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1-я КАФЕДРА ДЕТСКИХ БОЛЕЗНЕЙ
2-я КАФЕДРА ДЕТСКИХ БОЛЕЗНЕЙ

# ГЛОМЕРУЛОНЕФРИТЫ У ДЕТЕЙ

# GLOMERULONEPHRITIS IN CHILDREN

Учебно-методическое пособие

Минск БГМУ 2017

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Освещены вопросы этиологии, патогенеза, классификации, клинических и морфологических проявлений острых и хронических гломерулонефритов у детей. Приведены современные рекомендации по диагностике и лечению гломерулонефритов у детей.

Предназначено для студентов 4-го и 6-го курсов медицинского факультета иностранных учащихся, изучающих педиатрию на английском языке.

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## ABBREVIATIONS

APGN — acute post-streptococcal or post-infectious glomerulonephritis
ACE — angiotensin-converting enzyme
AG — antigens
AB — antibodies
ESR — erythrocyte sedimentation rate
GFR — glomerular filtration rate
GBM — glomerular basement membrane
GN — glomerulonephritis
IC — immune complex
RPGN — rapidly progressive glomerulonephritis

## DEFINITION

Glomerulopathies form the heterogeneous group of kidney diseases with initial glomerular lesion. The secondary involvement of other components of renal tissue (tubules, vessels or interstitium) may be observed later on. There is a huge variety of causes, pathogenetic patterns, clinical presentations and morphological features, as well as course (natural history) and outcome in the group of glomerulopathies.

## CLASSIFICATION GLOMERULONEPHRITIS

All glomerulopathies are divided in:

– ***primary or idiopathic*** — glomerular lesion occurs primarily in absence of any systemic condition, which may cause kidney disease;

– ***secondary*** — glomerular lesion is a result of systemic illness (more often systemic disease of connective tissue, for example systemic lupus erythematosus, systemic vasculitis, etc.).

According to the disease course glomerulopathy can be:

– ***acute*** (e.g. endocapillary glomerulonephritis (GN));

– ***chronic*** (e.g. membranoproliferative GN, IgA nephropathy, focal segmental glomerulosclerosis, etc.);

– ***rapidly progressive*** (extracapillary GN).

There are clinical classifications of glomerulopathies, which are based on clinical presentation and course of the disease, and morphological one, which is considered to be a “gold standard”, predominantly in case of chronic illness. However, not always morphological diagnostics is needed (especially in case of acute illness or hormone sensitive nephrotic syndrome). That is why both classifications, based on clinical manifestations and morphological diagnosis, remain of importance in clinical practice.

Often there isn't strong correlation between clinical pattern and morphological changes found on kidney biopsy. However, ***some clinical patterns may be designated***:

1. Nephritic syndrome, which is the most characteristic for acute poststreptococcal or post infectious (endocapillary) GN.

2. Nephrotic syndrome, which in young children is predominantly due to minimal changes disease.

3. Rapidly progressive GN, with nephrotic syndrome with hematuria and/or hypertension at presentation is characteristic for crescentic (extracapillary) GN.

4. Recurrent macroscopic hematuria (with or without proteinuria), which is often a sign of Berge's nephropathy.

According to the type of initial glomerular lesion glomerulopathies can be (figure 1).

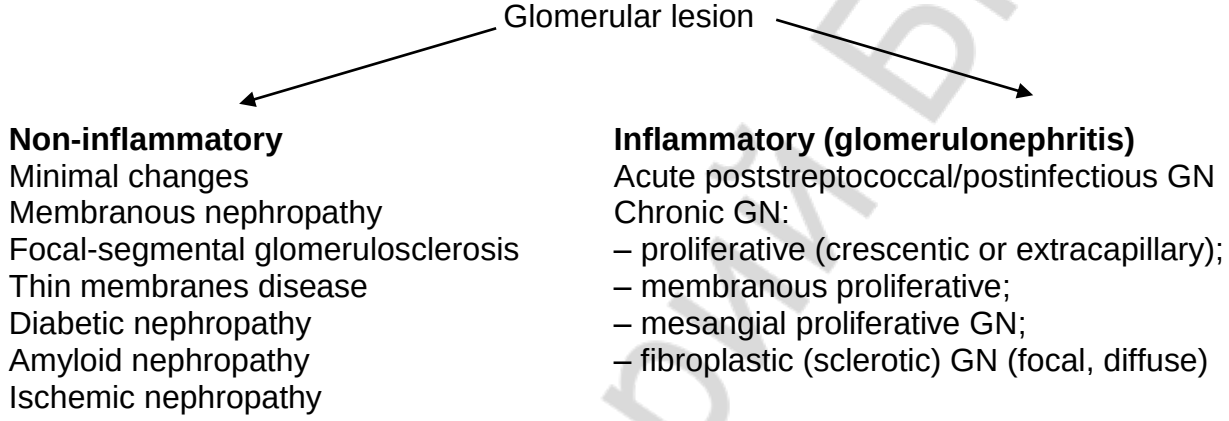



*Fig. 1*. Types of glomerular lesions

Non-inflammatory glomerulopathies are characterized by parenchymatous dystrophy or/and changes of glomerular basement membrane (GBM), disorganization or sclerosis of mesangial matrix. No or minimal signs of proliferation or glomerular infiltration can be observed. These caused by, in majority of cases, non immune-mediated damage, for example, amyloid deposition.

In case of immune injury (in minimal changes nephrotic syndrome), the attack is targeted at visceral epithelial cells, which are called podocytes, and the type of lesion is called podocytopathy.

In inflammatory glomerulopathies (true glomerulonephritis) immune attack is targeted at endothelial cells, mesangium, epi-, peri- and intramembranous structures. Classical signs of inflammation are observed: infiltration, proliferation, exudation, alteration and function impairment. Immune mediated injury involves immunoglobulin's deposition and inflammatory cells migration from blood flow in glomerulus, these both may be resulting in direct damage to glomerular cells and in inflammatory response of residential glomerular cells, mesangial proliferation and hyperproduction of mesangial matrix, thickening of glomerular basement membrane, proliferation of parietal epithelial cells with crescents formation.

Analysis of clinical manifestations in conjunction with morphological glomerular and tubulointerstitial lesions gives the most informative data concerning likelihood of disease progression and response to treatment.

For proper treatment and illness progression monitoring, morphological verification (kidney biopsy) should be considered.

## ACUTE GLOMERULONEPHRITIS

**Acute post-streptococcal or post-infectious GN** (APGN**)** is an acute immune kidney inflammation with predominant glomerular lesion. Exudation and endocapillary proliferation are observed in glomerulus on kidney biopsy.

Amounts 0.1–0.2 % of all kidney diseases in children.

Children of age 5–12 are mostly affected, males : females ratio 2 : 1.

***Etiology*:**

– throat (tonsillitis, scarlet fever) or skin (impetigo, streptodermia) infections, caused by streptococci («nephritogenous», β-hemolytic, group A, types 1, 2, 4, 12, 49, 55 et al.);

– other infections: viral (flu et al.), tuberculosis, salmonella typhy infection, etc.;

– vaccination (more often revaccinations);

In Belarus seasonality is observed — occurrence rises in February-March and October-November.

***Predisposing factors*:**

– familial history;

– familial sensibility to streptococci;

– chronic infections, hypovitaminosis;

– cold weather.

***Pathogenesis.*** APGN is a typical immune complex (IC) disease.

Streptococcal toxins and enzymes (streptolysine, hyaluronidase, streptokinase et al.) initiate specific antibodies (AB) production, followed by circulating immune complexes formation;

Circulating immune complexes are deposited in glomeruli capillary walls, causing the pro-infectious factors production by glomerular cells.

Endocapillary proliferation — immune cells, including neutrophils, concentrate in glomerulus, predominantly endocapillary. Blood flow in affected capillary loops slows, permeability of glomerular basement membrane increases for erythrocytes and protein.

Antigenic mimicry between streptococcal and glomerular antigens (AG) is of particular importance in the pathogenesis of APGN.

***Pathology.*** Kidneys look enlarged, with capsule easy to take off. Subcapsular hematomas' may be observed. Exudation and cells proliferation in glomeruli on light microscopy showed on figure 2 (hematoxylin-eosin stain) and figure 3 (silver stain).

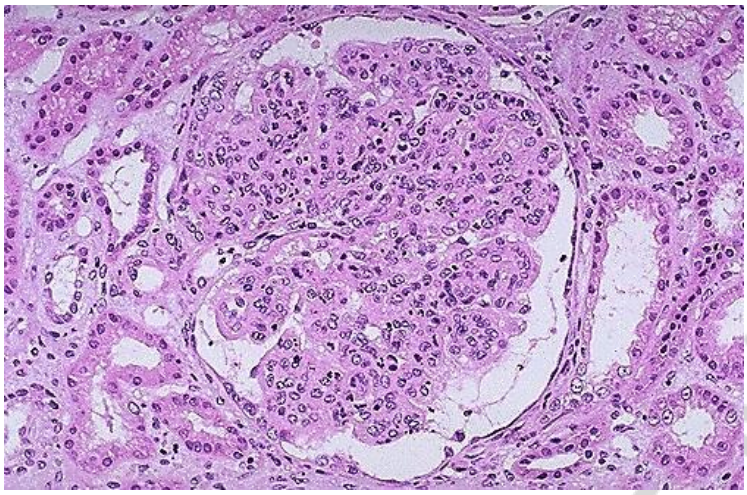


*Fig. 2*. Exudation and intracapillary proliferation in APGN. Numerous neutrophils can be seen in glomerulus (arrows). H&E stain, ×400

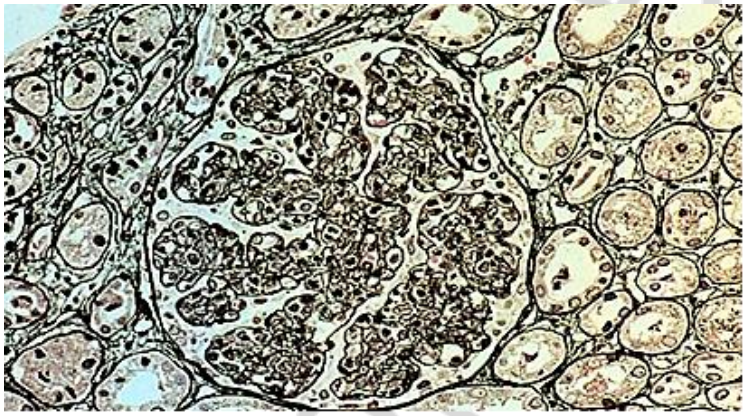


*Fig. 3*. Exudation and intracapillary proliferation in APGN, silver stain ×400

On electron microscopy, immunofluorescence or immunohistochemistry IgG or IgM deposits, C3 complement deposits are revealed (figure 4).

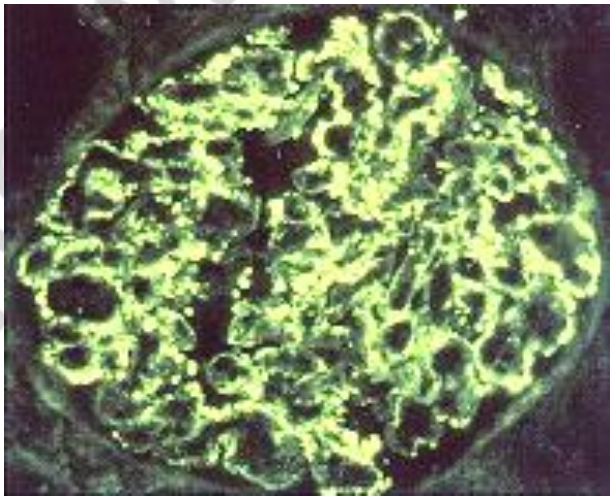


*Fig. 4*. Positivity for IgG on immunofluorescence

Duration of the changes in case of acute nephritis is up to 6 months.

***Clinical presentation.*** Nephritic syndrome is most common. Less frequently nephrotic syndrome, nephrotic syndrome with hematuria and hypertension or asymptomatic changes in urinalyses (hematuria, proteinuria) may be observed.

Natural history includes streptococcal infection 1–3 weeks prior to the disease onset. Child feels bad, becomes sleepy, complains of nausea, headaches, lack of appetite. Febrile or subfebrile fever may be observed. Sometimes complaints of stomachache or lower back pain can be present. Patient looks pale, puffy eyes (swollen eyelids), edema or pastosity of face and lower limbs can be found on clinical examination. Arterial hypertension, tachy- or bradycardia are present in majority of cases.

Patient develops **acute nephritic syndrome**, which includes:

– moderate proteinuria (1–2 g/l);

– hematuria: macrohematuria (when urine changes its color and becomes brown, reddish, coca-cola or beer like) or microhematuria (when urine discoloration is absent);

– urinary casts (hyaline, granular);

– decreased diuresis;

– arterial hypertension;

– edema.

***Laboratory findings***

– Blood tests: anemia, leukocytosis, neutrophilic shift, eosinophils. Erythrocyte sedimentation rate (ESR) is increased.

– Mild decrease in serum albumin, mild increase in α2 и γ-globulins.

– High ASLO blood test in case of poststreptococcal GN.

– Decreased C3 component of complement.

In typical cases kidney biopsy is not necessary.

***Morphological examination*** should be considered if:

– progressive course with high proteinuria, hematuria, increscent azotemia (urea, creatinine) and oliguria is observed (differential diagnosis with crescentic GN);

– systemic disease is suspected (lupus erythematosus, hemorrhagic vasculitis);

– C3-hypocomplementemia persists over 2–3 months;

– lack of effect of prior treatment;

– disease progression; persistent hypertension, lack of response to hypotensive treatment.

***Treatment.*** General principles include bed regimen, diet and symptomatic therapy. Medications are prescribed according to severity and manifestation of disease, and its cause.

Patients should stay in bed while edematous. Children are gradually allowed to leave bed when feeling better and after arterial hypertension is being controlled. Diet should be low in salt and spices, low-caffeine. Fluid is given according to previous-day diuresis. Extrarenal fluid losses should be considered. Upon

normalization of blood pressure and resolving of edema salt intake can gradually be increased starting at 1g/day. Protein intake should be lowered until normalization of blood creatinine and urea levels, as well as glomerular filtration rate is achieved.

***Pharmacotherapy*:**

1. Antibiotics are used in case of streptococcal infection. Aminopenicillines, cephalosporins of 1st generation are generally used. Macrolides can be chosen in case of allergy to beta-lactam antibiotics.

2. Symptomatic treatment (table 1):

– hypotensive (calcium-channel blockers, β-blockers);

– diuretics;

– in case of signs of hypercoagulation — anti-platelets (dipyridamole, pentoxiphylline).

*Table 1*

**Pharmacotherapy of APGN**

| Groups | Drug | Dosage |
|---|---|---|
| Calcium-channel blockers | Amlodipine | 0.06–0.2 mg/kg/day |
| | Nifedipine | 0.25–0.5 mg/kg/day |
| β-blockers | Metoprolole | 1–2 mg/kg/day |
| Diuretics | Furosemide | 1–2 mg/kg qd or bid |
| Anti-platelets | Dipyridamole | 5–7 mg/kg/day |

Angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers are used with caution because of risk of hyperkalemia (high potassium blood level).

Prognosis for survival and recovery of kidney function is favorable.

## RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

**Rapidly progressive GN (RPGN, crescentic GN, extracapillary proliferative GN)** is a type of nephritic syndrome, which is accompanied by glomeruli crescent formation seen on a kidney biopsy (in over than 50 % of affected glomeruli) and characterized clinically by a rapid loss of renal function (decrease of glomerular filtration rate (GFR) of at least 50 % over a short period). This form of GN is relatively rear, especially in children. It is also called fulminant GN due to highly aggressive course comparing to APGN and rapid progression of renal function deterioration.

Several groups of RPGN are described according to pathogenesis:

– anti-GBM antibody disease (Goodpasture's syndrome, if lung and kidney involvement are present; anti-GBM disease if only kidneys are involved);

– immune complex disease (lupus nephritis, post infectious, systemic vasculitis, lupus et al.);

– pauci immune disease (Granulomatosis with polyangiitis (Wegener's granulomatosis), microscopic polyangiitis (MPA), renal-limited necrotizing

crescentic glomerulonephritis (NCGN), Churg-Strauss syndrome). This group is characterized by absence of glomerular immune deposits on immunofluorescence. The vast majority of patients have circulating antineutrophil cytoplasmic antibodies (ANCAs).

***Pathology.*** Crescents in over 50 % of glomeruli are seen on kidney biopsy (figure 5, 6).

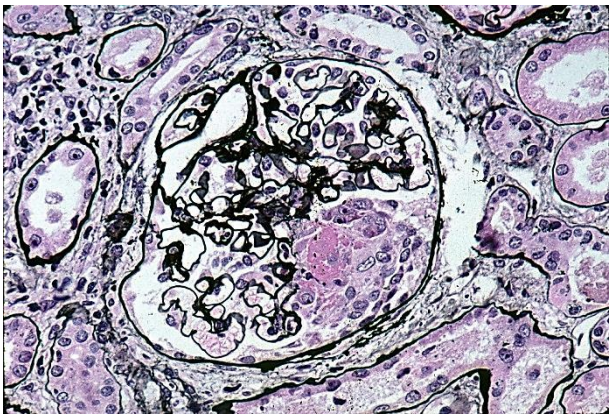


*Fig. 5*. Cellular crescent. H&E stain, ×400

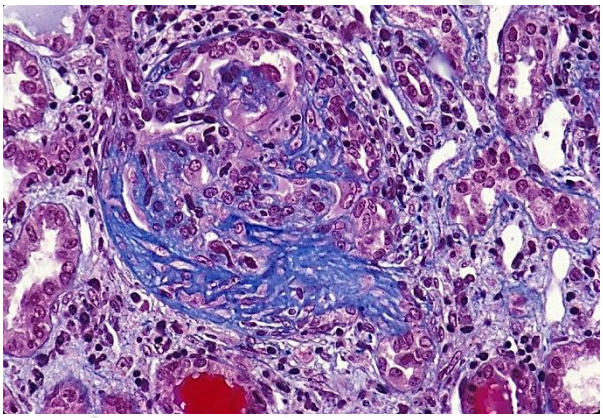


*Fig. 6*. Fibrous crescent. H&E stain, ×400

Presentation depends on type of RPGN, usually includes nephritic syndrome, or nephrotic syndrome with hematuria and hypertension. Patients are usually in severe condition. Symptoms include:

– severe paleness, severe arterial hypertension, edema, oliguria;

– proteinuria, macrohematuria, urine casts (hyaline, granular), hypostenuria;

– anemia;

– low serum protein;

– rapid decrease of glomerular filtration rate (more than 50 % over few days or weeks), accompanied by increase in serum creatinine and urea levels.

Diagnosis is made by results of morphological examination of kidney biopsy specimen, where over 50 % of glomeruli are found to be present with crescents.

***Treatment*:** aggressive immunosuppressive treatment is prescribed as soon as possible upon diagnosis is made.

***Pulse-therapy*:** methylprednisolone (30 mg/kg/day, max single dose 1000 mg) or cyclophosphamide (single dose of 500–750 mg/m$^2$) — 3 to 5 pulses synchronized with *plasmapheresis* (1 day — methylprednisolone «pulse», followed by plasmapheresis on the next day to remove pro inflammatory immune mediators, cytokines, antibodies).

Maintenance therapy includes *immunosuppressive therapy orally* (steroid 2 mg/kg/day + cytostatic agent) combined with anticoagulation therapy (heparin, low-molecular weight heparin, aspirin) and anti-platelets (dipyridamole, pentoxiphylline).

In most severe cases dialysis is needed (hemodialysis, hemodiafiltration et al).

Prognosis is poor for renal survival.

## CHRONIC GLOMERULONEPHRITIS

**Chronic GN** — heterogeneous group of chronic glomerulopathies, with predominant immune complex mechanism of glomerular lesion, different clinical and morphological presentation, course and outcome.

***Etiology*:** rarely develops as evolution of APGN. More common is a primary chronic course, i.e. without acute attack.

Four main groups of etiological factors are described:

– infections (bacterial, viral);

– mechanic and physical factors (traumas, cold weather, sun exposure);

– allergic toxins (food, chemical substances, drug abuse, medicines);

– vaccines.

***Morphological classification.***

*Not proliferative (non inflammatory)*:

– minimal changes nephropathy;

– membranous nephropathy;

– focal-segmental glomerulosclerosis.

*Proliferative (inflammatory)*:

– mesangial proliferative GN;

– mesangiocapillary GN;

– fibroplastic GN.

***Minimal changes nephropathy*** (lipoid nephrosis, small foot processes of podocytes disease, idiopathic nephrotic syndrome, minimal changes nephrotic syndrome) — the leading cause of nephrotic syndrome in childhood.

Boys : girls ratio 2 : 1.

Onset after upper respiratory tract infection, allergic reaction is common. Atopy can be predisposing factor. Nephrotic syndrome is usually steroid sensitive, arterial hypertension and hematuria are not characteristic for this condition. Although there can be relapses of nephrotic syndrome, kidney function however remains normal for a long time. In general, prognosis is favorable.

***Morphology.***

*Light microscopy*: glomeruli appear normal (figure 7).

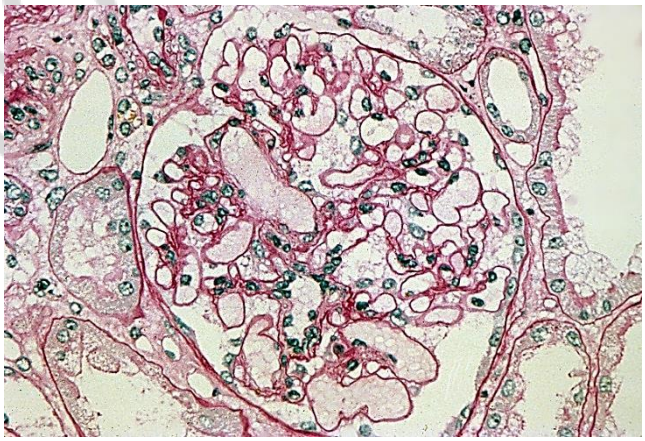
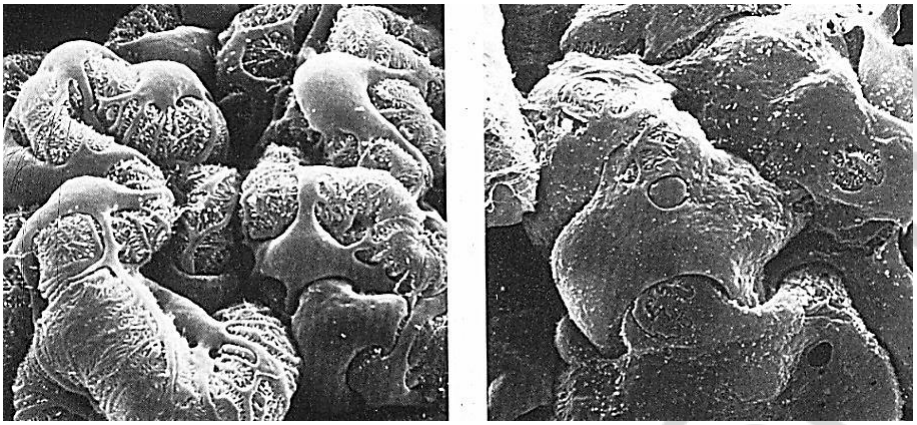


*Fig. 7.* Light microscopy — normal glomerulus. H&E stain, ×400

*Immunofluorescence*: absence of immune deposits.

*Electron microscopy*: normal podocytes (figure 8, *a*) and diffuse effacement of podocytes foot processes (figure 8, *b*).



***a*** ***b***

*Fig. 8.* Electron microscopy:
*a* — normal podocytes foot processes; *b* — diffuse effacement of podocytes foot processes

***Nephrotic syndrome*** includes 4 main criteria:

– massive proteinuria, mainly albuminuria (over 50 mg/kg/day);

– low serum protein level (low albumin, increased α2- and decreased γ-globulins);

– high blood cholesterol level (> 5,2 mmol/l);

– severe edema (the consequence of reduced oncotic pressure due to low serum protein).

*Pathology:*

– minimal changes nephrotic syndrome;

– focal-segmental glomerulosclerosis;

– membranous GN;

– mesangiocapillary GN.

*Treatment:*

1. *Standard protocol* — oral prednisolone 60 mg/m$^2$/24 h (2 mg/kg, max 80 mg per day), for 4 weeks (up to 6 weeks), than switch to alternate-day administration:

– 60 mg/m$^2$/48 h — 8 weeks;

– 45 mg/m$^2$/48 h — 2 weeks;

– 30 mg/m$^2$/48h — 2 weeks;

– 15 mg/m$^2$/48h — 2 weeks.

Treatment duration from 4 to 5 months.

2. Proton pump inhibitors — omeprazole 1 mg/kg/day for children older than 5 years, almagel, gefal — for younger children.

3. Calcium, vit. D (osteoporosis prophylaxis).

4. Albumin i.v. (if serum albumin level is lower 20 g/l and or ascites is present).

5. Heparin 100–200 IU/kg, aspirin for hypercoagulation correction.

6. Immunoglobulin i.v. in case of intercurrent infection.

Nephrotic syndrome can be divided into groups according to response to steroids:

1. *Steroid sensitive* — complete remission on standard regimen of prednisolone during 4 to 8 weeks.

*Steroid dependent* — relapse of nephrotic syndrome occurred at the time of steroid treatment (usually with low dose of prednisolone) or within 2 weeks of steroids have been stopped.

*Frequently relapsing* — 2 and more relapses within 6 months or 3 and more relapses within one year.

2. *Steroid resistant* — failure to achieve full clinical and laboratory remission when treated with prednisolone in standard regimen for 4 to 8 weeks (kidney biopsy should be considered), or after pulse-therapy with methylprednisolone (single dose 20–30 mg/kg) for 3 consecutive days.

*Frequently relapsing nephrotic syndrome*:

– chlorambucil (leukeran) — 0,2 mg/kg 8 to 12 weeks — almost is not using any longer;

– cyclophosphamide — 2 mg/kg/24 h for 8 weeks;

– cyclosporine A — 4–6 mg/kg/24h (under serum level control — target value 80–150 ng/ml) combined with alternate-day administration of oral prednisolone 1 mg/kg/48 h.

*Steroid dependent nephrotic syndrome*:

– cyclosporine A — 4–6 mg/kg/24 h (under serum level control — target value 80–150 ng/ml) combined with alternate-day administration of oral prednisolone 1 mg/kg/48 h, followed by mono therapy by cyclosporine up to 18–24 months;

– mycophenolate mofetil (MMP);

– tacrolimus;

– alkylating agents (chlorambucil, cyclophosphamide);

– MENDOZA protocol (table 2) is not used nowadays;

– ACE inhibitors (enalapril 0,05–0,5 mg/kg**)** or ACE receptors blockers (losartan 25–100 mg/day, irbersartan 75–150 mg/day).

*Table 2*

**MENDOZA protocol**

| **Duration, weeks** | **Metilprednisolone i.v.** | O**ral prednisolone** |
|---|---|---|
| 1–2 | 30 mg/kg/48 h | – |
| 3–10 | 30 mg/kg once a week | 2 mg/kg/48 h |
| 11–18 | 30 mg/kg twice per month | 2 mg/kg/48 h |
| 19–52 | 30 mg/kg once a month | 2 mg/kg/48 h |
| 53–78 | 30 mg/kg once per two months | 2 mg/kg/48 h |

*Kidney biopsy should be considered in case of:*

– steroid resistant nephrotic syndrome;

– steroid dependent and frequently relapsing nephrotic syndrome (3rd relapse);

– nephrotic syndrome with hematuria and hypertension.

– nephrotic syndrome in babies younger 1 year old (hereditary forms of nephrotic syndrome should be suspected — genetic testing) and in children older than 12 years old (renal disease secondary to systemic conditions, such as collagenoses or vasculitis, et al should be considered);

– treatment with cyclosporine A over 6 months — if serum creatinine level is increased, and urine gravity is decreased = cyclosporine nephrotoxicity should be considered).

***Nephrotic syndrome with hematuria and/or hypertension.*** Clinical manifestations are similar to ones in nephrotic syndrome, but:

– edema is less severe, but more persistent;

– high blood pressure;

– hematuria;

– anemia;

– increased serum γ-globulins.

Treatment includes steroids and cytotoxic agents.

***Focal-segmental glomerulosclerosis*** frequently (in over 80 % of patients) manifests as steroid resistant nephrotic syndrome. In less than one third of patients clinical symptoms include microhematuria and arterial hypertension.

*Light microscopy*: focal (in some of glomeruli) and segmental (in some of glomerular capillary loops) glomerulosclerosis and/or hyalinosis (figure 9).

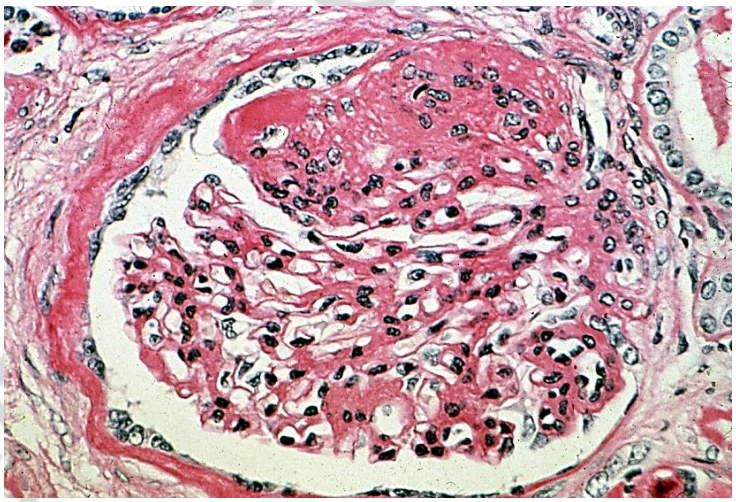


*Fig. 9.* Focal and segmental glomerulosclerosis. H&E stain, ×400

*Electron microscopy*: collapsed capillary loops in sclerosed segments, effacement of podocytes small foots in the rest of glomeruli.

*Immunofluorescence*: IgM, C3 deposits in sclerosed segments; negative in glomeruli, which appear normal on light microscopy (figure 10).

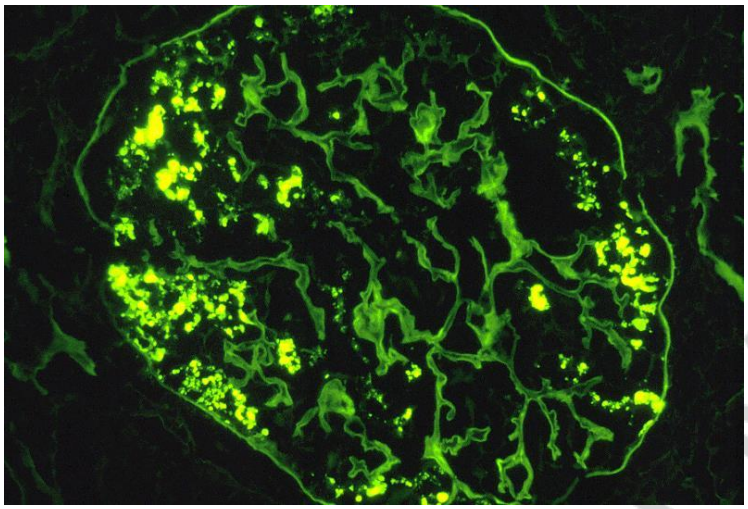


*Fig. 10*. IgM deposits in scleroses segments

*Treatment*:

1) cyclosporine A — 4–6 mg/kg/24 h (under serum level control — target value 80–150 ng/ml) combined with alternate-day prescribtion of oral prednisolone 1 mg/kg/48 h, treatment duration should not be less than 18 months (remission is achieved in 25–40 % of patients, however soon after the end of the treatment relapse often occurs);

2) cyclophosphamide;

3) tacrolimus;

4) mofetil mycophenolate.

***Membranous nephropathy*** manifests as nephrotic syndrome, or (less frequently) presents with persistent proteinuria, microhematuria and hypertension.

*Light microscopy*: diffuse thickening of glomerular basement membrane. Glomerular basement membrane has a lot of spikes on John's stain of kidney biopsy specimen-diagnostic feature (figure 11).

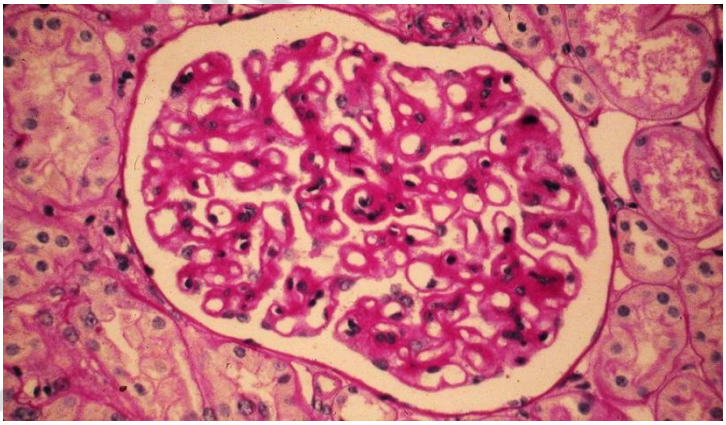


*Fig. 11*. Diffuse thickening of glomerular basement membrane. H&E stain, x400

*Electron microscopy*: subepithelial deposits, which are surrounded by electron-densitive substance, produced by podocytes — «membranous transformation» (figure 12).

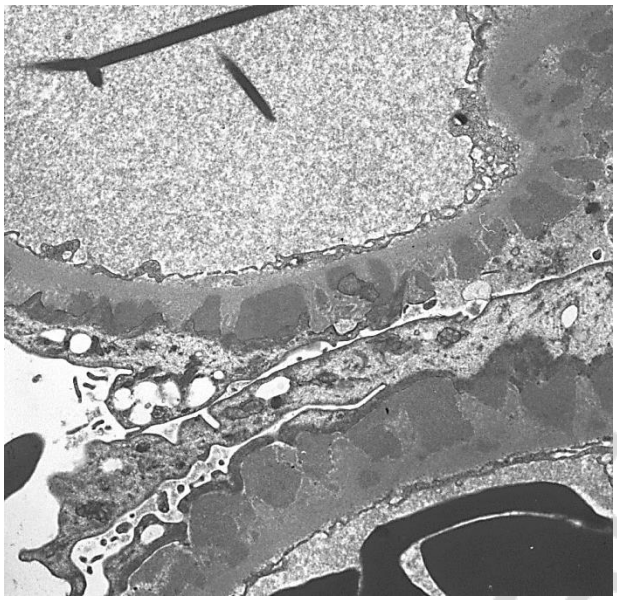


*Fig. 12*. Subepithelial deposits on electron microscopy

*Immunofluorescence*: granular IgG, C3 deposits, less frequently IgM or IgA (figure 13).

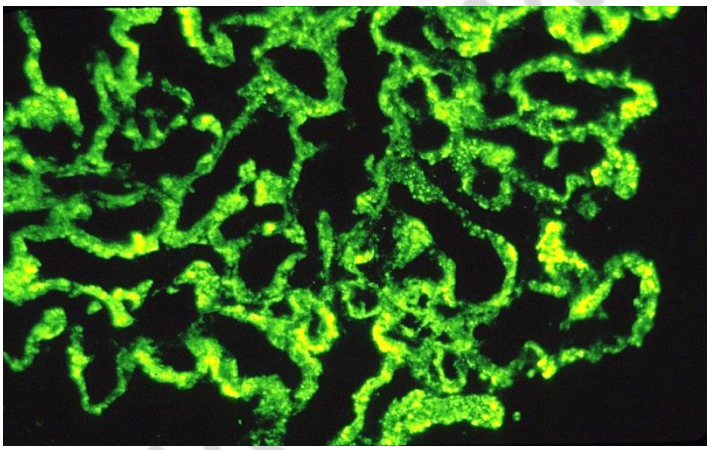


*Fig. 13*. Granular IgG deposits on immunofluorescence

There are no controlled studies on treatment of membranous nephropathy in children. According to symptoms can be used:

– ACE inhibitors in proteinuric patients;

– steroids for years long in nephrotic patients: oral prednisolone 2 mg/kg, max 60 mg per day for 4 to 8 week, than switch to alternate-day administration 2 mg/kg/48 h with gradual reduce to 10–30 mg/48 h for at least 6 months, up to 5 years;

– cyclophosphamide, cyclosporine A, monoclonal antibodies (rituximab);

– treatment of underlying condition (hepatitis B et al.).

***Mesangial proliferative GN*** in children is often appears to be primary. Can present as nephritic syndrome at onset with consequent development of nephrotic syndrome with hematuria and arterial hypertension. Low serum levels of C3 and C4 complement can be persistent.

*Light microscopy*: diffuse mesangial expansion due to mesangial proliferation and mesangial matrix overproduction (figure 14).

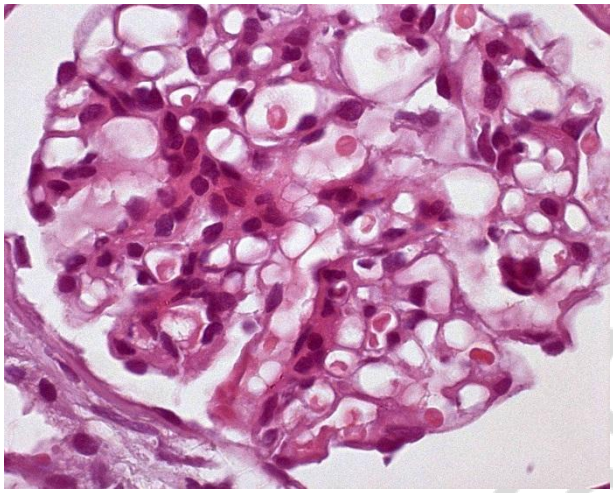


*Fig. 14*. Diffuse mesangial expansion due to mesangial proliferation and mesangial matrix overproduction. H&E stain, x400

*Electron microscopy*: mesangial matrix enlargement, mesangial deposits.

*Immunofluorescence*: granular diffuse mesangial IgG, IgM, IgA, C3 complement deposits (figure 15).

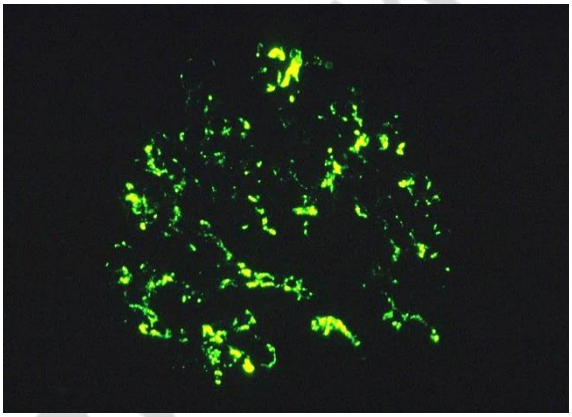


*Fig. 15*. Granular diffuse mesangial IgA deposits

***Berger's nephropathy*** is a mesangial proliferative GN with predominant IgA deposition in mesangium (IgA nephropathy) (figure 16). In children an idiopathic IgA nephropathy is more common, secondary disease is less frequent (hemorrhagic vasculitis, systemic lupus erythematosus, intestinal diseases etc.).

Berger disease is highly variable, both clinically and pathologically. Clinical features range from asymptomatic hematuria to RPGN. Recurrent macrohematuria is considered to be most characteristic for IgA nephropathy. These episodes are often associated with upper respiratory tract infections (mainly tonsillitis or pharyngitis), and develop simultaneously or within a couple of days after the infection begins. Gross hematuria persists several days and can be accompanied by loin pain in a third to half of patients. Urine becomes brown or coca-cola like, sometimes fever and dysuria can be present.

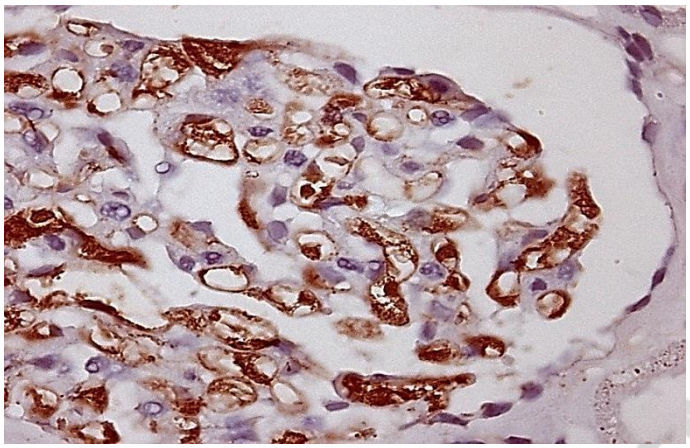


*Fig. 16*. Brown colored mesangial IgA deposits

*Treatment:*

– no special treatment is necessary in hematuric patients without or accompanied with mild proteinuria;

– in nephrotic patients steroids (60–30–15 mg/m$^2$ for 3 to 5 years);

– in proteinic patients omega-3 fatty acids (fish oil 4 g daily for 2 years), ACE inhibitors for a long time.

*Prognosis*: IgA nephropathy is used to be considered a disease with favorable prognosis. However recent data from adult nephrologists show that 30–35 % of patients develop end stage renal disease by third or fourth decade of life.

***Mesangial capillary GN*** can be variable in clinical manifestations and pathological changes.

*Light microscopy*: diffuse thickening and splitting of glomerular basement membrane (tram tracking), severe mesangial proliferation (figure 17).

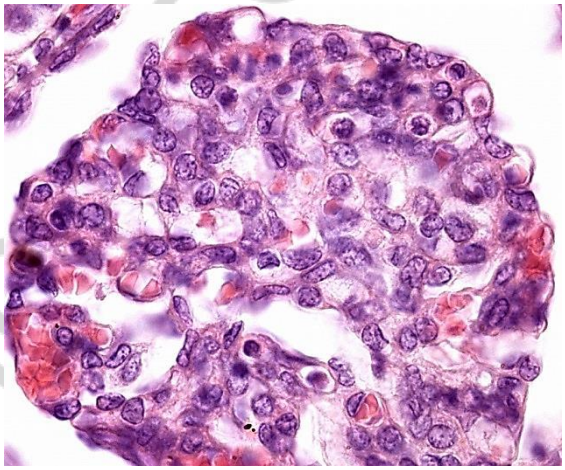


*Fig. 17*. Diffuse thickening and splitting of glomerular basement membrane, severe mesangial proliferation. H&E stain, ×400

*Electron microscopy*: splitting of glomerular basement membrane, mesangial expansion and hypercellularity.

*Immunofluorescence*: periferal, large deposits of C3 complement, rarely deposits of IgG, IgA, C4, fibrin (figure 18).

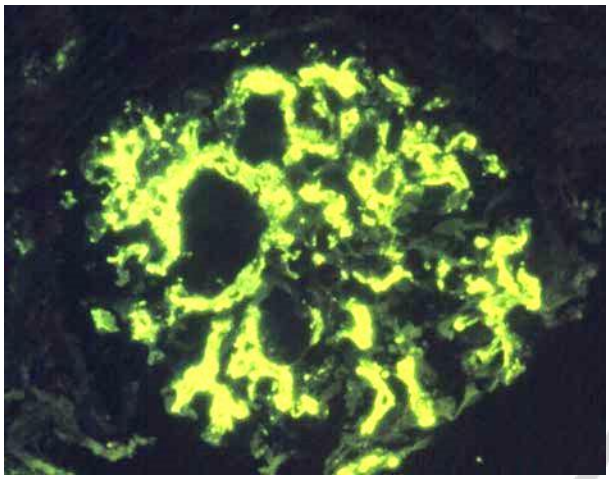


*Fig. 18.* Peripheral, large deposits of C3 complement

***Pathology.*** 3 types are described:

– I type — with subendothelial deposits;

– II type — dense deposits disease (this type is considered to be a distinct disease);

– III type — transmembrane deposits.

There are no clinical differences between these types: different clinical manifestations such as proteinuria (from mild to nephrotic range), edema, nephrotic syndrome with hematuria and/or hypertension, asymptomatic changes in urinalyses (hematuria, proteinuria) can be seen in all types.

*Etiology*: the disease is idiopathic in majority of cases.

Children 7–10 years of age and older are mostly affected.

Males : females ratio 1 : 1.

There are different approaches to treatment of mesangial capillary GN.

– no special treatment is necessary in hematuric patients without or accompanied with mild proteinuria;

– in nephrotic patients steroidsfor1 to 5 years, sometimes after pulse-therapy with steroids;

– cyclosporine A;

– ACE inhibitors for a long time.

Prognosis: the disease has a progressive course with loss of renal function and progression to end-stage renal disease (10 year survival is 32 %).

**LITERATURE**

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**CONTENTS**

Abbreviations ..... 3
Definition ..... 3
Classification of glomerulonephritis ..... 3
Acute glomerulonephritis ..... 5
Rapidly progressive glomerulonephritis ..... 8
Chronic glomerulonephritis ..... 10
Literature ..... 18

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# ГЛОМЕРУЛОНЕФРИТЫ У ДЕТЕЙ

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Учебно-методическое пособие

На английском языке

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