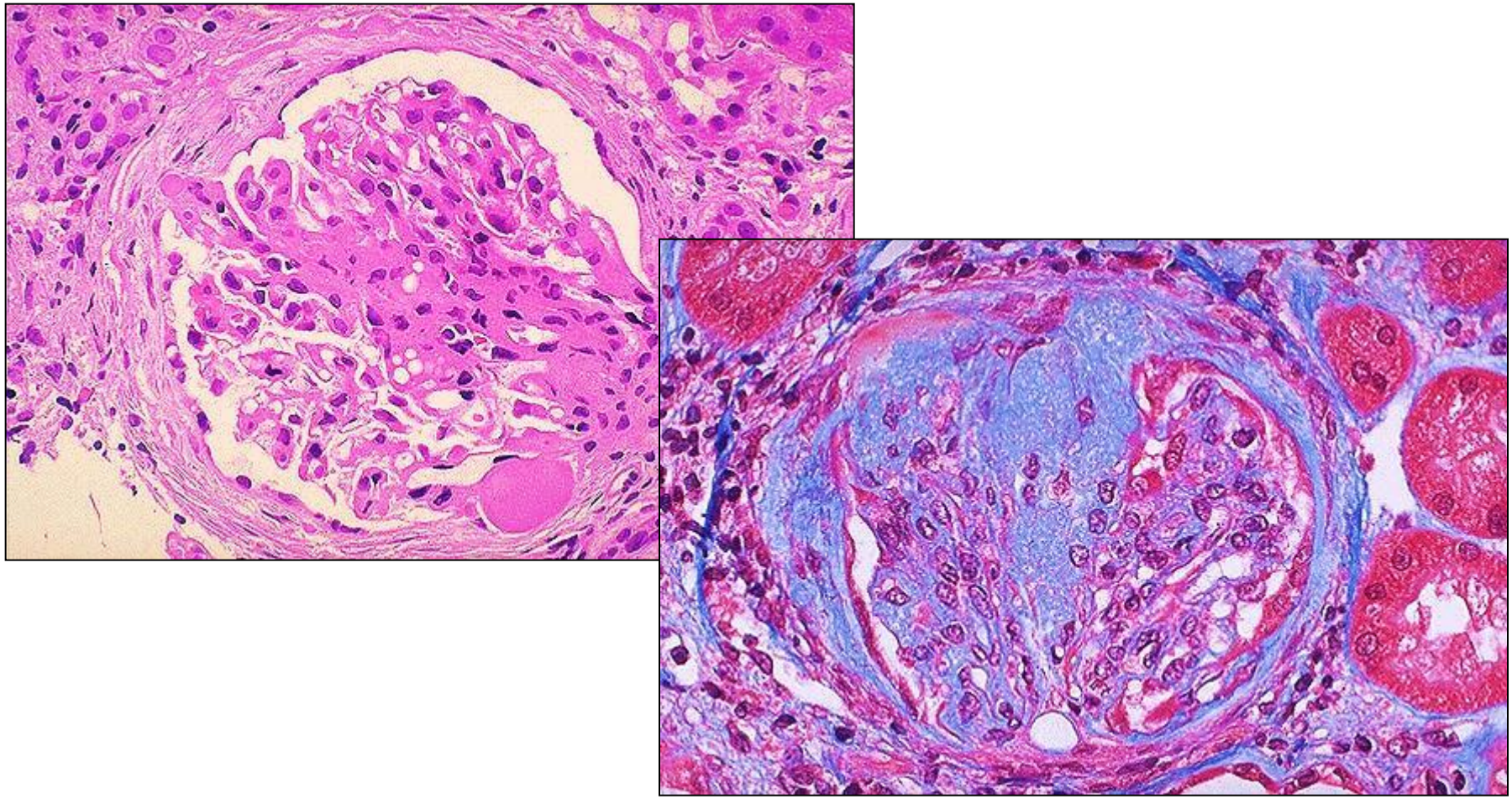
Focal-segmental glomerulosclerosis / hyalinosis

- It occurs in both adults and children.
- It accounts for about 10 - 15% of all observations of the nephrotic syndrome.
- Clinically, it flows unfavorably, ending on average after 10 years with chronic renal failure.
- Does not treated with corticosteroid therapy.

Focal-segmental glomerulosclerosis / hyalinosis

- With light microscopy, the following changes are observed:
  - Affected individual glomeruli, initially juxtamedullar glomeruli (focal changes), which are scleroses some segments of the vascular bundle (segmental changes).
  - The remaining glomeruli at the early stage look normal. In the sclerosed segments, a collapse of the glomerular basement membrane, an increase in the mesangial matrix, and the accumulation of hyaline masses (hyalinosis), often with lipid droplets.

Focal-segmental glomerulosclerosis / hyalinosis



Focal-segmental glomerulosclerosis / hyalinosis

- As the disease progresses, more and more coils are involved in the pathological process, and sclerosis affects each glomerulus.
- Over time, all this leads to total sclerosis of the glomeruli, grown atrophy of the tubules and interstitial fibrosis.
- Immunofluorescence microscopy reveals IgM and C3-immune deposits in the glomerular basement membrane.

Tubulopathies

- Group of diseases (conditions) of the kidneys with predominant involvement of tubules.

- On the etiology of tubulopathy are divided into:
  - Hereditary,
  - Acquired.

Tubulopathies

- Hereditary tubulopathies are a large group of enzymopathies of childhood:
  - Syndrome de Toney - Debre - Fanconi,
  - Albright's syndrome,
  - Tubulopathy with nephrolithiasis and nephrocalcinosis,
  - Others.

- Acquired tubulopathies by the nature of the pathological process are divided into:
  - Necrotizing:
    - Necrotic nephrosis of various etiologies,
  - Obstructive:
    - Gouty (urate) nephropathy,
    - Myeloma nephropathy.

Acute renal failure (ARF)

- Acute renal failure (ARF) is a syndrome or complication of various diseases, morphologically manifested by necrosis of the epithelium of the renal tubules (necrotic nephrosis) and severe disorders of the renal circulation.

- Patients develop an acute oliguria (less than 100 ml of urine per day).

Acute renal failure

- The main causes of ARF are:
- Ischemic injury:
  - At various kinds of a shock and a collapse (infections, burns, traumas, hemorrhages)
- Toxic damage of nephrocytes:
  - Bilirubin for jaundice (hemolytic-uremic syndrome),
  - Salts of heavy metals (lead, mercury, gold, etc.);
  - Organic solvents (carbon tetrachloride, chloroform);
  - Glycols (ethylene glycol, propylene glycol, etc.);
  - Medicinal substances (metacycline, sulfonamides, polymyxin, cephalosporins, NSAIDs);
  - Iodine-containing radiopaque substances;
  - With crush syndrome (prolonged crushing).

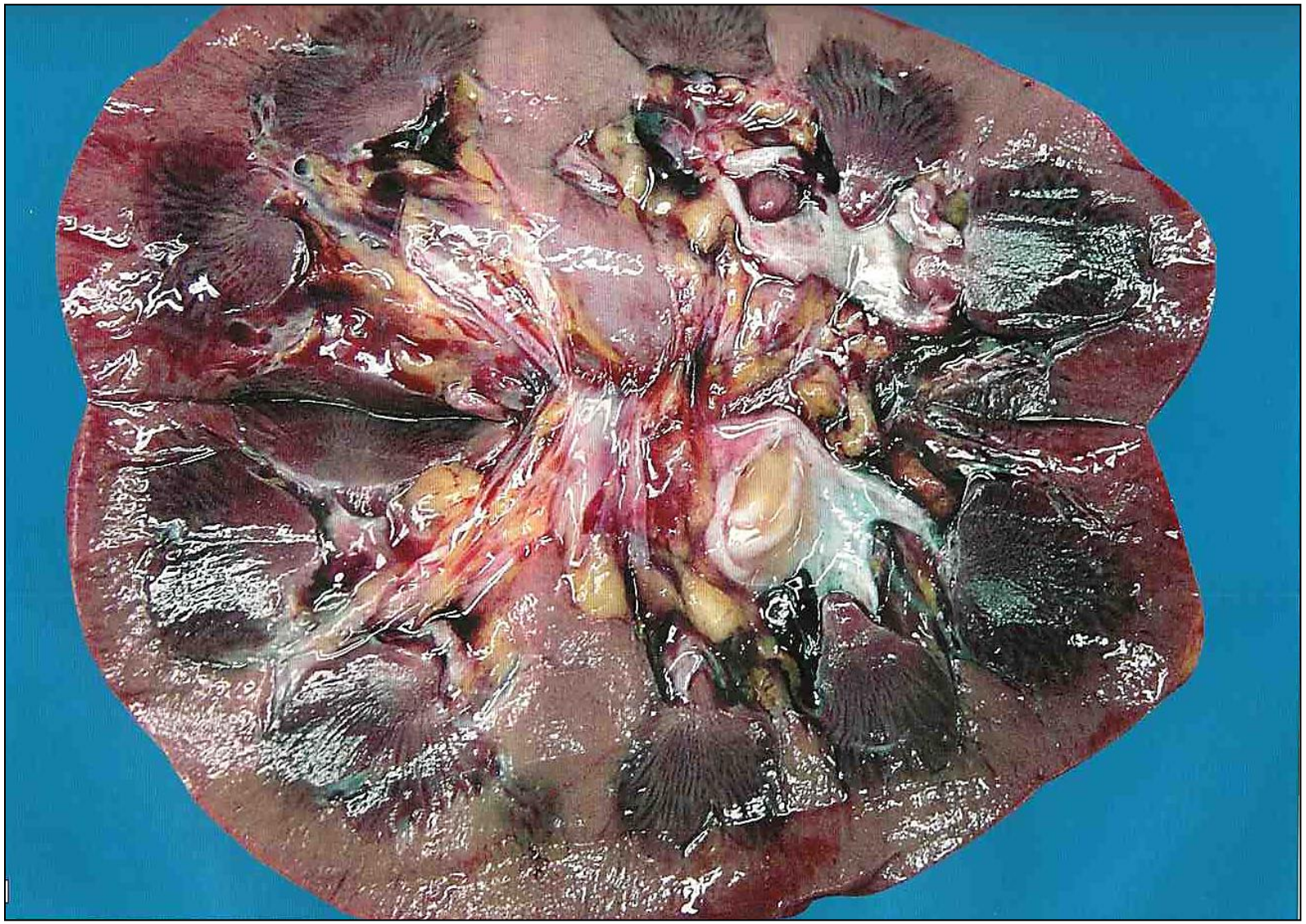
Stages of ARF

- In its development, necrotic nephrosis passes through several stages:
  - Initial (shock),
  - Oligo-anuric,
  - Recovery of diuresis,
  - Convalescence.

Initial stage

- It is manifested by a pronounced fullness of the intermediate zone and pyramids, ischemia of the cortical layer (1st day).
- Macroscopic picture:
  - Kidneys are enlarged in size,
  - The capsule is tense, it slides from the cortical substance,
  - The bark is swollen, pale,
  - The pyramids are dark red.
- Microscopic picture:
  - In the epithelium of the tubules, hyaline-drop, hydrophilic or fatty degeneration,
  - The lumen of the tubules is unevenly expanded, and may contain cylinders.

Shock kidney



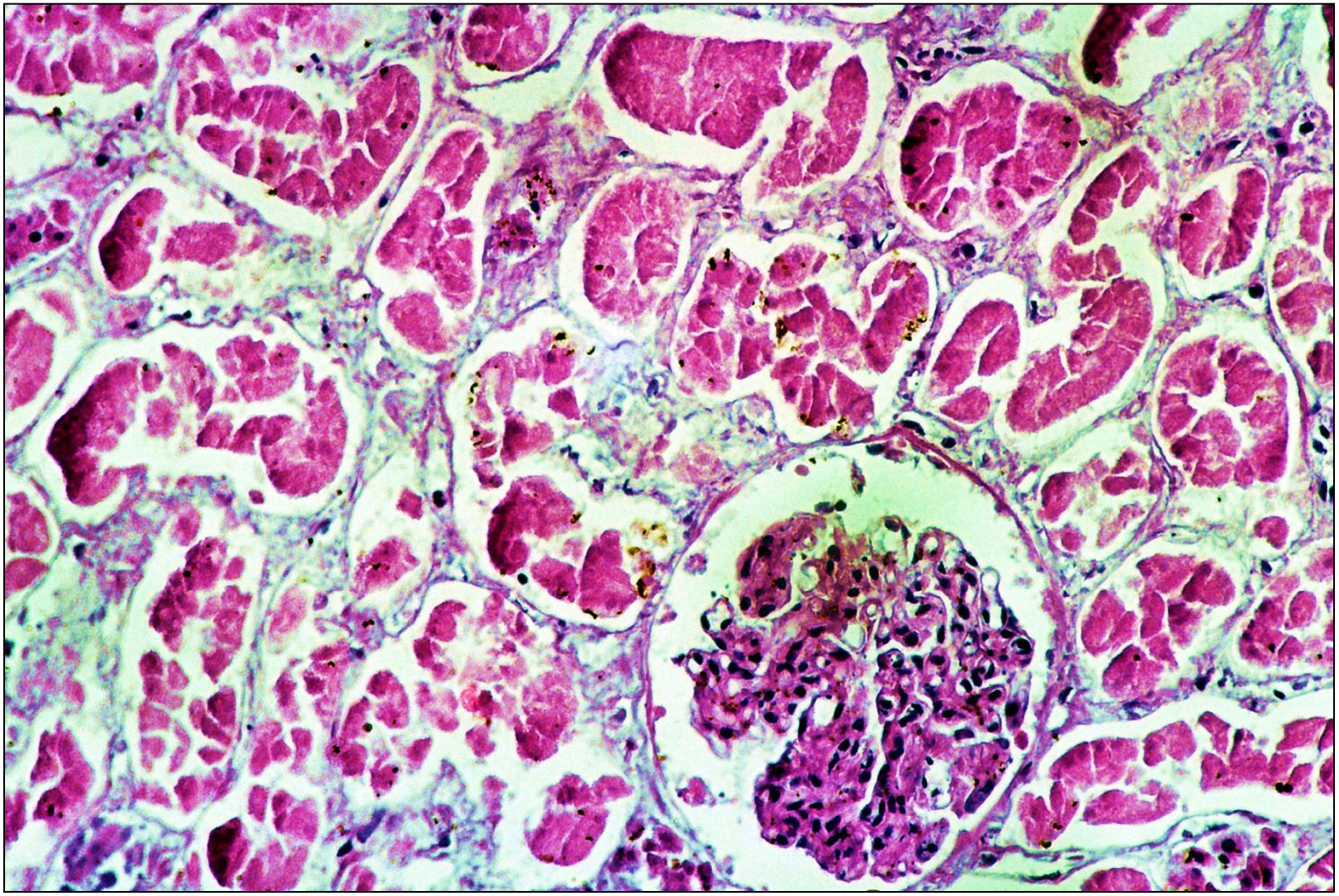
Oligo-anuric stage

- Characterized by the growth of necrotic changes in the epithelium of tubules (2 - 9th day).
- The first to necrotize the distal tubules.
- There is an increase in edema and leukocyte infiltration of the interstitium of the kidneys, hemorrhages appear.
- The destruction of tubules and cylinders make it difficult to drain primary urine from the glomerulus capsules.
- In the areas where the basal membrane of the tubules has disintegrated, connective tissue begins to form.

Recovery of diuresis stage

- It starts on the 10th-21st day.
- Edema and infiltration of the kidneys are reduced.
- Ways of regeneration of the epithelium of the tubules alternate with foci of necrosis and sclerosis.
- In the tubules with the preserved basal membrane there is a complete recovery of the epithelium.
- If there is a destruction of the basement membrane, connective tissue grows.

Necrotic nephrosis



Causes of death patients with ARF

- Death can occur in the shock and oligoanuricheskuyu stage of uremia or electrolyte disorders.

- Especially dangerous is hyperkalemia, which leads to cardiac arrest.

Stromal diseases

- A group of diseases with primary lesion interstitial kidney.
- As a rule, these are acquired diseases, which are inflammatory.
- Presented by tubulo-interstitial nephritis and pyelonephritis.

Tubulointerstitial nephritis (TIN)

- Disease of an infectious-allergic nature, characterized by bilateral non-inflammatory inflammation of the interstitial tissue of the kidney with secondary involvement of the nephron.
- Occurs under the influence of the following factors:
  - Toxic:
    - Drugs (analgesics - especially dangerous combination of aspirin with phenacetin, some antibiotics - gentamicin, cephaloridine, sulfonamides, cytostatics, etc.)
    - Salts of heavy metals (lead, mercury);
  - Infectious (bacteria, viruses);
  - Metabolic disorders, etc.

Tubulointerstitial nephritis

- The pathogenesis of tubulointerstitial nephritis has much in common with the pathogenesis of glomerulonephritis: it can be caused by the action of circulating immune complexes in the blood, antibodies or being a manifestation of the reaction of HRT.

- In this case, the basal membrane of the tubules is damaged, and the inflammatory reaction unfolds in the interstitium of the kidney.

- The disease can be acute or chronic.

Tubulointerstitial nephritis

- Clinically, tubulointerstitial nephritis in both forms differs from glomerular diseases by the absence in the early stages of such major signs of glomerular damage as nephritic and nephrotic syndromes.

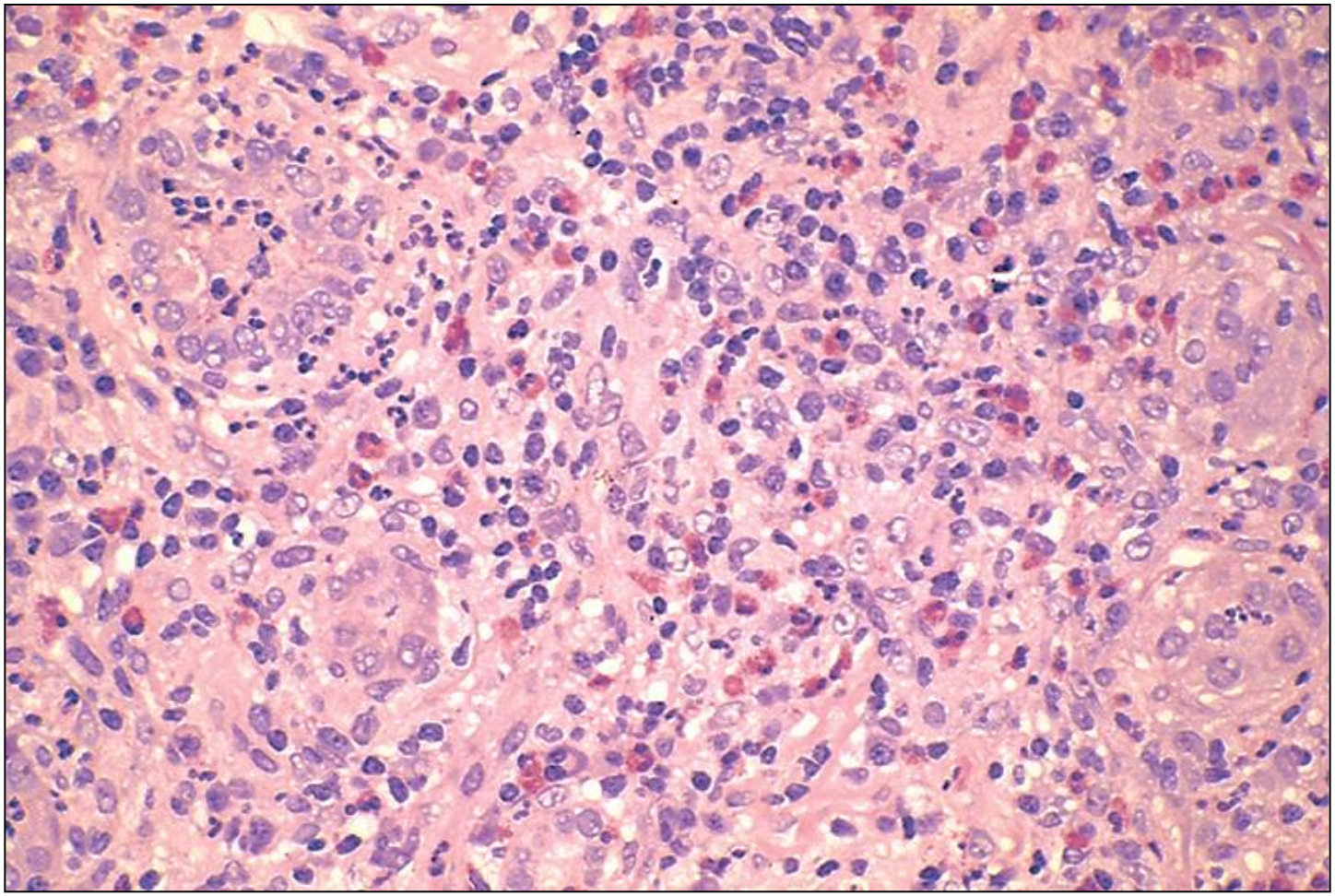
- Functional disturbances can be insignificant: violation of urine concentration (polyuria), loss of salt, metabolic acidosis, isolated defects of tubules of reabsorption and secretion.

- Developed forms, however, can be difficult to distinguish from other diseases that lead to kidney failure.

Acute TIN

- Clinically it has an acute onset.
- Microscopic picture:
  - Varying degrees of edema of the interstitial tissue, Infiltration of the stroma (lymphocytes, histiocytes, monocytes, neutrophilic leukocytes, plasma cells, eosinophils - in drug forms and allergic reactions),
  - Focal necrosis of tubular epithelium.

Acute drug-induced TIN



Chronic TIN

- Microscopic picture:
  - Pronounced infiltration of the stroma with mononuclear cells,
  - Sclerosis of the stroma,
  - Atrophy of tubules,
  - Periglomerular sclerosis.

Pyelonephritis

- Pyelonephritis is a purulent inflammation of the kidneys involving the cup-and-pelvic system with a predominant lesion, interstitium caused by various microbes.
- The most frequent etiologic factor is E. coli
- Infect enters the kidney in the following ways:
  - Descending (hematogenous),
  - Ascending (from the urethra, urinary bladder, ureters).

Pyelonephritis

- The following factors predispose to the development of pyelonephritis:
  - Short urethra in women;
  - Obstruction of the urinary tract (stones, strictures, tumor compression, prostatic hyperplasia, etc.);
  - Pregnancy (hyperprogesteronemia reduces the contractile activity of SMC, which leads to a stasis of urine);
  - Operations on the kidney and urinary tract;
  - Urinary tract catheterization;
  - Vesicoureteral reflux;
  - Diseases of the genitals;
  - Diabetes mellitus.

Pyelonephritis

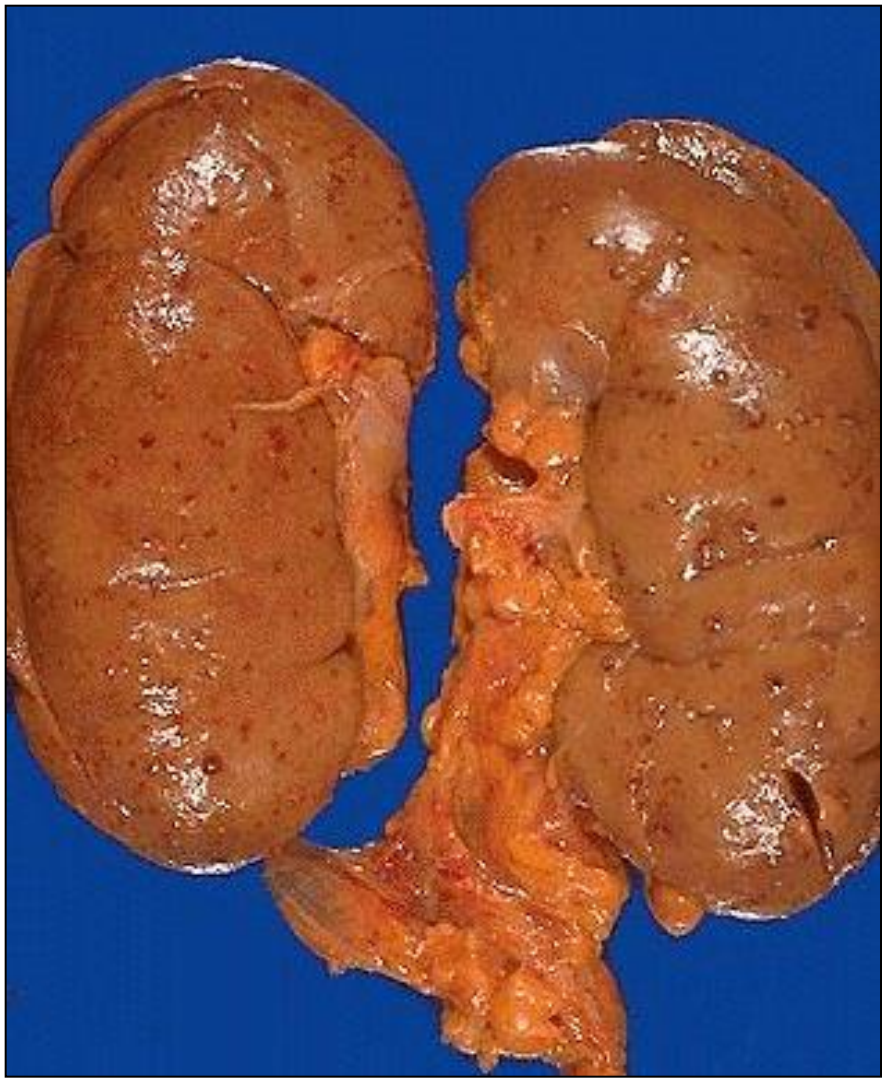
- There are the following types of pyelonephritis:
- By localization:
  - unilateral,
  - bilateral,

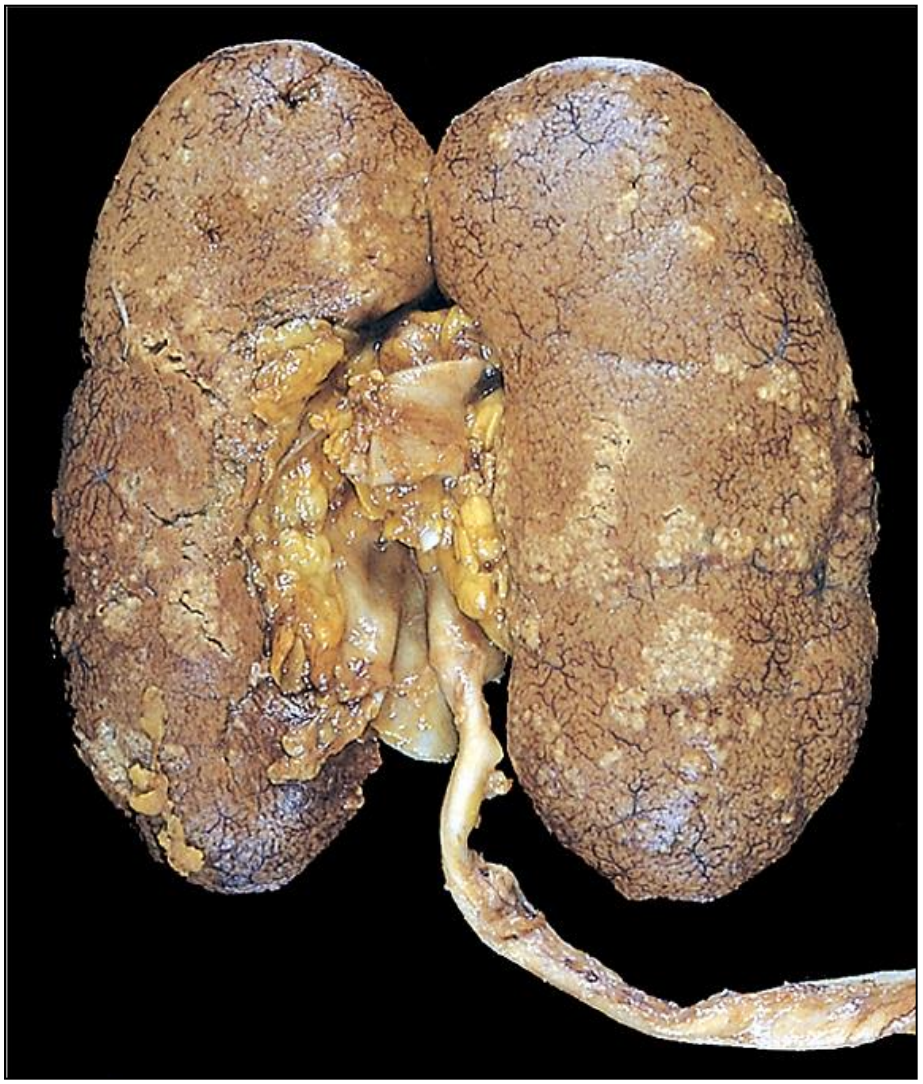
- According to the clinical course:
  - acute,
  - chronic.

Acute pyelonephritis

- Macroscopic picture:
  - The kidneys are enlarged,
  - The capsule is strained, after its removal, gray-yellow patches and bands are detected;
  - In some cases in the cortex and medulla of visible pustules different sizes (apostematozny pyelonephritis);
  - The mucous membrane of pelvis and calyx is dull, with small hemorrhages, sometimes covered with purulent-fibrinous overlap.

Apostematous pyelonephritis

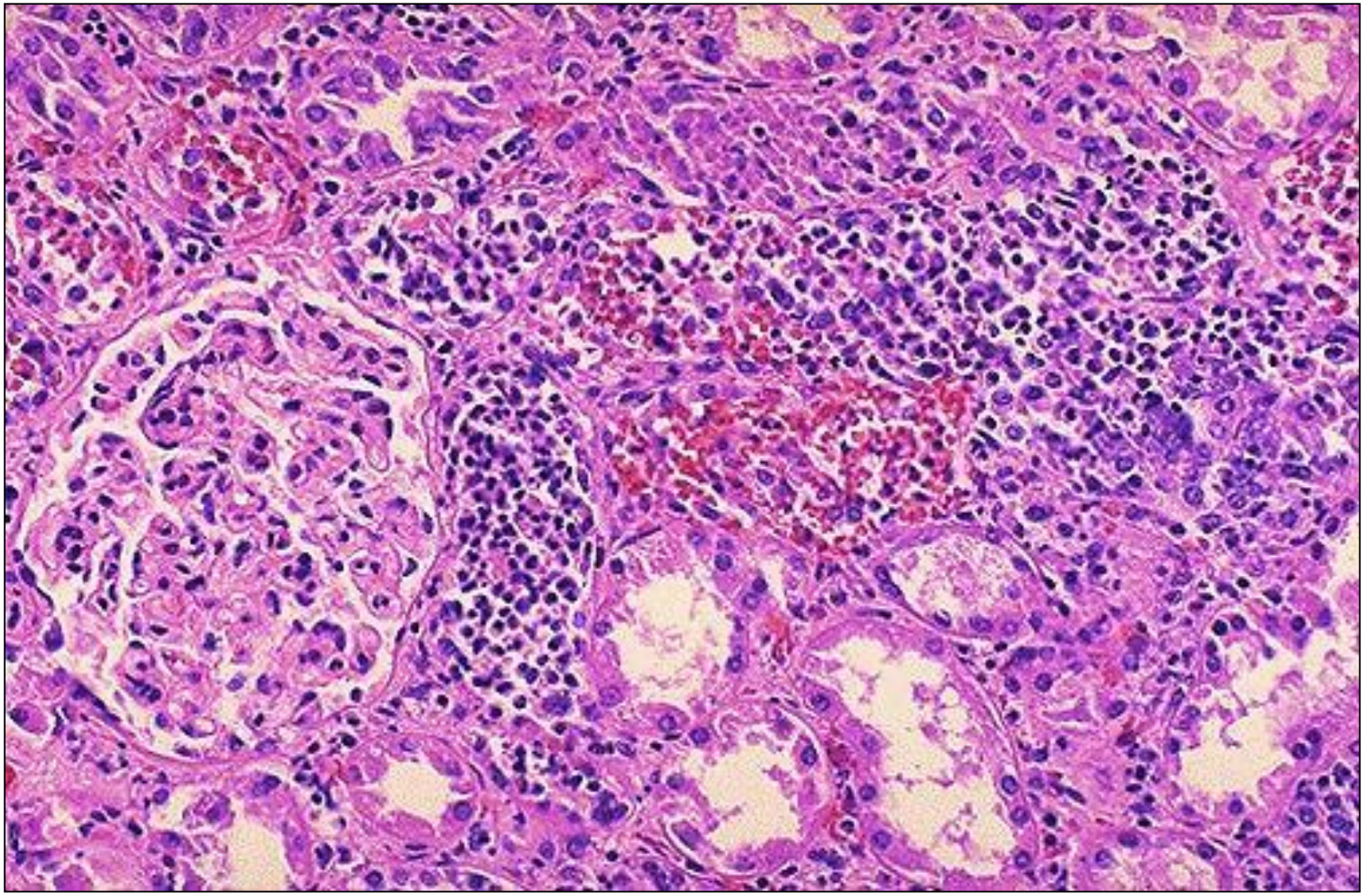




Acute pyelonephritis

- Microscopic picture:
  - Focal or diffuse infiltration of the stroma of both cortical and brain matter by neutrophilic leukocytes,
  - Small areas of necrotic tissue,
  - In the lumen of the tubules, a large number of neutrophilic leukocytes is determined,
  - In the center of the pustules there can be colonies of microbes (with descending pyelonephritis).

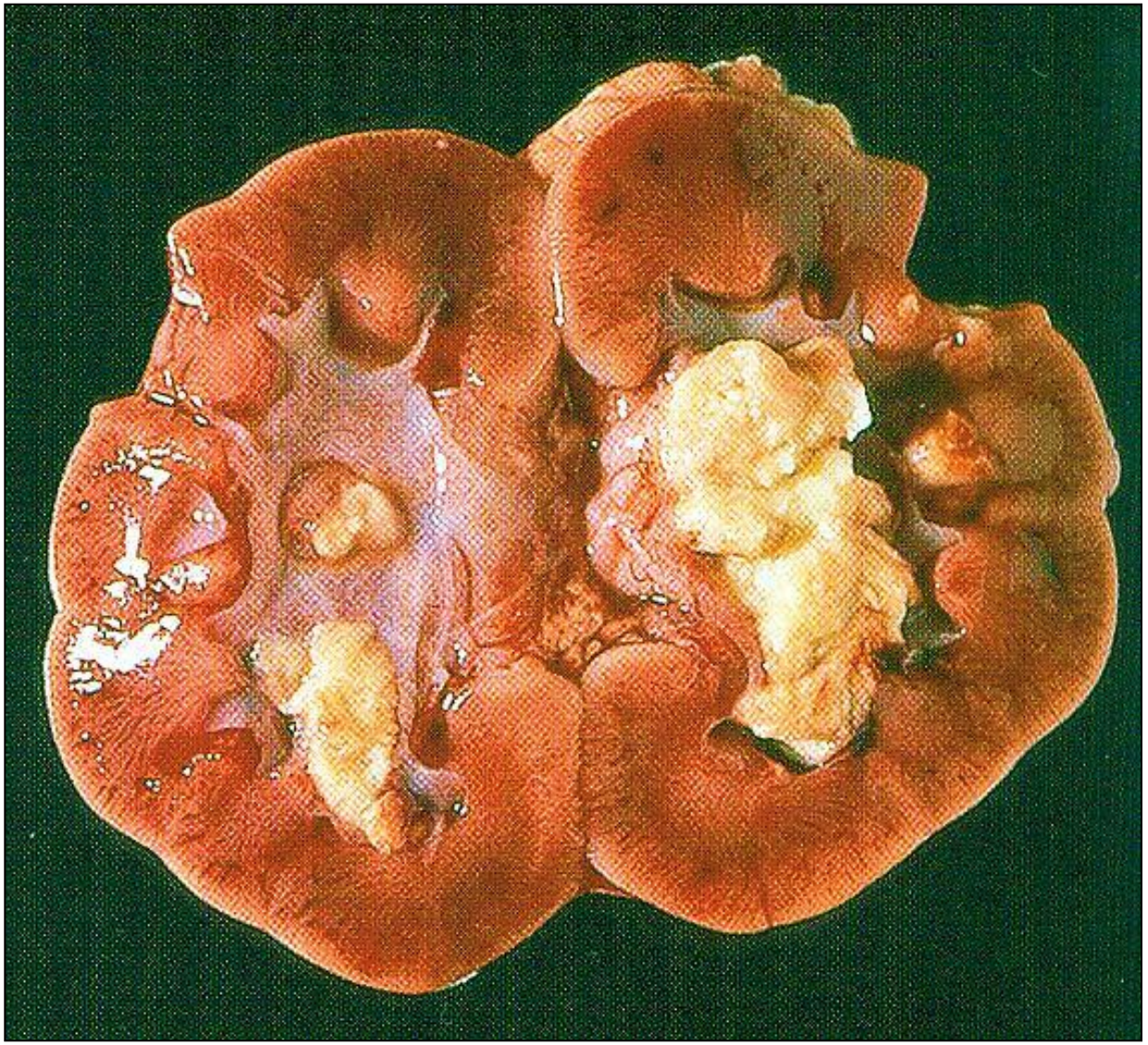
Acute pyelonephritis



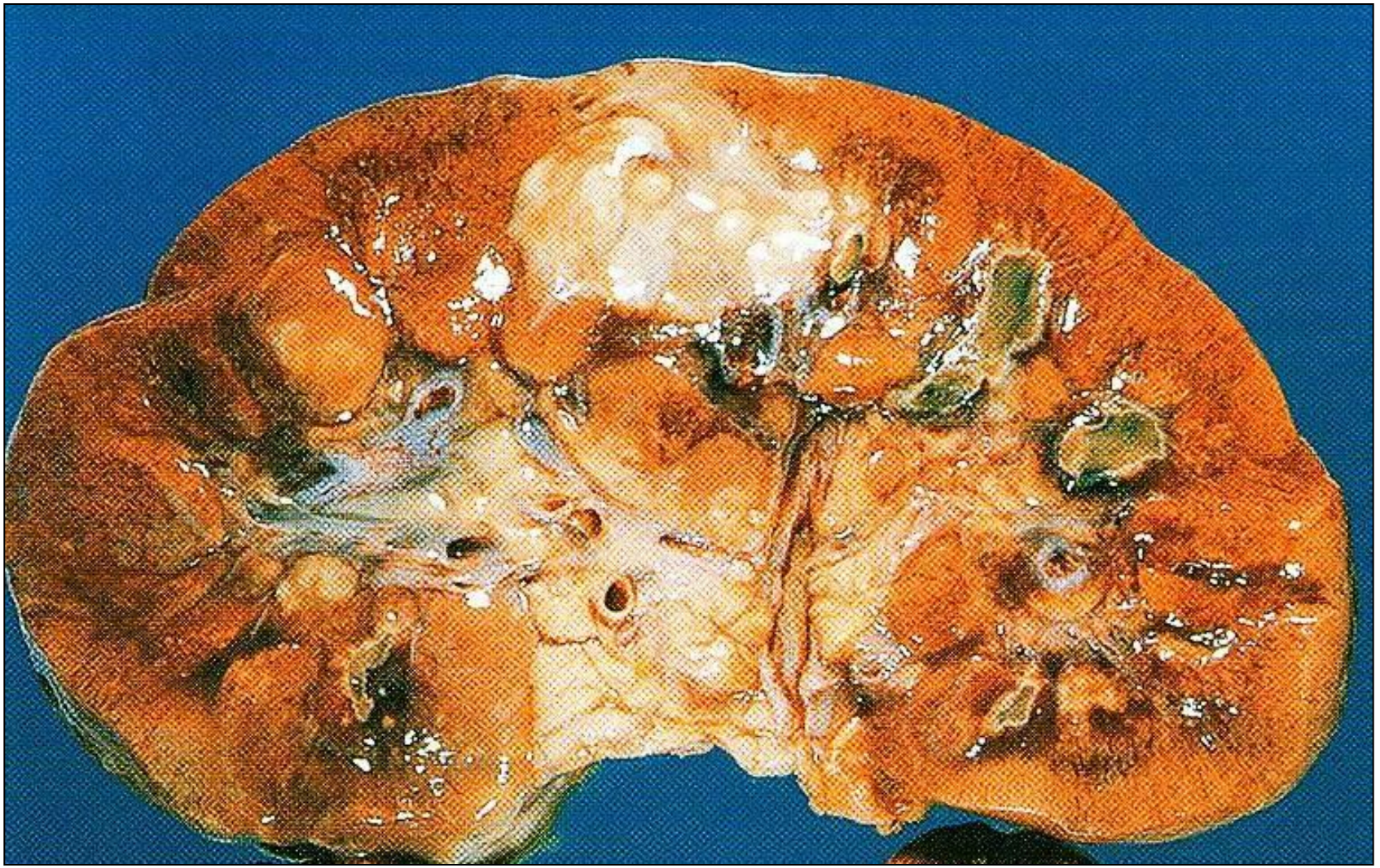
Complications of acute pyelonephritis

- Complications of acute pyelonephritis are:
  - Pionephrosis,
  - Perinephritis (inflammation of the capsule of the kidneys),
  - Paranephritis (inflammation of the perineum cellulose),
  - Urinogenic sepsis,
  - Necrosis of the papillae of the pyramids of the medulla with the development of acute renal failure (rarely).

Pionephrosis



Necrosis of the papillae of the pyramids



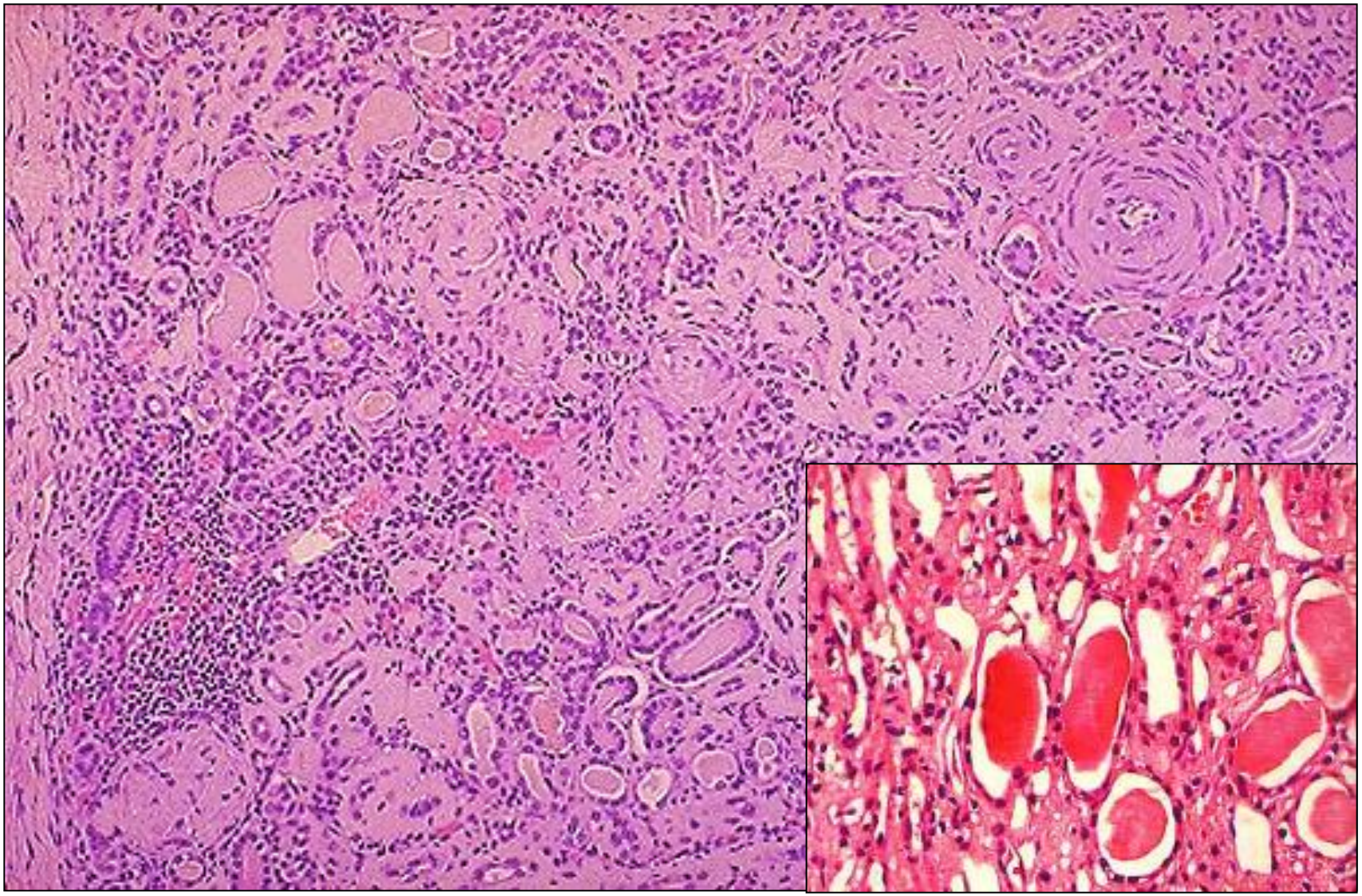
Chronic pyelonephritis

- Microscopic picture:
  - The epithelium of the tubules is dramatically atrophied, the lumens of their cystic dilated with the appearance of dense eosinophilic masses and resemble in structure the follicles of the thyroid gland ("kidney thyroidization", "thyroid kidney"),
  - Focal lympho-macrophagal infiltration of the renal stroma,
  - Sclerosis of the stroma, periglomerular sclerosis.

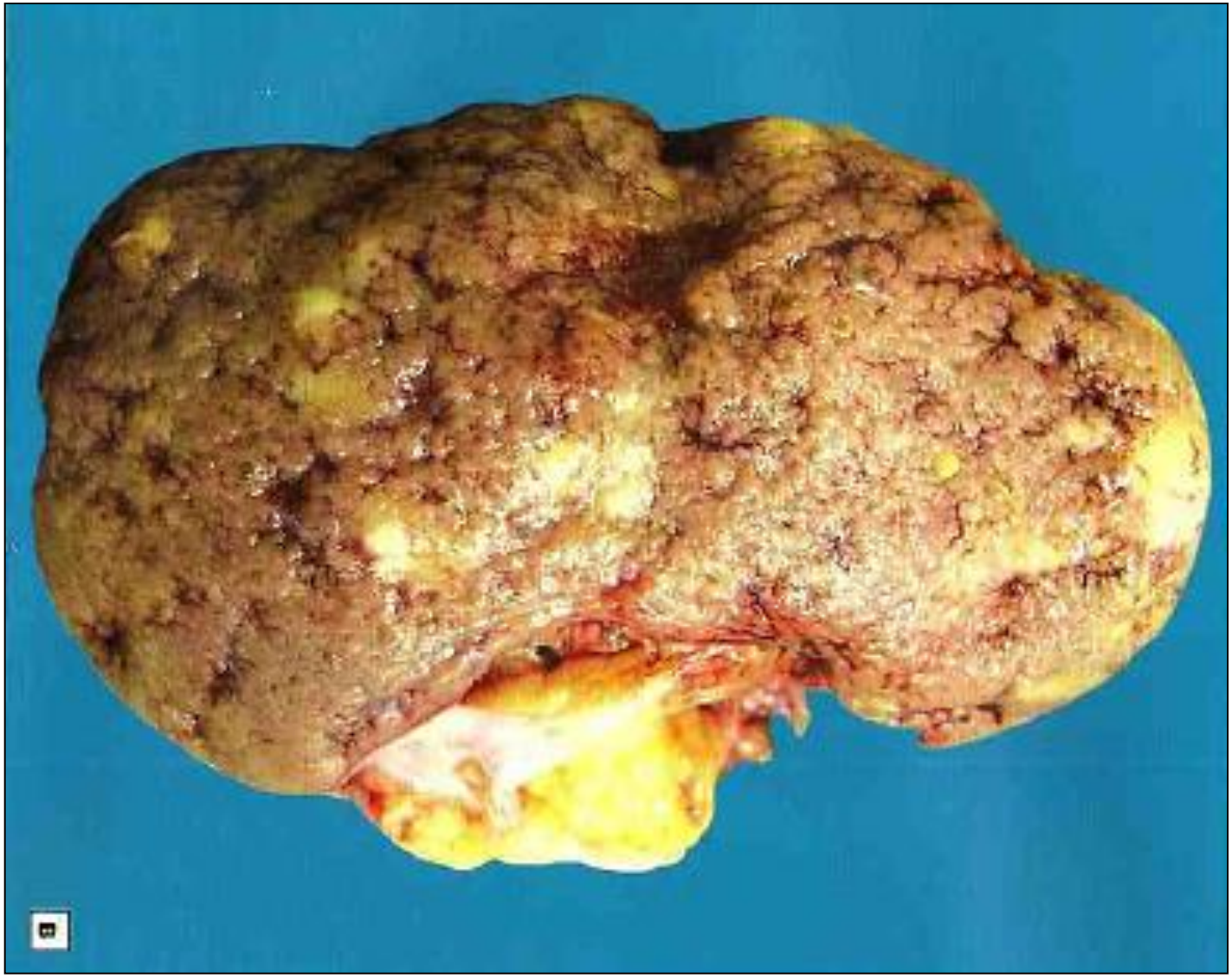
- The disease can be accompanied by nephrogenic arterial hypertension.

- In the kidney, sclerotic changes develop with the outcome of a secondary-wrinkled kidney and CRF.

Kidney thyroidization



Secondary-wrinkled kidney



Chronic renal failure (CRF)

- Chronic renal failure (CRF) is a symptom complex caused by the irreversible gradual death of nephrons in chronic progressive kidney diseases.

- This is in most cases an irreversible progressive process leading to the development of uremia in the terminal stage.

- Morphological substrate is nephrosclerosis.

Chronic renal failure

- With development of chronic renal failure are ends:
  - Chronic kidney disease (glomerulonephritis, pyelonephritis),
  - Diffuse connective tissue diseases that occur with kidney damage (SLE, scleroderma),
  - Metabolic diseases (diabetes mellitus, amyloidosis, gout),
  - Cardiovascular disorders (arterial hypertension, atherosclerotic stenosis of the renal arteries),
  - Obstructive nephropathy (urolithiasis, tumors of the genitourinary system).

Stages of CRF

- In the **latent (reversible)** stage of CRF:
  - Diuresis is preserved and can be somewhat strengthened (polyuria), which is due to a decrease in water reabsorption in the distal tubules of the nephron and the concentration ability of the kidneys (hypoisostenuria);
  - Increases blood pressure;
  - The picture is typical for a state where up to 50% of nephrons die.

Stages of CRF

- In the **azotemic (stable)** stage of CRF:
  - Marked decrease in the glomerular filtration rate;
  - Azotemia, hyperkalemia, hyperphosphataemia, renal acidosis, anemia, edema, hypertension;
  - The number of functioning nephrons is reduced from 50 to 20%.
- In the **uremic (progressing)** stage of CRF:
  - Develop oliguria and uremia, autointoxication;
  - The number of functioning nephrons is reduced to 5%.

Uremia

- Uremia is a clinical syndrome of progressive renal failure, characterized by metabolic and functional impairments in many organs and systems (multiple organ failure).

- Uremia can develop with an unfavorable outcome of ARF, regularly occurs in the terminal stage of CRF and is characterized by a number of functional and metabolic disorders.

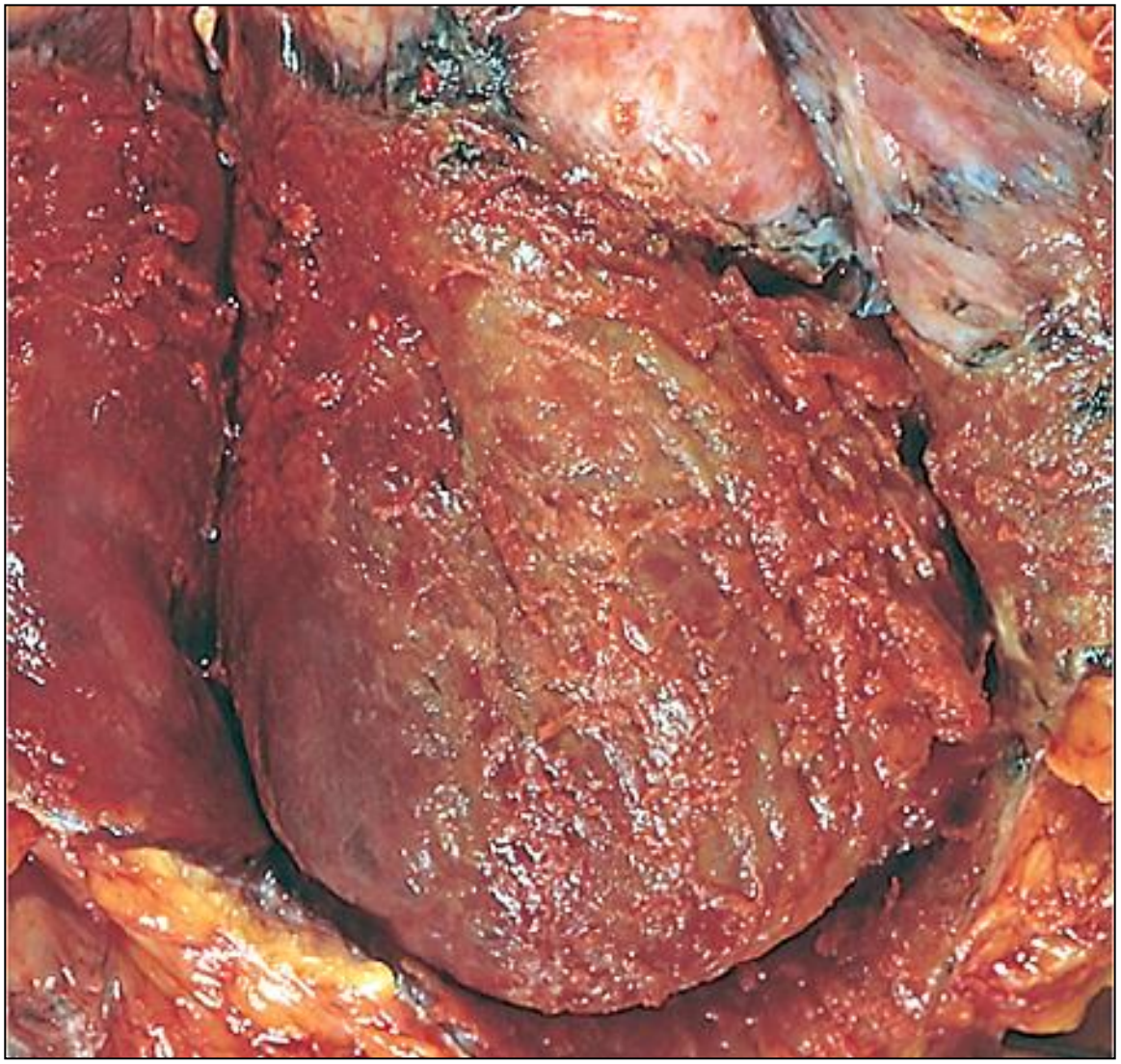
- Uremia often ends with renal coma, which is manifested by loss of consciousness, hypo- and areflexia, terminal state of the body.

Morphology of uremia

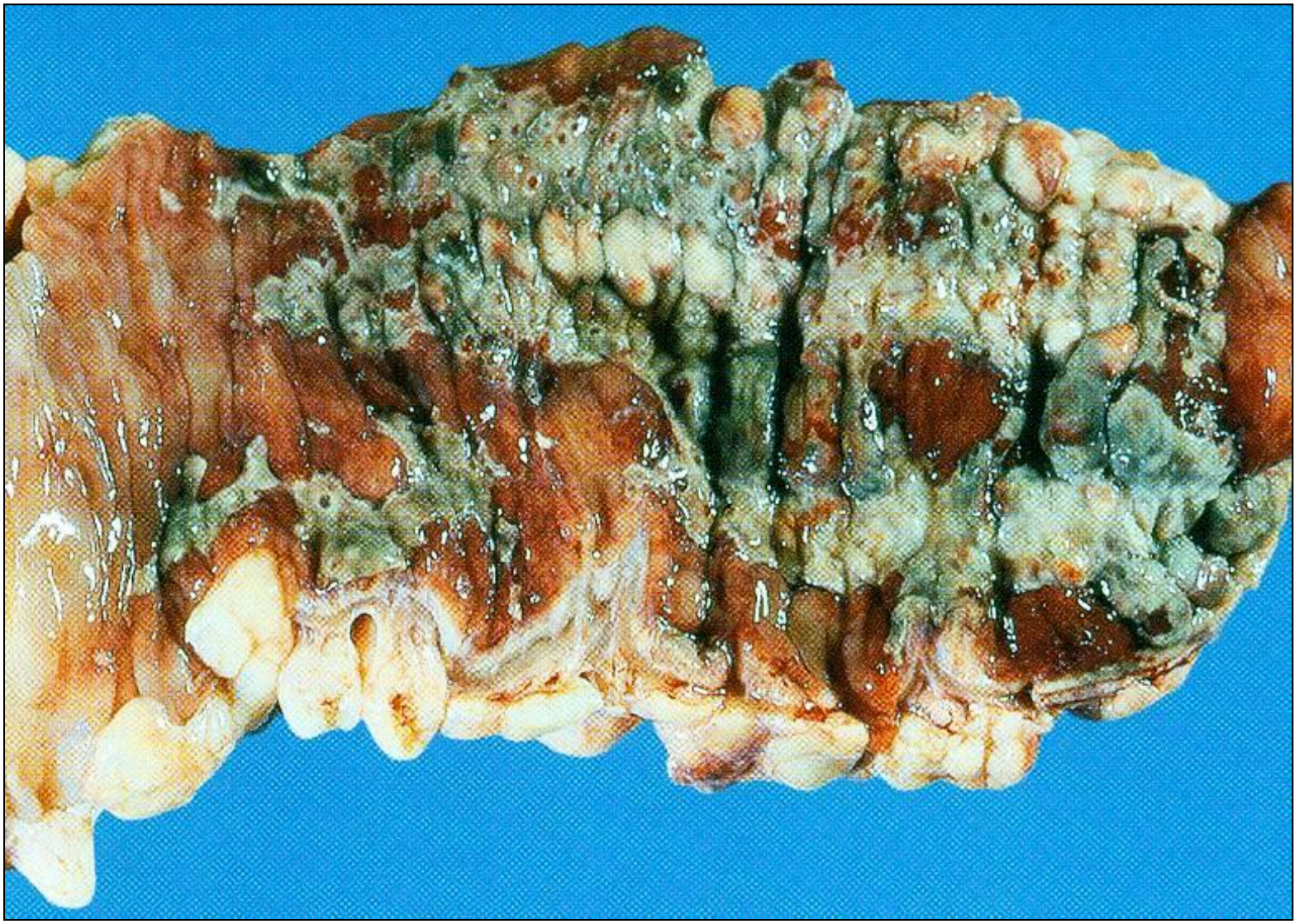
- The morphological picture of uremia is characterized by the pathology of the extrarenal excretory system with the development of serous, hemorrhagic or fibrinous inflammation:
  - Fibrinous pericarditis ("hairy heart");
  - Catarrhal or fibrinous gastritis, enteritis, colitis;
  - Pulmonary edema and fibrinous pneumonia.

- On the skin of patients (more often in the area of the elbows and armpits) there is a white powdery coating and the smell of urine.

Fibrinous pericarditis



Fibrinous colitis



Kidney cancer

- Among malignant epithelial tumors in adults, most often there are various variants of renal cell carcinoma (kidney adenocarcinoma).

- Because of the bright yellow color of the tumor and the similarity of tumor cells with light cells of the adrenal cortex, renal cell carcinoma is called hypernephritic kidney cancer.

Kidney cancer

- Distinguish the following histological variants of renal cell carcinoma:
  - Clear cell;
  - Papillary (chromophilic);
  - Chromophobic;
  - Carcinoma of collecting tubules.

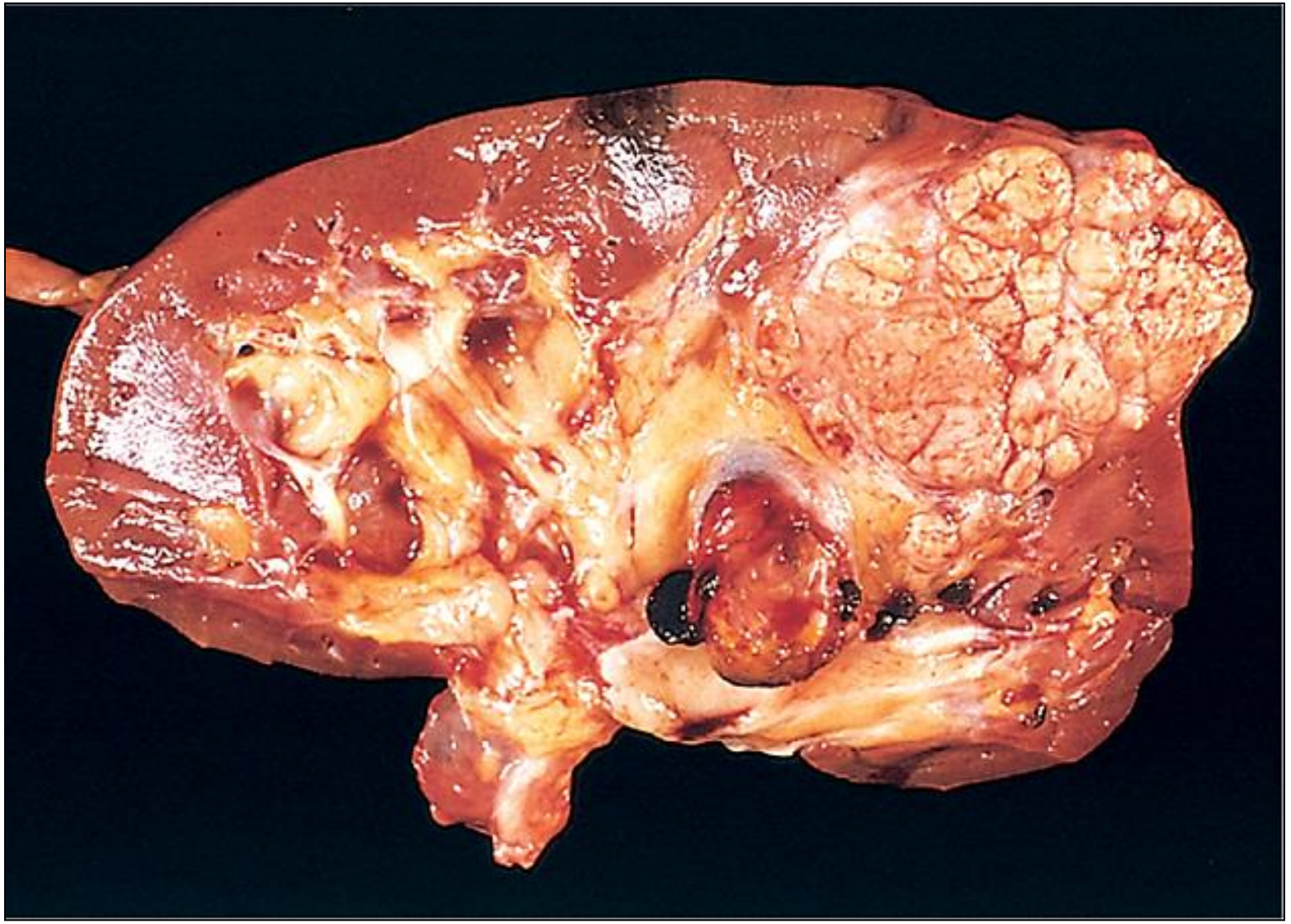
- All these variants arise in the cortical substance from the stem cells of the tubular epithelium.

- The most frequent and typical cancer of the kidneys is the clear-celled cancer (up to 80%).

Hypernephritic kidney cancer

- Macroscopic picture:
  - The tumor has the form of a node,
  - On a cut the tissue of its bright yellow (similar to the tissue of the adrenal gland - hypernaroid cancer) or a variegated species with the presence of foci of necrosis and hemorrhages of various prescription;
  - Cysts with a clear, brownish or bloody fluid are often found.

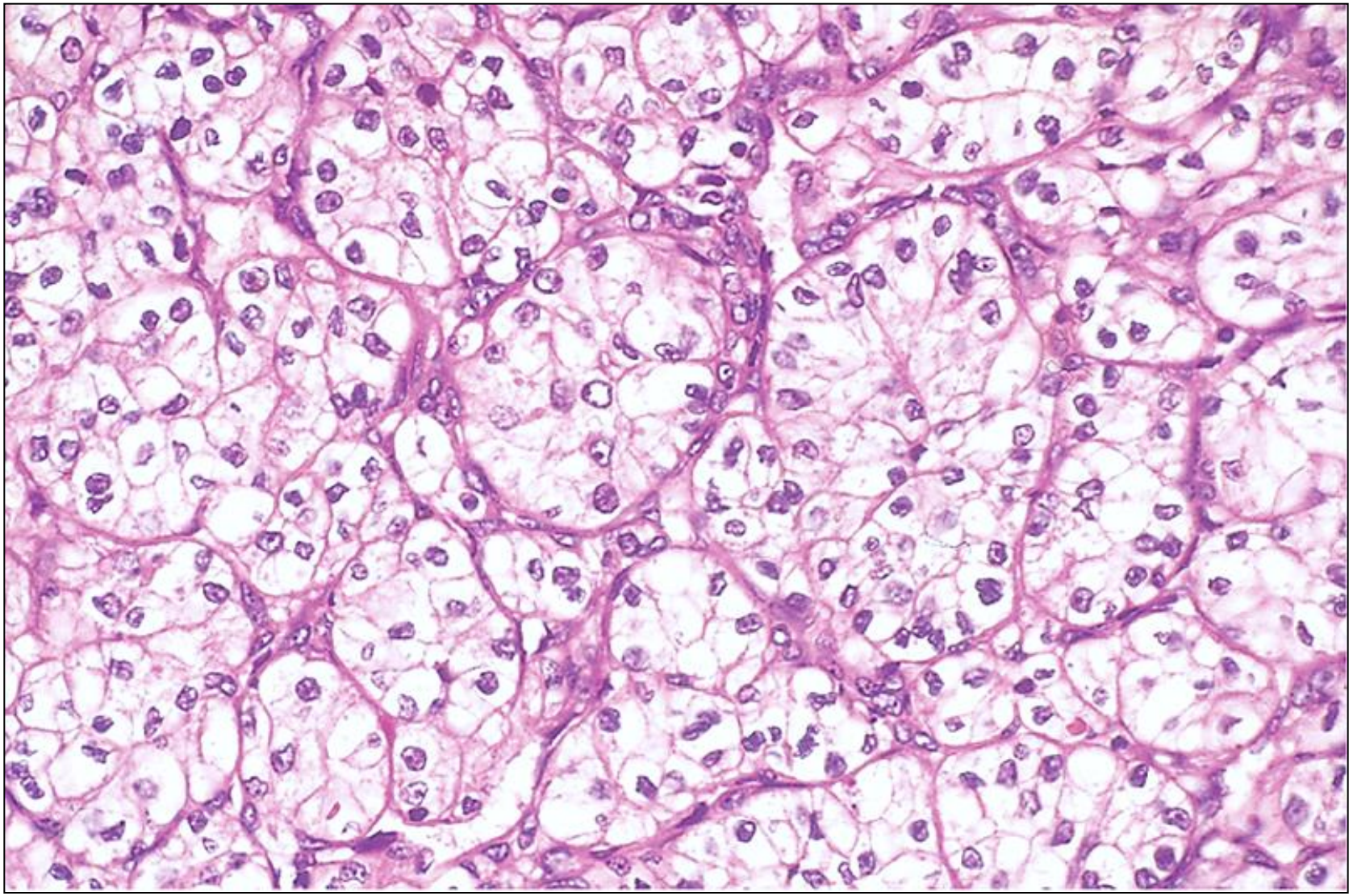
Hypernephritic kidney cancer



Clear cell kidney carcinoma

- Microscopic picture:
  - Tumor cells have a polygonal shape and contain rounded hyperchromic nuclei located in the center,
  - The light color of the cytoplasm is due to the fact that it contains a large amount of glycogen and lipids,
  - Complexes of tumor cells form alveoli and lobules, separated by narrow interlayers of connective tissue containing a large number of thin-walled blood vessels,
  - Characterized by foci of necrosis and hemorrhage,
  - Crystals of cholesterol, deposits of calcium salts are often found.

Clear cell kidney carcinoma



Metastasis of kidney cancer

- For renal cell carcinoma, the tumor tissue of the pelvis grows and grows through the veins until the inferior vena cava enters the right atrium with the formation of clots containing tumor cells.
- Breaking off, such blood clots are often the cause of fatal embolism.
- Kidney cancer gives early multiple hematogenous metastases to the lungs, bones, liver, adrenals, the opposite kidney, the brain.
- Early lymphogenous metastases are detected in the lymph nodes of the kidneys, near-aortic lymph nodes.

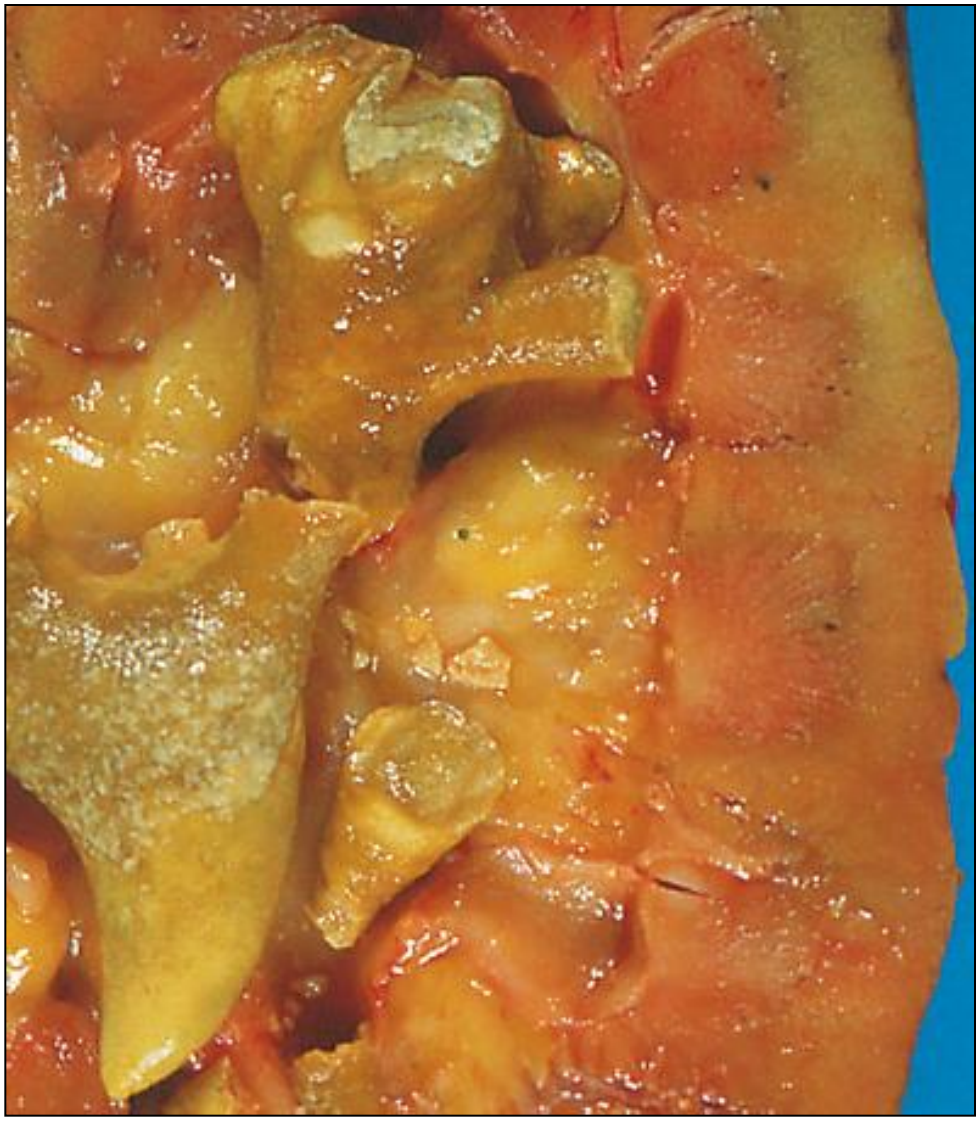
Kidney stone disease

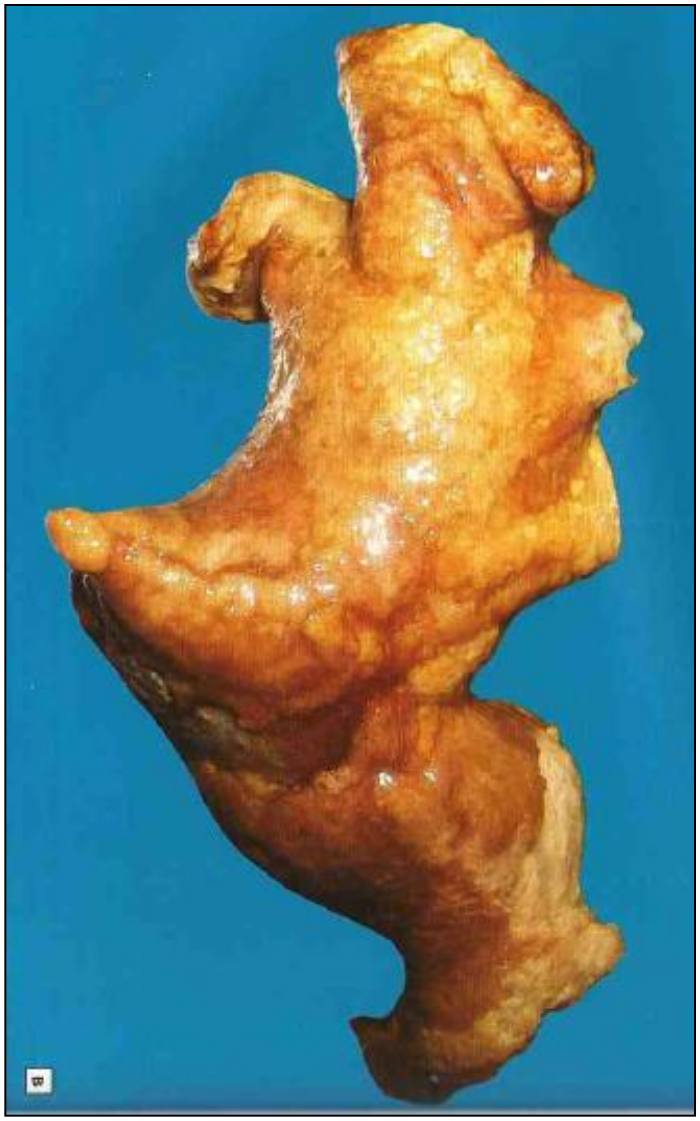
- Kidney stone disease (nephrolithiasis, urolithiasis) is a disease in which calculus-calculous kidneys form concretions (stones).
- Factors promoting stone formation:
  - Increase in the concentration of salts in the urine;
    - With a decrease in the volume of urine;
    - With an increase in the excretion of salts by the kidneys;
  - Violation of urine outflow;
  - Inflammation (pyelonephritis);
  - Deficiency of stabilizing factors (citrates, amino acids, etc.).

Kidney stone disease

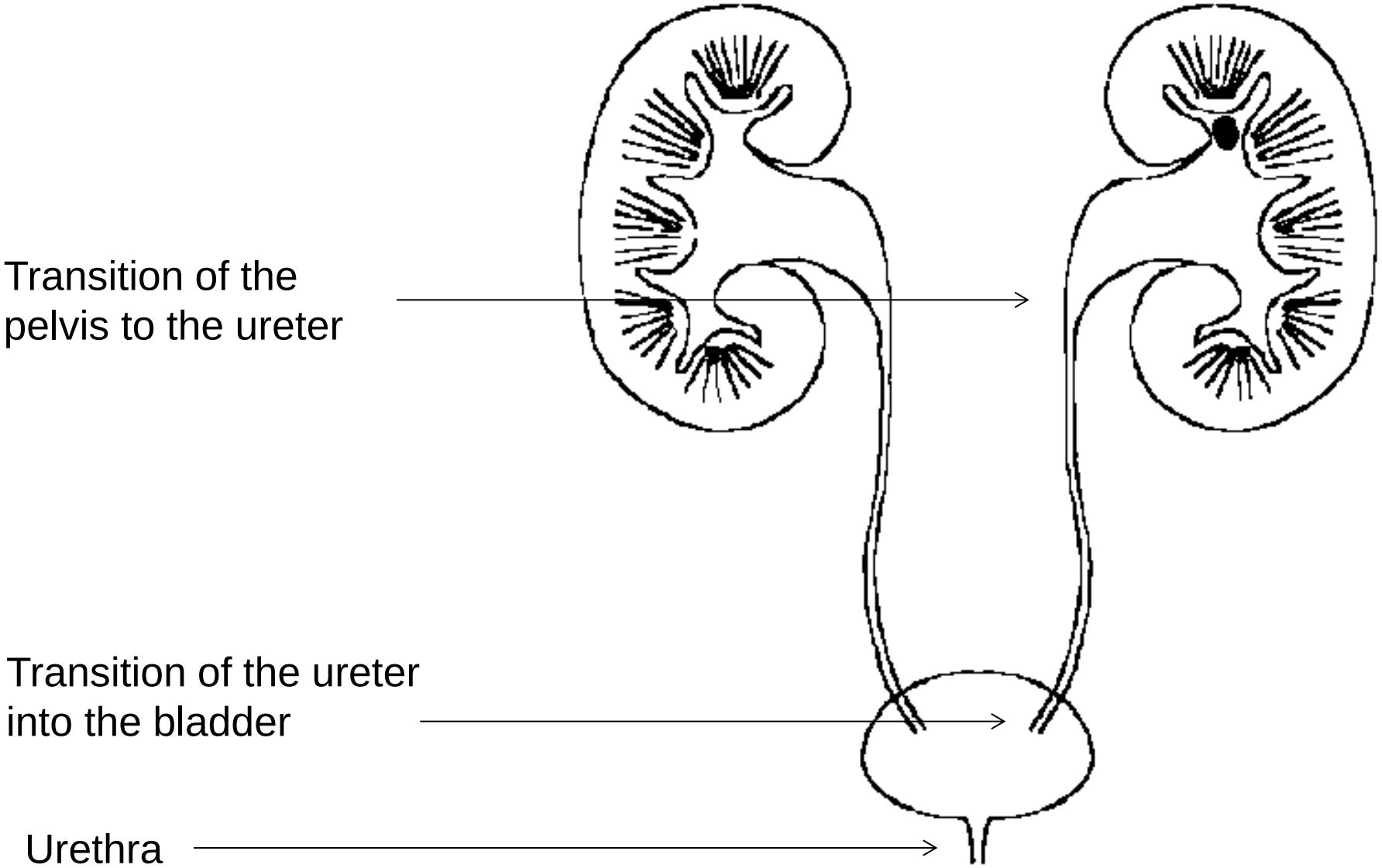
- Composition of stones:
  - Urates;
  - Phosphates;
  - Oxalates;
  - Mixed.
- By the size and shape of the stones can be very diverse.
- A special type of concrement is the coral stone, which has a characteristic shape and reaches a large size (7-9 cm).
- Complications:
  - Obstruction of the urinary tract (hydronephrosis);
  - Acute and chronic pyelonephritis, cystitis.

Coral kidney stone





Obstruction of urinary tract with stone



Hydronephrosis