GLOMERULONEPHRITIS

Methodic materials for international students (IV-VI year)

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Definition: Glomerulonephritis is an inflammatory process primarily involving the glomerulus, though at times the renal vasculature, interstitium, and tubular epithelium may also be affected, that leads to progression of the disease and, finally, to chronic renal failure.

Epidemiology:

Glomerulonephritis occupies the 3rd place among all renal diseases. Its prevalence is 10-15 per 10 000 of adults. Last decades, the increase of glomerulonephrtis prevalence is observed, which is due to the ecological situation and immune system changes.

Most often young people are affected, with 2-3 fold males dominating.

Aethiology:

- depends on the form of glomerulonephritis
- in all cases the defect of the youngest T-lymphocytes subpopulation may be present (TdT-lymphocytes, containing terminal desoxynucleotidiltrans-ferase); with trophic and regenerating properties. These cells participate in regeneration of the affected tissue in any organ or system. In kidneys, if defect of this subpopulation is present, immune complexes may form as a result the impaired regeneration.

Morphology:

Glomerular inflammation can result in damage to any of the three major components of the glomerulus:

- basement membrane
- mesangium
- capillary endothelium.

Identification of the specific histopathologic pattern of glomerular injury by renal biopsy is often the most helpful technique available for defining the cause of glomerulonephritis.

Mophological peculiarities of the glomerulus inflammation are the base of the morphological classification of glomerulonephritis.

Classification (also see at the end)

1. Some authors classify glomerular diseases according to whether they present as either a **nephritic or a nephrotic syndrome:**

A Glomerular diseases presenting as **nephritic syndromes** are associated with:

- a clinical presentation of hypertension
- edema
- urine sample showing red blood cells, red blood cell casts, and a moderate degree of proteinuria.

B. Glomerular diseases presenting as **nephrotic syndromes** are characterized by:

- heavy proteinuria (> 3.5 g/24 h)
- hypoalbuminemia
- hyperlipidemia
- edema.

However, most of glomerular diseases can present with components of both.

2. Diseases causing glomerulonephritis can also be classified according to whether they cause only renal abnormalities **(primary renal diseases)** or whether the renal abnormalities result from a systemic disease **(secondary renal diseases).**

3. **The recent classification includes following principles:**

Morphological changes	Clinical manifestations	Types of course	Functional state of kidneys
I. Proliferative -focal or diffuse	- isolated changes in urine	**I type** – rare exacerbations	**Chronic renal failure**: stage.
1. Extracapillary	(haematuria,	(more rare	In case of

<table>
<tr><td>2. Membranous-proliferative
a. with subendothelial deposits
b. with dense deposits
c. mixed
3. Mesangioproloferative
- immune negative
- immune positive
a. with IgG deposits
b. with Ig M deposits
c. with mixed deposits</td><td>proteinuria)</td><td rowspan="8">than every 10 years)</td><td rowspan="8">normal results special tests should be performed</td></tr>
<tr><td>4. IgA-nephropathy (Berger’s)</td><td rowspan="7">- nephrotic syndrome and arterial hypertension</td></tr>
<tr><td>5. Focal-segmental glomerulosclerosis</td></tr>
<tr><td>II. Non-proliferative</td></tr>
<tr><td>1. Minimal</td></tr>
<tr><td>2. Membranous (I,II,III,IV stage)</td></tr>
<tr><td>III. Sclerotic (fibroplastic)</td></tr>
<tr><td colspan="4">Primary (idiopathic), secondary or innate origin of glomerulonephritis also should be mentioned in diagnosis.</td></tr>
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4. Acute and chronic glomerulonephritis:

Acute disease onset doesn’t mean that acute glomerulonephritis is present; it may be acute manifestation of chronic, slowly (before the acute exacerbation) progressing disease. So, the diagnosis of acute glomerulonephritis should be confirmed morphologically. **It should be mentioned, that morphological diagnosis doesn’t change with time; only sclerotic changes may increase.**

Acute endocapillary diffuse proliferative glomerulonephritis (sometimes called postinfectious or poststreptococcal glomerulonephritis)

Definition: Acute endocapillary diffuse proliferative glomerulonephritis is the disease, which is a result of infection, leading to immune-inflammatory glomeruli affection with proliferative and exccudative changes.

In some definitions the role of nephritogenic strain of group A (β-hemolytic) streptococci, especially type 12 is underlined. However, nowadays other types of bacterial and viral infections were found to cause the same disease.

Epidemiology:

Rate in adults: 3-5% of all cases of glomeruli affection with increase of revealed cases number in last years.

Age: ¾ of cases - 5-20 years old

Gender: males: females ratio is 2:1

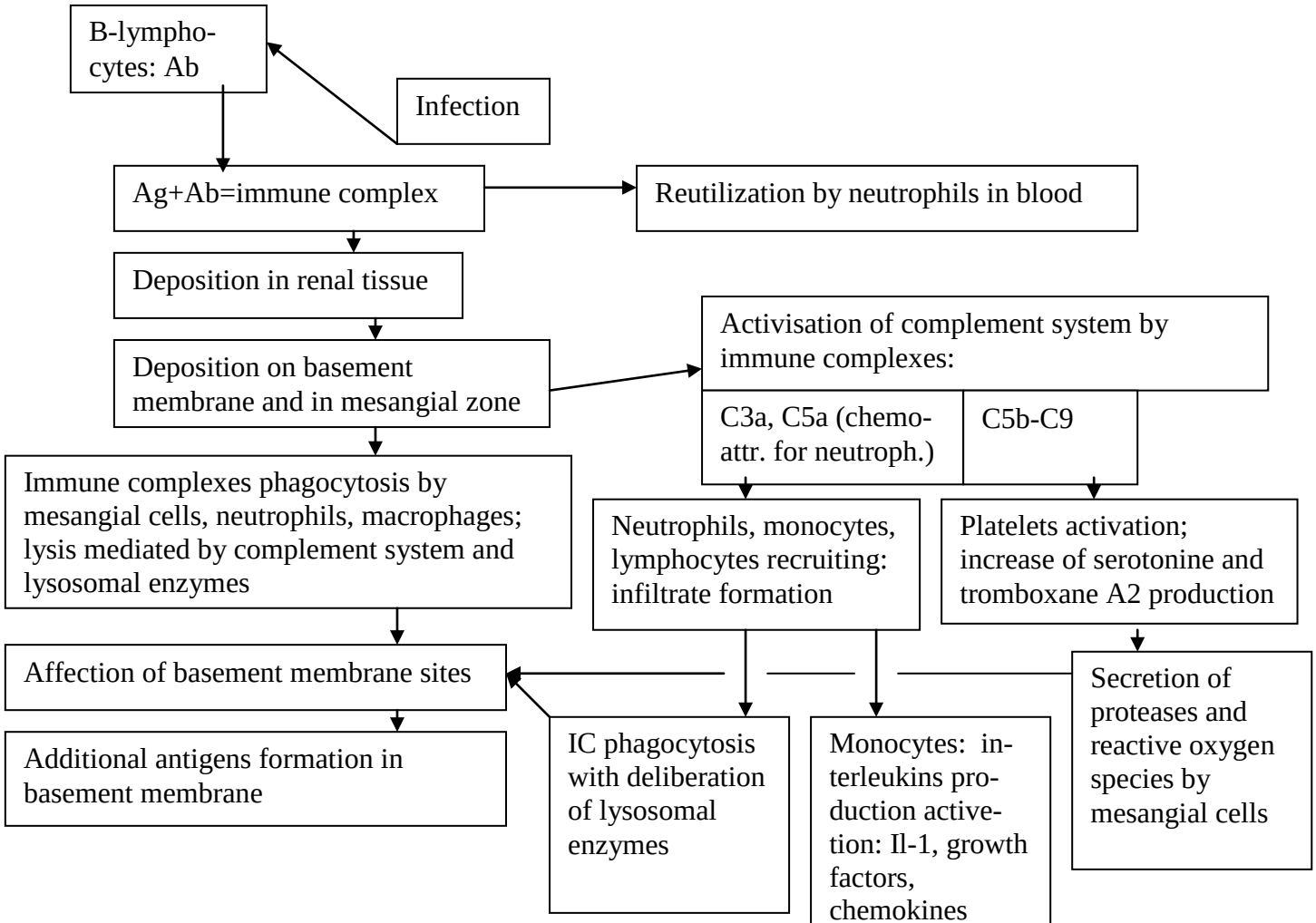
Areas: in cold and damp climate the prevalence is usually higher.

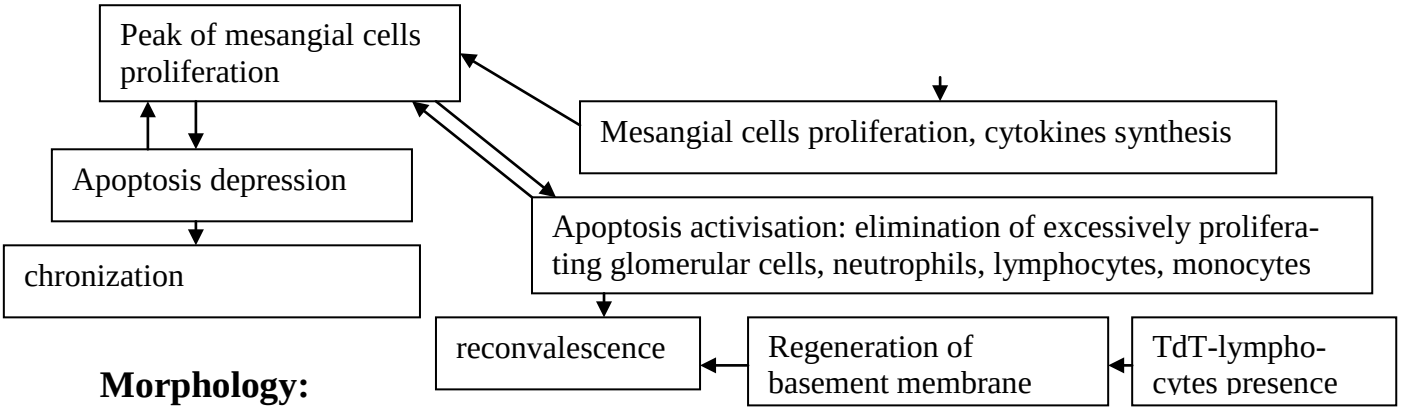
Aethiology:

1. Infection precedes the disease with the latent period 3-4 weeks.
2. Aethiological factors:

- Streptococci: group A (β-hemolytic); types 1, 3, 4, 12, 49 (more often 12) are the cause of glomerulonephritis in 15-20% of cases; most commonly presents following infections of the throat (pharyngitis) or skin (impetigo)
- other bacterial and viral agents
- vaccination

Pathogenesis:





Morphology:

Light microscopy: diffuse proliferative glomerulonephritis.

1. affection of almost all glomeruli
2. 3 phases:

- exccudative: haemorrhagic exccudate in glomeruli
- exccudative-proliferative:
- proliferative

3. The glomeruli are increased in size, increase of total cells count, increase of endothelial cells of capillars and mesangial cells proliferation; mesangium infiltration by neutrophils and monocytes.
4. The changes are revealed during several months, rarely – more than 1 year

Immunofluorescence:

shows IgG and C3 in a granular pattern along the capillary basement membrane and in mesangial regions or large, dense subepithelial deposits or "humps".

Types of Ig deposition:

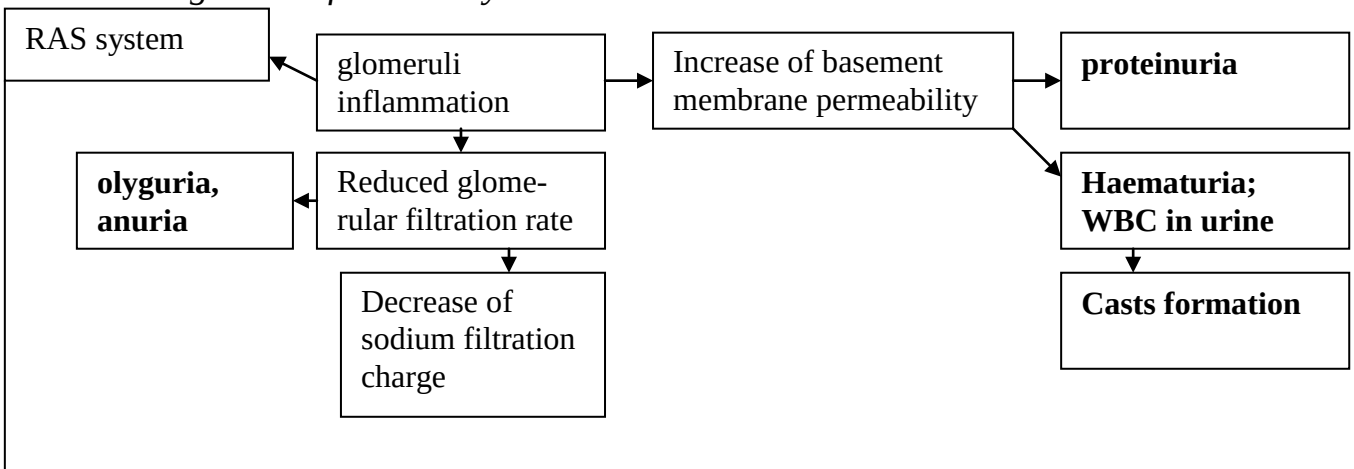
I. "Stars in the sky" – granular small deposits along the capillary walls of glomerulus
II. Mesangial type – IgG and C3 in mesangial area
III. Large dense deposits ("humps") in capillary walls.
IV. Immune-negative type – neither Ig nor complement deposits are revealed

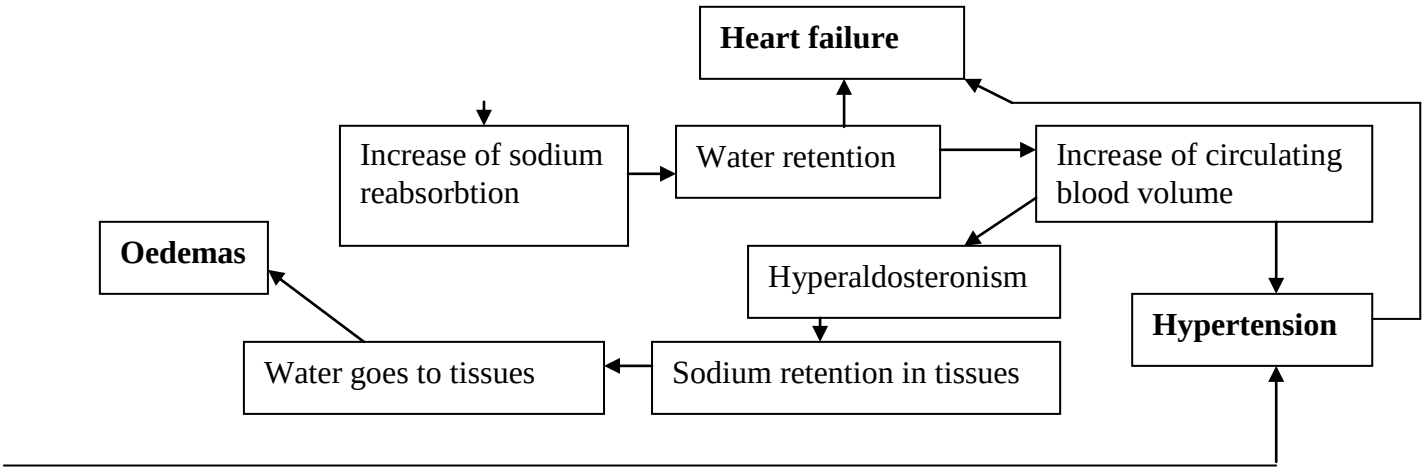
Clinical manifestations (4 main syndromes are marked):

Symptom/ syndrome	**Characteristics, causes**	**Prevalence, duration**
Cardiovascular system		
1. Hypertensive syndrome	Usually moderate, 150/180/90-100 mm Hg; due to renin-angiotensin-aldosteron and water retention mechanisms	1st days – 100% of cases; later in most of patients – normal BP (normalization in 1-2 weeks)
2. Heart failure	Due to water retention, hypertension	very rare (3%)

	and heart muscle dystrophy	
3. Bradycardia	due to increase of vagus tone	33-50% of cases
Water retention		
- Diuresis reducing (olyguria, anuria)	May be up to 700-500 ml; its duration has a prognostical value	The earliest sign; in case if lasts more than 1 week – prolonged course of the disease
4. Thirst	May be present	¼ of cases
5. Oedemas	In most cases not severe, localized on face	early sign, the first to disappear after treatment
6. Nephrotic syndrome	- Oedemas – may be severe, including hydrothorax, hydropericardium, ascitis - hypoproteinemia; hypoalbuminemia - severe proteinuria - hypercholesterolemia	may be present (not common)
7. Pain in back area	Due to renal parenchyma oedema; symmetric aching pain in both sides	early sign
8. Headache	Due to intracranial pressure rise	early sign
9. Eclampsia	Cramps attacks; the same cause	very rare – 8% (children)
Other symptoms		
10. General symptoms	Decrease of working abilities, weakness;	early sign
11. Dyspnea	Heart failure; nephrogenous pulmonary oedema	rare
Changes in urine		
12. Urinary syndrome:	In general: tea-colored urine Moderate: - proteinuria - haematuria - cylindruria; - in nephrotic syndrome – leucocyturia Renal tubular cells, leukocytes, and hyaline and granular casts may occur	1 months – 1 year

Pathogenesis of clinical syndromes:





Clinical course types:

- **monosymptomous** (only changes in urine, mild/moderate hypertension in first days of the disease is not diagnosed)
- **full complex of symptoms:** oedemas, hypertension, changes in urine
- **nephrotic** – nephrotic syndrome and hypertension

Prevalence: In 60-80 the monosymptomous type dominated; nowadays – nephrotic or full complex of symptoms.

Course:

Cyclic: at first – acute appearance of all symptoms; then – their gradual disappearance.

1st period – all above mentioned symptoms; with the beginning of treatment oedemas disappear first of all, then (in 1-2 weeks) – BP normalizes; changes in urine persist for 1-12 months; if longer – that is the sign of chronization.

Complications: rare

1. **Heart failure,** more often accompanied by rare pulse
2. **Encephalopathy (eclampsia)** – cramps attacks; usually in children (8%), develops during oedemas increase and in high BP; due to increase of intracranial pressure. Duration of each attack is several seconds/1-10 min with following sleepiness. Positive Babinsky symptom may be revealed during the attack. Attacks may be frequent (10-100 times a day). Spinal punction stops the attack.

3. **Renal failure – 1%:** acute; characterized by anuria. Emergency dialysis is necessary in this case.

Laboratory and instrumental investigations

1. Dipstick and microscopic evaluation will reveal evidence for:

A. proteinuria:

- monosymptomous type – 1-3 g/l (<1 g daily)
- nephrotic and full complex of symptoms: 3-6 g/l (1-10 and mire g daily)

Proteinuria lasts for 1 month with gradual decrease up to 2nd month; trace amounts - from the end of 2nd month.

B. Urine sediment: RBC, casts, in nephrotic type - WBC

2. **Reberg test (or more detailed complex functional examination of kidneys, including level of creatinine, urea and ions = sodium, potassium, calcium, magnesium, chlorine, phosphates levels; clearance of serum creatinine, daily proteinuria, reabsorbed fraction):**

Method of assessement:

8.00 in the morning – urination to toilet

Since 8.00 – urine is collected into a bottle; last urination into a bottle – 8.00 next day. At the same time with last urination venous blood is taken. Levels of creatinine and other substances are evaluated both in blood and urine.

Clearance, fractional excretion and other indices are calculated.

- increase of daily proteinuria (see above)
- serum creatinine clearance may be changed (decrease of glomerular filtration rate)
- low urinary sodium, fractional excretion often less than 0.5%

3. Biochemical blood analysis:

- nephrotic syndrome signs: hypoproteinemia (total plasma protein less than 60 g/l); hypoalbuminemia (plasma albumin less than 30 g/l); hypercholesterolemia (plasma cholesterol more then 7 mmol/l).

4. **X-ray investigation:** to exclude urological diseases

5. **Ultrasonic investigation:** excludes stone disease; in nephrotic syndrome – oedema of pyramides is revealed
6. **Radiological investigation:** exclude other kidneys diseases
7. **Renal biopsy: obligatory** for confirmation of the diagnosis, differential diagnosis between acute and chronic glomerulonephritis and definition of morphological variant of the disease.
8. **Immunological studies**: Antistreptolysin O (ASO), antistreptokinase, and antihyaluronidase titers may rise, but this rise may be blunted by previous treatment with antibiotics. There is usually a decrease in serum complement levels, both total hemolytic complement (CH50) and the level of C3

Diagnosis:

May be considered as confirmed in cases of renal biopsy results were investigated by light and immunofluorescence microscopic investigation.

Prognosis:

Prognosis is usually determined by the morphological type (worse if "hump"-like deposits are revealed); depends on age (worse in middle-aged and aged) and in time hospitalization (early hospitalizations are associated with more favorable prognosis).

Outcomes:

- **Reconvalescence;** self-limiting disease course (80%, in children – 90%); no extrarenal symptoms are revealed (disappearance in 1-2 month), minimal changes in urine may be revealed up to 6 or 12 month.
- **Reconvalescence with defect** – clinical reconvalescence with moderate urine change persistence. **Nowadays considered as chronization.**
- **Chronization** – 5% (more often – in aged and middle-aged). As a marker of chronization anuria persistence for 7 and more days at the beginning of the disease may be considered. Heart failure, renal failure, eclampsia also are the factors, worsening prognosis.
- **Death** – very rare, due to the complications

Treatment

1. **Hospitalization: absolutely indicated (even in case of suspected diagnosis)**
2. **Strict regimen: lying in bed only for 1-2 weeks** (not walking); lying improves intrarenal haemodynamic (position leads to increase of renal blood flow; remaining in bed leads to constant warming of the back region). Such regimen must be kept up to 1-2 weeks or up to the period of BP normalization, disappearance of oedemas and 10-times reduction of proteinuria and erythrocyturia.
3. **Diet**

A. Full complex of symptoms or nephrotic syndrome:

- 1-2 days of strict fasting: nothing should be eaten; volume of consumed water shouldn't be more than daily diuresis.
- 2-3 days: rise and potatoes (rich by potassium): eating 4-5 times a day; each time 200 g of milk rise porridge or 200 g of potatoes. Severe restriction of salt. Volume of fluids don't exceed daily diuresis +500 ml
- One apple day may be administered if that diet is not tolerated: 1.5 kg of apples with reduction of water volume.
- Since 4-6 days: Protein: 40 g/24; Carbohydrates: 280-320 g; fats – 80-120 g; Potassium – 50-60 mmol/l, Calcium 400 mg daily, Sodium 30-40 mmol/l. Total calorage – 2500-3000 kkal; total salt – 4-5 g daily.
- This diet (severe protein and salt restriction) should be kept no less than 6 month. Milk and milk products also should be restricted due to high phosphate and proteins' amount.

B. **Isolated urinary syndrome** – without fasting; from the 1st days – restriction of proteins and salt.

4. **Drugs:**

A. symptomatic:

- oedemas: diuretics – Furosemid 40-80 mg daily or once 2 days per os up to oedemas disappearance. In case of severe oedemas – intravenous Lasix 80-300 mg/day once 2 days.

- Hypertension: ACE inhibitors

B. Antiinflammatory:

Indicated: if symptoms persist for 2 days from the beginning of treatment

Prednizolone:

- 200-300 mg daily (i.v.) – first 3 days,
- then 60-80 mg daily per os – 1-2 weeks
- reducing the dose – 0.5 tab every 3 days up to 40 mg
- 40 mg daily – 1 month (if symptoms persist)
- gradual dose lowering up to 20 mg daily and treatment with this dose up to 6 months
- if urinary and extrarenal symptoms persist – up to 1 year.
- If only urinary changes remain – Prednizolone treatment should be stopped. The chronization of the disease should be excluded.

Chronic glomerulonephritis.

Definition: Chronic glomerulonephritis – is a group of the diseases with different origin and morphological signs which are characterized by glomerular apparatus, canals and interstitium affection. In case of frequent exacerbations glomerular sclerosis and canals (dystrophy, atrophy) and interstitium (sclerosis) affection develops.

Chronic glomerulonephritis is not the outcome of an acute one, it develops as a primary chronic disease.

Epidemiology

Prevalence: 15-20 cases/10 000 of population with the increase of the cases number last years. Young and middle-aged patients dominate (40% of cases – under 30 years old). Men: women ratio is 2:1.

In Russia chronic glomerulonephritis is the main cause of chronic renal failure and thus the main cause of death among the renal diseases.

Aethiology:

- infection
- “cold” situations (working in cold places, walking in cold weather etc)
- vaccination (in children more often)

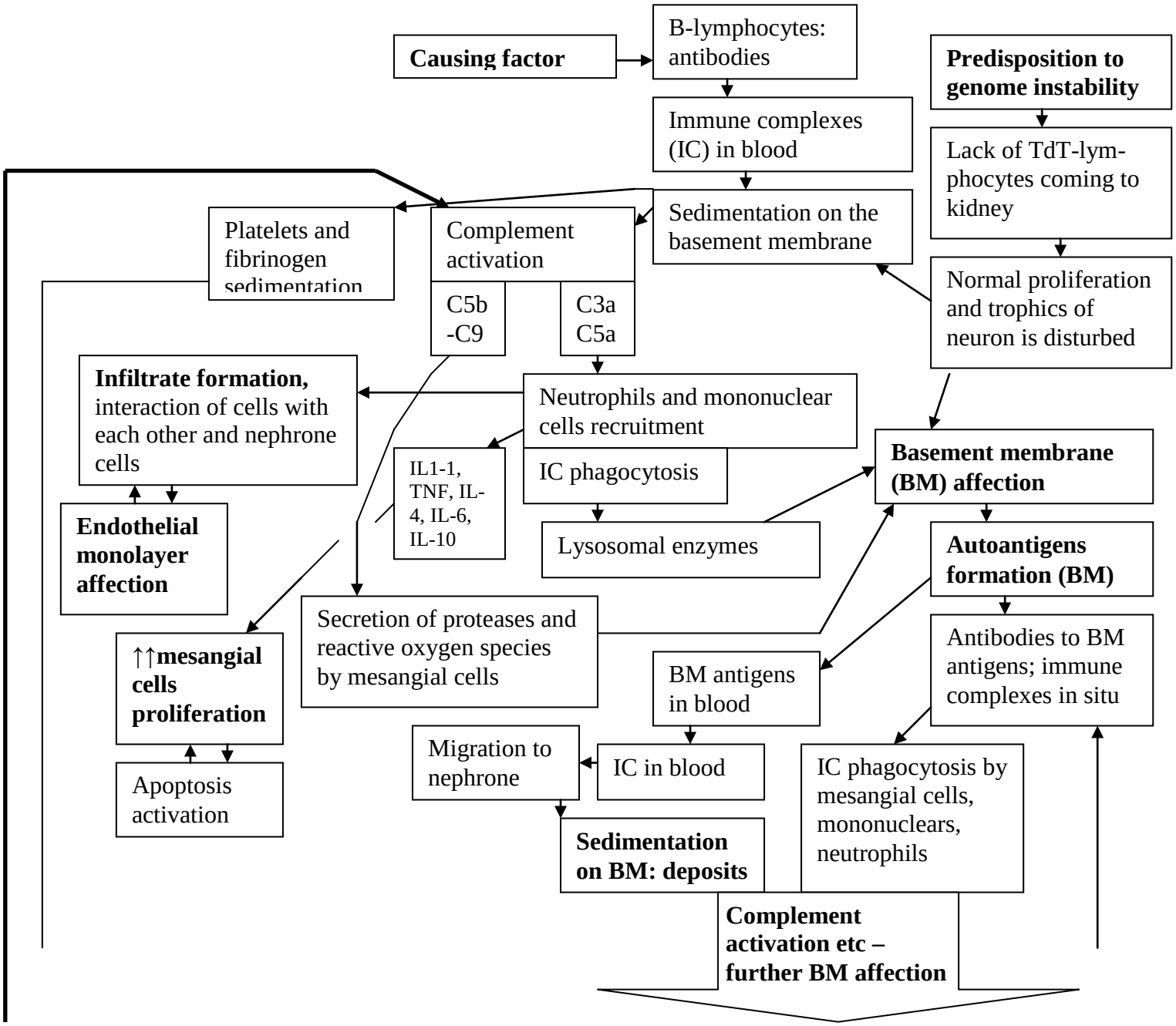
In 50% of cases aethiological factor remains unknown

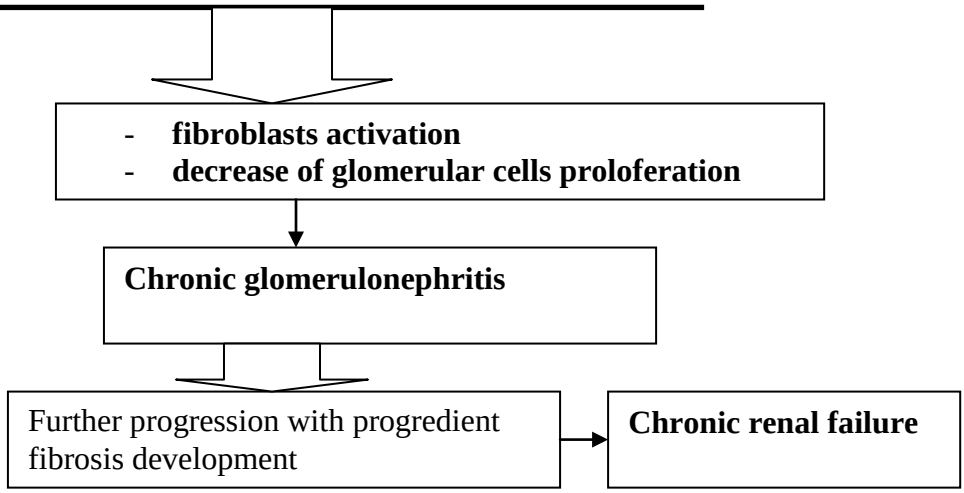
Pathogenesis

At the first stage, pathogenetic mechanisms are the same than these in acute glomerulonephritis.

The differences are:

- defect of young trophic and regeneratory subpopulation of T-lymphocytes: TdT-lymphocytes.
- thus, defect of basement membrane trophics and regeneration is present, so immune complexes sedimentation takes place on the affected part of the membrane; further regeneration (after affection by lysosomal enzymes) is also disturbed
- that leads to further progression of the inflammation, development of irreversible changes of basement membrane, formation of autoantibodies (to the affected zones of the basement membrane) and deposition of immune complexes.





Clinical manifestations

I. Main syndromes:

1. Oedemas
2. Arterial hypertension
3. Urinary syndrome
4. Nephrotic syndrome may be present

Pathogenesis of the syndromes is the same than that in acute glomerulonephritis.

II. Exacerbation and remission criteria:

Exacerbation	**Incomplete remission**	**Complete remission**
Sudden development of **nephrotic syndrome** (persisting is not taken into attention)	Disappearing of nephrotic syndrome	-
Appearance of uncontrolled (uncorrectable)**hypertension**	Controlled hypertension	Normalizing of BP (with normalizing of urine syndrome)
Increase of **proteinuria** from the initially stable level: 10-fold in urine dipsticks	Proteinuria in dipsticks reduces to 0.033 g/l	Trace proteinuria
Erythrocyturia: more than 10-fold increase in urine dipsticks		Normal values of RBC in urine
Increase of urine level of Lactatdehydrogenase and alkaline phosphataze		

Disproteinemia: increase of β- and γ- globulins blood levels		
Rapid changes of immunological data		

Morphological forms of chronic glomerulonephritis:

I. Mesangioproliferative glomerulonephritis

Prevalence: The most common variant of the disease (70% of all cases of glomerulonephritis)

Classification:

Renal biopsy immunofluorescence investigation		
Immune positive (Ig deposits in glomeruli and interstitium)		Immune negative (no deposits are revealed)
Ig A deposition – Ig A nephropathia	Ig M deposition – Ig M nephropathia	
Aethiology		
Idiopathic	Secondary: systemic lupus erythematosus, Shonlein-Henoch sdisease, Alport syndrome	

1. Idiopathic mesangioproliferative glomerulonephritis

Prevalence: more often in young males

Aethiology: more often unknown (revealed during preventional medical examinations, when occasionally urine changes are found); in women may manifest as nephropathia of pregnant.

Morphology:

1. Light microscopy

Focal variant	Diffuse variant

- only some glomeruli involved - segmental (some of the glomerular loops) mesangial cells proliferation - dystrophy and atrophy of some canals	- diffuse proliferation of mesangial cells; increased mesangial matrix - thinned basement membrane - sclerosis (globular or segmental) - inosculations between glomerular loops and capsule

2. Immunofluorescent investigation:

In immunopositive forms – focal or linear Ig deposits

3. Electron microscopy:

Increase of number and size of mesangial cells, thinnering of basement membrane; electron-dense deposits of immune complexes.

Clinical manifestations:

Urinary syndrome: for the long time – the only syndrome of the diseases

Oedemas and hypertension: appear when the sclerotic changes in glomeruli develop; oedemas are usually mild and located in suborbital regions.

Laboratory and instrumental investigations:

Proteinuria: 0.03-1.0 g/l in dipsticks; in daily urine – 0.5-1 g/24 h; proteinuria increases in exacerbations

Sediment: RBC - up to 10 one in field (dipsitck)

X-ray and ultrasonic: no changes; in advanced sclerotic changes ultrasonic investigation reveals increase of renal parenchyma density

Course: I type: years of asymptomatic course; rare exacerbations. Gradual increase of glomerular sclerosis, however, leads to chronic renal failure development.

Prognosis: chronic renal failure - 15-20 years after the onset of the disease.

Treatment:

1. Regimen: to avoid cold
2. Antiinflammatory: only in exacerbations

Prednisolone

- 1 month - 60 mg daily with subsequent gradual reducing of dose up to 20 mg daily

- up to 1 year – 20 mg subsequent intake

3. Antyhypertensive: ACE inhibitors when hypertension develops.

3 morphological subtypes of mesangioproliferative glomerulonephritis, having clinical course peculiarities, are divided in special subgroups and discussed separately.

1. Focal mesangioproliferative glomerulonephritis

Due to focal affection – minimal clinical manifestations.

Oedemas – absent

BP – normal

Urinary syndrome: moderate proteinuria up to 1 g daily

Course: very slow progression.

Treatment: only regimen (avoid cold) and diet (moderate restriction of salt and proteins)

2. Mesangioproliferative glomerulonephritis, immunopositive with IgM deposits (IgM-nephropathy)

Prevalence: very rare, 1% of all glomerulonephritis cases. Males under 40 dominate.

Aethiology: unknown

Morphology: typical picture of mesangioproliferative glomerulonephritis with IgM deposits.

Clinical manifestations:

1. Active onset and course of the disease
2. **Oedemas** – from the first day of the disease, marked; with subsequent
3. **Nephrotic syndrome** development
4. **Arterial hypertension:** present, appears sometimes later than oedemas

Laboratory and instrumental investigations

1. **Urinary syndrome:**

- Proteinuria: marked – more than 3 g/24h

- Erythrocyturia – moderate
- Leucocyturia – may be present

2. **Biochemical blood analysis:** nephrotic syndrome signs

- total protein less than 60 g/l
- albumins less than 30 g/l
- cholesterol more than 7 mmol/l

Course and prognosis: III type (progressive)

Chronic renal failure development –5-7 years after onset

Treatment:

1. Patogenetic:

Cyclophosphan=Endoxan=Cyclophosphamide (cytotoxic drug - alkiling agent):

-first 3 days – i.v. 200-400 mg; than – same dose per os with subsequent lowering the dose

- Blood WBC level and hepatic enzymes serum level should be controlled during treatment

2. Symptomatic:

- diuretics (loop - furosemid)
- in marked hypoproteinemia – plasma or albumin transfusion.

3. Mesangioproliferative glomerulonephritis, immunopositive with IgA deposits (IgA-nephropathy)=Berger's disease

Prevalence: the most frequent variant of mesangioproliferative glomerulonephritis (60-70% of all glomerlonephritis cases)

Dominate males (80% of patients); more often young or children.

Aethiology:

Direct links between onset of the disease and infections (pharyngitis) have been found, different microbes associations an viruses are revealed.

Morphology

I. Light microscopy

1. Focal (some glomeruli affected) and segmental (some loops of glomeruli affected) character of glomeruli involvement is revealed.
2. Mesangial cells proliferation; mesangial expansion appearing like a tree trunk.
3. Thin basement membrane

In active disease areas of tuft necrosis manifesting by fibrin exudates and leucocyte infiltration are found. Small crescents are frequently associated with these lesions and, on occasion, circumferential crescents may be seen, but these are uncommon. The second probably represents healed areas of tuft necrosis, and consists of segmental glomerular scars with associated synechiae joining the tuft to Bowman's capsule. In long-standing disease, areas of tuft collapse and sclerosis with hyalinosis occur. These are most frequently seen in progressive disease, in which there is progressive glomerular obsolescence.

Mononuclear cells and neutrophils surround glomeruli with active areas of tuft necrosis and crescents. Interstitial scarring, tubular atrophy, and hypertensive vascular changes complicate long-standing disease.

Electron microscopy

Confirms that picture; immune deposits are revealed between mesangial cells and under basement membrane

Immunofluorescent microscopy

Deposits containing of IgA light chains are revealed in mesangium; C3 is also revealed in mesangium.

Classification:

A. Idiopathic

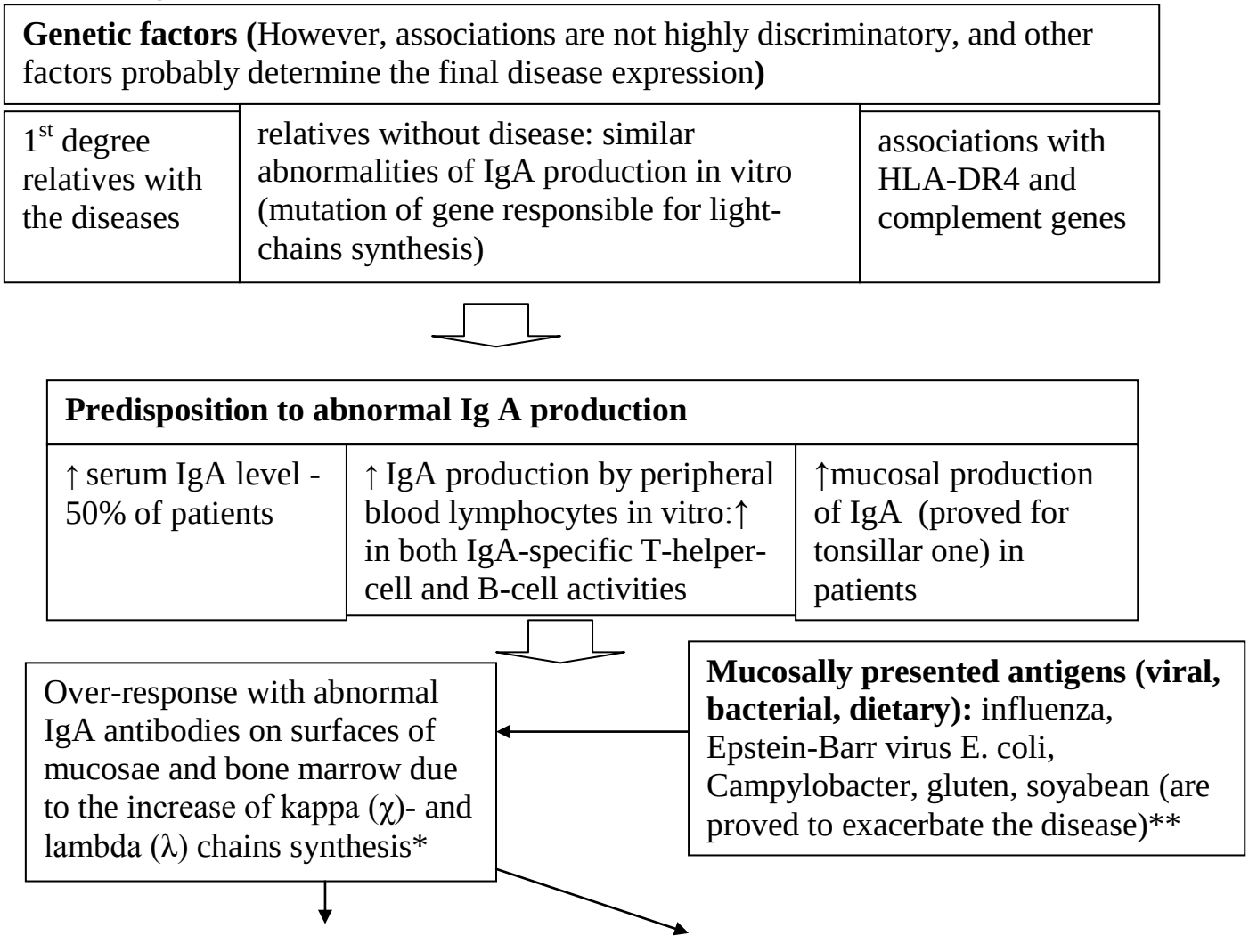
B. Secondary

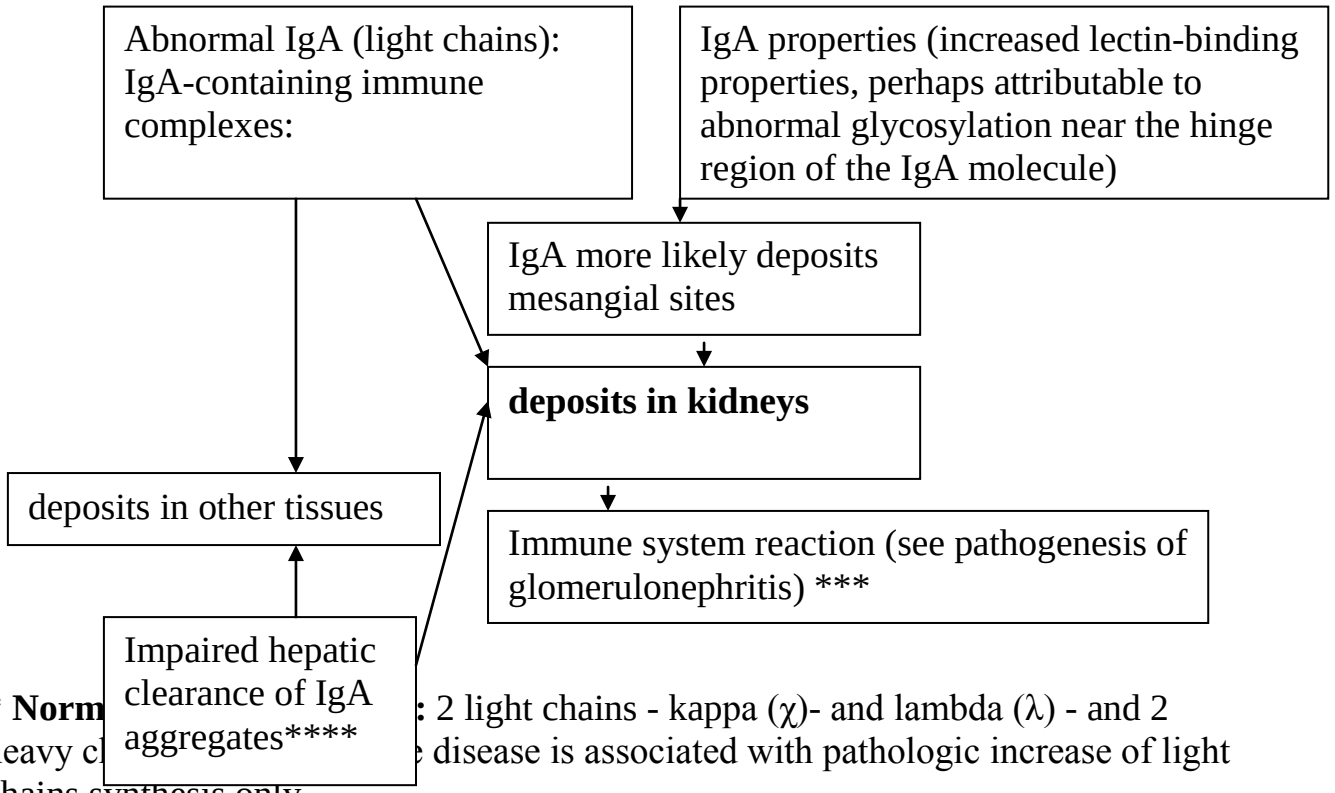
- herpetic infection
- liver cirrhosis
- coeliac disease
- Crohn's disease
- mucin-secreting carcinomas, wherein disorders of antigen processing may occur, leading to overproduction of IgA

- other diseases where there is a clearly demonstrable immuno- globulin response of the IgA class: dermatitis herpetiformis, ankylosing spondylitis, and IgA monoclonal gammopathy.

Henoch-Schounlein purpura, the commonest disease associated with Berger's disease, was revealed to have common pathogenetic mechanisms with it.

Pathogenesis





* **Norm** **:** 2 light chains - kappa (χ)- and lambda (λ) - and 2 heavy c[illegible] disease is associated with pathologic increase of light chains synthesis only

** Alcohol (probably by increasing gut permeability to a multiplicity of macromolecules) was also proved to exacerbate disease, presumably by an increased immune complex load and subsequent glomerular deposition.

***__Autoantibody reactivities__ are also identified. These include rheumatoid factors, mesangial antibodies (these are IgA class), IgA-ANCA (antineutrophil cytoplasmic antigen), and fibronectin-IgA aggregates.

**** Impaired in vivo hepatic clearance of IgA aggregates has been shown. This might reflect saturation of receptors, resulting from the original IgA immune complex load. Further support for this premise comes from the observed occurrence of mesangial IgA deposits in cirrhotic patients and in animal models of cirrhosis.

Clinical manifestations

1. Infection signs: (throat, bronchial, gastrointestinal, bladder, female genital tract, and breast infections**).**

2. Urinary syndrome (clinical):

- macroscopic haematuria beginning between 1 and 5 days after infection – the first symptom; the same accompanies all the exacerbations; the urine looks frankly bloody

- pain during urination (gripping character)

2. **Hypertension:** usually BP is normal; hypertension appears in about 10 years and is due to glomerular sclerosis

3. **Oedemas:** usually not present at the beginning of the disease, may occur several years later.

4. **Nephrotic syndrome:** quite rare, but may occur

Laboratory and instrumental investigations

1. Urinary syndrome (laboratory):

A. proteinuria is moderate (up to 1 g/l)

B. Sediment:

- numerous dysmorphic erythrocytes
- granular and red cell casts

2. Immunology: elevated serum concentrations of IgA and, at times of disease activity, elevated circulating concentrations of IgA immune complexes – in 50% of patients; autoantibodies reactivities (rheumatoid factor, IgA-ANCA)

3. X-ray: no changes

4. Ultrasonic: differential diagnosis with urinary stone disease.

Diagnosis:

Includes morphological and clinical characteristics.

Example of diagnosis formula:

IgA-nephropathy. Mesangioproliferative glomerulonephritis, isolated urinary syndrome with dominating haematuria. Renal function isn't impaired. I type course.

Course and prognosis:

Fluctuating course with spontaneous remissions, not caused by treatment. Common cold, flu etc are always accompanied by exacerbations with haematuria (sometimes severe).

I type of course, with slow progression.

Chronic renal failure: 10-15-20 years after disease onset.

Treatment:

1. Treatment of the cause in case of secondary disease
2. In case of idiopathic:
    A. prevention of colds and respiratory infections;
    B. Symptomatic treatment
    C. Pathogenetic treatment – only in exacerbations:

- Prednizolone – 40-60 mg daily
- Or cyclophosphane 100-200 mg daily

Pathogenetic treatment duration: 6-12 months

Control:

- hepatic enzymes and blood WBC (in case of cyclophosphane treatment)
- renal function – every 3 months

III. Membranoproliferative glomerulonephritis (other terms – mesangiocapillary glomerulonephritis or MCGN)

Definition: membranoproliferative glomerulonephritis is a group of the diseases with mesangial cells proliferation and basement membrane changes.

Prevalence: Usually found in age below 30, with equal rate of men and women. Revealed in 20-30% of glomerulonephritis cases and in respectively 8% (in children) 14% (in adults) of nephrotic syndrome cases.

Aethiology:

In most cases idiopathic, but a similar histological appearance may be seen in infectious endocarditis, hepatitis B and C infections, systemic lupus erythematosus, Henoch-Schunlein purpura, mixed cryo- globulinaemia, Candida infections.

Pathogenesis: see above.

Complement abnormalities, indicating predominant activation of the alternative pathway of complement, may play a certain role in pathogenesis of this variant: **low C3 and, less commonly, C4 levels** were found in patients; a special **C3 nephritic factor (C3Nef)** was revealed, which is an IgG autoantibody directed at determinants on C3bBb, the alternative pathway convertase. Binding of C3Nef factor to C3bBb prevents its inactivation and this leads to continuous activation of the alternative pathway, with the generation of C3b and ticking over of this pathway.

A small proportion of patients with MCGN have been reported to have inherited deficiencies of the complement proteins C2, factor B, C6, C7, and C8.

Morphology:

1. Light and electron microscopy

A. Primary changes

- increase of mesangial cells number
- mesangium expansion
- Ig, fibrine, complement fractions deposits

B. Secondary changes:

- Basement membrane affection – 3 variants:

I type – subendothelial deposition of immune complexes

II type – dense deposits inside the basement membrane (disease of dense deposits)

III type- severe increase of deposits number causing splitting of the basement membrane and contacts between intramembraneous and subendothelial deposits; sometimes with duplicated appearance of the glomerular basement membrane.

Immunofluorescent

2. Immunofluorescence:

C3, Ig A, G, M-containing deposits

Classification:

1. Aethiological

A.Idiopathic

B. Secondary: system connective tissue diseases, tumors, liver diseases

2. Morphological type – see above

Clinical manifestations

1. Acute onset of the disease with simultaneous appearance of all the 3 main syndromes
2. **Urinary syndrome (clinical):** macroscopic haematuria in 20% of cases
3. **Hypertension:** high BP from the 1st days of the disease in 60% of cases
4. **Oedemas:** usually marked, in case of nephrotic syndrome hardly respond to treatment and are associated with high activity of the disease

5. **Nephrotic syndrome:** in 50% of patients

Laboratory and instrumental investigations:

1. **Urinary syndrome (laboratory):**

A. Proteinuria: constant and marked; in case of nephrotic syndrome – more than 3 g/24h. Usually non-selective (albumines, globulines). Proteinuria is constant, lowering in remissions and increasing in exacerbations.

B. Sediment:

- RBC
- Casts (red-cell ones)
- WBC in case of nephrotic syndrome (not due to the inflammatory process)

2. **X-ray, Ultrasonic:** enlarged kidneys without severe structural changes. In nephrotic syndrome, triangle pyramids (sign of kidneys oedema) are revealed.
3. **Renograms (perfusion scanning):** symmetric curves with wide long-drawn curves in case of renal functions disturbances (the earliest sign of renal function impairment, even before biochemical markers appearance).
4. **Renal biopsy**

Diagnostic formula (example):

Membranoproliferative glomerulonephritis, I type, immune positive with IgA, M and G deposits in glomeruli and interstitium, exacerbation. Nephrotic syndrome. Secondary hypertension (date), III type of course. Initial disturbances of renal function.

Course and prognosis:

Usually III type of course, with frequent exacerbations. Remissions are short and exacerbations occur without visible causes.

Prognosis is serious due to constant progression of the disease.

Chronic renal failure: occurs in 5-7 years and needs active treatment

Treatment: begins just after diagnosis verification

1. Symptomatic (hypotensive, diuretics)
2. Pathogenetic:

A. Plasma exchange therapy – 500-700 ml of blood 3 times

B. Steroids:

- 1st 3 days – 500 mg of Prednizolone daily i.v.
- then (1st 2 months) – per os 60-80 mg daily
- then 2-fold decrease of the dose
- up to 1 year and more – Prednizolone treatment

C. Cyclophosphane may be used instead of steroids:

- 1 month – 200-400mg daily
- then per os 100-200 mg daily
- control of liver ensymes and blood WBC

Extracapillary diffuse proliferative glomerulonephritis=rapidly progressive glomerulonephritis=diffuse crescentic glomerulonephritis

Definition: The term rapidly progressive glomerulonephritis is used to describe those cases of glomerulonephritis which progress from onset to endstage renal failure within weeks or months. The characteristic histological appearance is of a focal necrotizing glomerulonephritis with crescent formation.

Prevalence: usually in young, up to 30-40 years old, both men and women (equal). Rate is about 1% of all glomerulonephritis types.

Aethiology:

- Idiopathic (some authors suspect it to be a renal-limited form of systemic vasculitis)
- Antiglomerular basement membrane disease
- Primary systemic vasculitis: Wegener's granulomatosis, polyarteritis nodosa
- Other systemic diseases: systemic lupus erythematosus

Often cold or tonsillitis precedes the development of the disease.

Morphology:

1. **Light microscopy**

- marked diffuse cells proliferation; cells are located extracapillary and form crescents (present in no less than 50% of glomeruli, usually – in 60-80%). Crescents are situated extracapillary inside the Boumen’s capsule. Crescents

consist of proliferating capsule cells, monocytes and lymphocytes, sometimes fibrin is revealed.

- Crescents squeeze loops and initial part of proximal part of Henle loop
- Gradual increase of fibrin amount in crescents – further squeezing and glomerular obsolescence.
- As a result – glomerular capillary loops necroses
- Further mesangial cells proliferation

2. **Immunofluorescence:** Ig G and C3 deposits

Clinical manifestations:

1. Acute onset with marked symptoms
2. **Urinary syndrome (clinical):** severe decrease of diuresis up to olyguria
3. **Oedemas:** frequent increase (mass increase – 6-10 kg during 1st week), localized on face and lower extremities; ascitis, hydrothorax, hydropericardium.
4. **Hypertension:** high BP (malign AH may be present)
5. **Nephrotic syndrome**
6. **Heart failure symptoms:** may be present in aged patients
7. **Other symptoms:** headache (water retention, intoxication); thirst, absence of appetite; pallor

Course and prognosis: rapid progression; most of patients die in first months of the disease, in spite of active treatment, due to chronic renal failure or complications of malign arterial hypertension (stroke, myocardial infarction).

Chronic renal failure: 1st months of the disease

Laboratory and instrumental investigations

1. Urinary syndrome (laboratory):

A. Proteinuria: more than 3 g/24

B. Sediment:

- RBC
- red cells casts

2. Haemogram:

- Anaemia
- Increased ESR

3. Biochemical blood analysis:
- signs of nephrotic syndrome
- signs of renal failure may be present

4. X-ray: nothing; ultrasonic: triangle-like pyramids (oedema of renal parenchyma)

5. Renograms (scanning): increase of time parameters (renal function disturbances)

Diagnosis formula:

Extracapillary diffuse proliferative glomerulonephritis, immune positive with IgG and C3 deposits, rapidly progressing. Nephrotic syndrome. Secondary arterial hypertension (date). Initial signs of renal failure (date).

Differential diagnosis:

Secondary rapidly progressing glomerulonephritis:

Wegener's granulomatosis (necrotizing vasculitis – necrotic changes of upper airways and lungs; arthritis); polyarteritis nodosa, Goodpasture's syndrome (lungs involvement: haemorrhagic necrotizing alveolitis with haemopthisis, pulmonary haemorrhage).

More rare rapidly progressing glomerulonephritis may occur in systemic lupus and cryoglobulinemia

Treatment

1. Plasma exchange therapy: 3-5 sessions with removing of 500-600 ml of blood; RBC are returned to patient and plasma is removed. The efficacy of treatment is due to possible removal of P-proteins , which block cells receptors. In case of nephrotic syndrome with hypoproteinemia removed volume of plasma can be replaced by solutions (albumin)

2. Steroids: Prednizolone 0.05
- initial dose – 500-800 mg i.v. 3-5 days

- then per os 80 -100 mg daily (2 mg/kg daily) – 1 month
- 2-times lowering the dose (up to 40-50 mg), the dose is lowered ½ tab once 2 days
- 40 mg dose – 6 months
- 2-times lowering the dose for 1 year
- The further therapy is planned afterwards if the patient is still alive.

3. Instead of Prednizolone Cyclophosphan can be administered:
- 200 mg daily i.v. – 1 month
- per os 100 mg - 6 months
- if treatment is effective – 2-times lowering of dose and 1-year treatment course.

Cautions: WBC level control, hepatic enzymes control; in case of long-time treatment – possible cancerogenic effect and (in men) azoospermia.

3. In case of renal failure: dyalisis; however, it is usually minimally effective and patients die.

Focal segmental glomerulosclerosis (FSGS).

Definition: glomerulonephritis with focal and segmental (affection of some capillars of glomerulus) nephrone affection.

Prevalence: rather rare (0.5-1% of all glomerulonephritis types; in adults – 10% of all glomerulonephritis types, presenting with nephrotic syndrome, in children – 7% of these). Predominantly in young people, in children peak age is 6-8 years old; in adults – 20-30 years old (but rarely occur in age over 70).

Aethiology: unknown

Pathogenesis: discussed above

Peculiarities:

In experimental models focal segmental sclerosis can develop from different pathogenic mechanisms. These include toxic injury (puromycin nephropathy),

immunological injury (antiglomerular basement membrane nephritis), the nephritis of NZB/NZW lupus, and hyperfiltration injury from five-sixths nephrectomy). Some of these models have clinical counterparts and the diversity of pathogenic mechanisms may explain the variability in the clinical presentation of FSGS as well as responses to therapy.

There are suggestions that the glomerular injury in FSGS is caused by a lymphokine. The rapid development of heavy proteinuria following renal transplantation in some patients with FSGS suggests that the glomerular injury is caused by a circulating factor.

Morphology

1. Light microscopy

- focal and segmental affection (only some loops of glomerular capillars)
- hyaline masses in glomeruli, with the progressing of the disease hyaline masses are replaced by sclerosis
- focal obsolescence of glomeruli, mesangial matrix increase, moderal hypercellularity of mesangium, focal canals changes

2. Electron microscopy

Absence of diffuse foot process effacement

3. **Immunofluorescent microscopy:**

deposits of IgM, G and C3 may be seen in the sclerotic areas.

Classification

1. Primary=idiopathic
2. Secondary: intake of gold preparations (rheumatoid arthritis), lithium, some antibiotics, narcotics (heroin). May develop in lymphomas, Alport's syndrome.

Clinical manifestations

1. Acute onset with marked symptoms from the beginning of the disease
2. **Oedemas:** marked
3. **Nephrotic syndrome**
4. **Hypertension:** high BP

5. **Urinary syndrome:** see laboratory investigations

6. Heart failure, tachycardia

7. Pallor

Course and prognosis:

Rapid progression with poor response to treatment; III type of course. In case of good response to steroid treatment, remission is possible; in patients without response – end stage of chronic renal failure within 5-10 years in 30-50%. Nephrotic syndrome is a factor worsening prognosis.

Laboratory and instrumental investigations:

1. Urinary syndrome:

A. Proteinuria – more than 3 g daily; poorly selective

B. Sediment: rich (RBC, red cells casts, WBC)

2. Biochemical blood analysis: signs of nephrotic syndrome

3. X-ray: at the early stage - increase of kidneys' size

4. Ultrasonic – triangle form of pyramids (oedema)

5. Perfusion scan renograms: increase of time parameters (function impairment)

Diagnosis formula:

Focal segmental glomerulosclerosis, exacerbation. Nephrotic syndrome. Secondary hypertension. III type of course. Moderate impairment of renal function.

Differential diagnosis: with all forms of rapidly progressing glomerulonephritis; diagnosis is proved by biopsy.

Treatment:

1. **Steroids:** in most studies, patients with classical FSGS and a nephrotic syndrome have been treated with steroids (the same schemes). The response to treatment is poor. Only 10 to 30 per cent of patients respond by going into remission. These patients have a good prognosis and do not develop progressive renal failure. However, the prognosis in patients who do not respond to steroids is poor. Between 30 and 50 per cent of these patients develop endstage renal failure over 5 to 10 years.

2. Cyclophosphamide at the same doses and duration as used in minimal change nephropathy has been given to some patients with FSGS who are resistant to steroids. A useful remission was induced in 25 per cent of cases and this approach may be tried in patients with a severe nephrotic syndrome.

3. Cyclosporin A in focal segmental glomerulosclerosis

Several studies have examined the effects of cyclosporin A in patients with FSGS and a nephrotic syndrome. In general, the responsiveness to cyclosporin A has been poor and has paralleled steroid responsiveness. Those patients who were steroid resistant achieved little or no benefit from cyclosporin A.

Membranous glomerulonephritis (nephropathy)

Definition: Membranous nephropathy is a disease which is characterized by predominant affection of basement membrane without mesangial cells proliferation.

Prevalence: 3-10% of all glomerulonephritis types and no less than 30% of all cases with nephrotic syndrome (2-5% of these in children). More often middle-aged and aged (most commonly in the fifth and sixth decades), more often men.

Aethiology: usually in patients with chronic infections

Pathogenesis: see above

Peculiarities:

- Predisposition - HLA system: In Europe there is a strong association between membranous nephropathy and the major histocompatibility complex haplotype HLA-A1 B8 DR3; in Japan the association is with HLA-DR2. By contrast no such association is seen in the United States.
- antibodies: in rats, administration of antibodies to renal tubular epithelial antigen leads to a membranous nephropathy that histologically resembles human membranous nephropathy. The antibody responsible for this Heymann nephritis in rats binds to epitopes on glomerular epithelial cells and leads to the development of

subepithelial deposits. There is no evidence that a similar mechanism plays a role in human membranous nephropathy.

Morphology

1. Light microscopy:

- diffuse thickening of the glomerular basement on light microscopy, usually with argyrophyllic subepithelial spikes (Johnson's coloring).

4 degrees of basement membrane affection

I degree: basement membrane thickening and increase of density, no spikes are present

II degree: large subepithelial deposits separated by spikes of basement membrane

III degree: deposits incorporated into a thickened basement membrane with many spikes

IV degree: a very thick irregular basement membrane with no spikes and resorbed deposits. Some sites of basement membrane arte thickened, others are wrinkled. Glomerular sclerosis.

2. **Electron microscopy**: the same findings

3. **Immunofluorescent or immunoperoxidase microscopy:** basement membrane thickening is shown to be due to the presence of immune deposits consisting of usually IgG and C3 on the subepithelial surface of the glomerular basement membrane. The presence of mesangial proliferation, mesangial immune deposits, and IgA and C1q on immunofluorescent microscopy raises the possibility that the membranous nephropathy is secondary to systemic lupus erythematosus.

Classification:

1. Idiopathic

2. Secondary (20-25 of adults):

- Malignancy, usually a carcinoma and rarely Hodgkin's lymphoma or non-Hodgkin's lymphoma 3 – 7% this rises to 16 per cent in patients aged over 60 years. The most common tumours are carcinoma of the bronchus, colon, kidney, breast, stomach, and prostate.

- Gold and penicillamine therapy are prominent causes of membranous nephropathy, and this complication is more common in individuals who carry the HLA-DR3 gene.
- systemic lupus erythematosus – 3%; suggested SLE – 2%
- in northern Europe about 1 per cent of patients with membranous nephropathy have positive hepatitis B serology, although this probably causative association is much more common in South-East Asia and in Africa.
- diabetes, thyroiditis, and mixed connective tissue disease are also reported to be associated with membranous nephropathy

Clinical manifestations

1. Onset: gradual, from mild/moderate proteinuria (I morphological degree of basement membrane affection) appearing and disappearing; becoming more and more marked; stable marked level is reached in several years (quicker in secondary glomerulonephritis); by that time symptoms appear

2. Oedemas: more and more marked with disease progression up to nephrotic syndrome

3. Nephrotic syndrome: usually appears at III-IV morphological degree

4. Hypertension: at III-IV degree

5. Urinary syndrome: macroscopic haematuria in 10-20% of children, but rare in adults

6. Strokes, angina and congestive heart failure may occur (hypertension, age, atherosclerosis progression in patients with nephrotic syndrome)

7. Chronic renal failure

8. Renal vein thrombosis: 5-10%; due to hypercoagulable state of the nephrotic syndrome and not a primary cause of membranous nephropathy.

Laboratory and instrumental finding:

1. Urinary syndrome:

A. Proteinuria: moderate – I degree, severe – III-IV ones

B. Sediment: RBC, WBC, red cells casts

2. Biochemical blood analysis: nephrotic syndrome

3. Haemogram: anaemia, increased ESR

4. X-ray: nothing in kidneys; however chest X-ray may reveal lung cancer

5. Ultrasonic: nephrotic syndrome: triangle form of pyramids: renal oedema

6. Scan renograms: in case of renal failure, even initial – changes of time parametres

Diagnosis formula:

1. Membranous glomerulonephritis, I degree wih Ig G and M deposits. Isolated urinary syndrome with moderate proteinuria (date). Course: I type, without renal function impairment

2. Membranous glomerulonephritis, III degree, exacerbation with IgA, G,M deposits. Nephrotic syndrome. Secondary hypertension (date) . Impairment of water-discharge renal function. Course II-III type.

Differential diagnosis: all types of glomerulonephritis, secondary membranous glomerulonephritis (search for carcinomas!!!)

Course:

Fluctuating, initially – long-time period of fluctuating proteinuria (I type), which gradually increases and becomes stable, accompanied by nephrotic syndrome (II and III types).

In secondary glomerulonephritis the course and prognosis depend on the aethiology. Treatment of the main disease (for example, radical operation in tumor) leads to regression of the glomerulonephritis.

Renal failure: After a mean follow-up of 4.5 to 6 years, between 9.5 and 22 per cent of patients are in endstage renal failure, 9.5 to 19 per cent have significant impairment of renal function, and 23 to 50 per cent are in remission. Actuarial survival shows that about 75 per cent of patients are alive at 10 years and 60 per cent have functioning kidneys.

Treatment

1. Pathogenetic treatment: according to above mentioned schemes (steroids) only in exacerbation period.

As a cytotoxic agent, Chlorambucil was reported to be effective in patients in whom renal function deteriorates more rapidly; alternating schemes (monthly for 6 months) of high-dose methyplrednizolone and chlorambucil exist.

2. Symptomatic treatment: hypertension – ACE inhibitors

3. Diet (salt and water restriction)

4. Regimen – avoid cold and respiratory infections.

Glomerulonephrtits with minimal changes

(Minimal change disease=Lipoid Nephrosis=Nil Disease)

Definition: Glomerulonephrtits with minimal changes is a disease with marked clinical manifestations but without significant morphological changes.

Prevalence: Most common in children 2-5 years old (under 6 years old – 80%); sometimes may be revealed in adults (middle-aged, even aged). In adults revealed in 0-3% of glomerulonephritis cases (25% of these with nephritic syndrome); men: women ratio is 2:1.

Aethiology and classification:

A. Idiopathic: aethiology is unknown, but disease occur following:

-viral upper respiratory tract infections

- immunizations,

- bee stings.

B. Secondary:

- Hodgkin's disease (paraneoplastic)

- Gold preparations use in rheumatoid arthritis patients

- Lithium preparations use

- Antibiotics

- NSAIDs (non-steroid anti-inflammatory drugs)
- narcotics (heroin)

Pathogenesis: see above

Morphology:

1. Light microscopy following variants (WHO, 1982):
- absence of changes
- focal obsolescence of glomeruli
- minimal increase of mesangial matrix without changes of mesangial cells number
- focal changes in canals
- minimal mesangial hypercellularity

2. Electron microscopy:

characteristic "fusion" of the epithelial foot processes, which is not a specific finding for this disorder but occurs in all glomerular diseases associated with significant proteinuria

3. Immunofluorescence:
- negative
- in some patients, diffuse mesangial deposits of IgM and C3. These individuals tend to have more marked hematuria and hypertension than these with “pure” disease

Clinical manifestations

1. Acute onset with marked symptoms

2. Oedemas: rapidly progressing up to nephrotic syndrome

3. Nephrotic syndrome with ascitis, hydrothorzx, hydropericardium

4. Hypertension: infrequent (9%); may be revealed at the late stages (10 and more years after the onset)

5. Urinary syndrome: see laboratory investigations

6. Symptoms due to nephrotic syndrome (complications):
- High susceptibility to infections with gram-positive microorganisms (due to severe hypoproteinemia), in children - in particular cellulitis and pneumococcal peritonitis

- thromboembolic events
- severe hyperlipidemia
- protein malnutrition.

Laboratory and instrumental investigations:

1. Urinary syndrome

A. Proteinuria – severe, highly or moderately selective

B. Sediment: moderate changes

2. Biochemical blood investigations: signs of nephrotic syndrome; hypoproteinemia may be marked (albumins less than 10g/l)

3. X-ray: big kidneys

4. Ultrasonic: nephrotic syndrome: triangle form of pyramids due to kidneys oedema.

5. Perfusion scanning: no changes

Diagnosis formula:

Minimal changes glomerulonephritis. Nephrotic syndrome (date). I type of course. Normal renal function (date).

Differential diagnosis:

All cases of nephrotic syndrome

Course and prognosis:

Relapsing course with remissions even without any treatment. Good and rapid response to steroids (in adults – 80%). Survival rate (5 years) is 90% (if antibiotics are used). Only 20% of adults have multiple relapses or are steroid-dependant. Long-lasting remissions are possible; i one study, 62.5 per cent of patients treated with cyclophosphamide were in remission at 10 years.

Treatment:

1. Pathogenetic:

A. Steroids – long-time treatment (for several years)

- In adults with nephrotic syndrome – i.v. Prednoizolone 300-500 mg daily – 3-5 days
- then – per os 60-80 mg daily - 1 month
- then – lowering the dose gradually up to minimally possible to avoid proteinuria (usually 10-20 g daily)

This disorder tends to respond to prednisone, 1 mg/kg/d, after 4–6 weeks. However, a significant number of individuals will relapse when steroids are discontinued and will require additional doses of steroids; some will become steroid-dependent, relapsing every time steroids are discontinued.

In adults response to steroids is less than in children, but occurs in 80% of cases; however it needs more time (up to 16 weeks).

B. Cytotoxic agents (Cyclophosphane) in patients with contraindications to steroids, frequent relapses and steroid-dependent individuals; beginning with i.v. administration, then – per os.

C. Cyclosporin A: is indicated in patients with multiple relapses or steroid toxity or dependence. Cyclosporin A appears to be effective at blood levels of 100 to 200&g/ml, and at these levels significant short-term nephrotoxicity and hypertension are uncommon.

Sclerotic (fibroplastic) glomerulonephritis

Definition: Sclerotic (fibroplastic) glomerulonephritis is the outcome of all other morphological variants and clinically manifests as chronic renal failure.

Prevalence: relates to the prevalence of glomerulonephrtits; in patients with confirmed diagnosis males below 40 years old dominate.

Aethiology: all types of glomerulonephritis

Pathogenesis: see above

Peculiarities: haemodynamic changes in glomeruli dominates, which causes intraglomerular hypertension and acceleration of sclerosis.

Morphology

Sclerosis, glomerular obsolescence and tubulointerstitial fibrosis with no difference between morphological types.

Classification: is not classified.

Clinical manifestations:

1. In general: more marked features of the main form of glomerulonephritis
2. **Hypertension:** uncontrolled
3. **Oedemas:** marked, severe, resistant to treatment
4. **Nephrotic syndrome** – often present
5. **Chronic renal failure**
6. **Congestive heart failure** due to hypertension and severe water retention
7. **IHD** signs may appear

Course and prognosis:

Rapid progression of renal failure; due to poor prognosis patient should be prepared to active treatment methods (dialysis).

Laboratory and instrumental investigations

1. Urinary syndrome

A. Proteinuria: usually more than 3 g daily

B. Sediment: RBC, red cells casts

2. **Biochemical blood analysis**: nephrotic syndrome signs in 50% of patients.

3. Urograms: good quality of urograms is usually not available; so renal tomograms are needed to evaluate the position of kidneys and degree of increase of renal parenchyma density

4. Ultrasonic:

Small kidneys; signs of sclerosis; density of kidneys is equal to that of liver

5. Renograms: increase of time parameters (impairment of renal functions)

Treatment:

1. Pathogenetic: at that stage is not used

2. Symptomatic

- Oedemas: Furosemid – 40-80 mg daily; if ineffective – i.v.(Lasix) 80-100-200 mg daily – 3-7 days
- Hypertension: ACE inhibitors with non-hydropiridin calcium antagonists (Verapamil 80 mg 2-4 times a day); calcium antagonists can't reduce intraglomerular pressure, so don't influence on renal failure progression

2. Patient should be prepared to dialysis

In some western textbooks all cases of chronic glomerulonephritis are divided in 3 big groups, basing simultaneously on clinical, morphological and pathogenetic principles

I. More often manifesting with nephrotic syndrome: Idiopathic glomerulonephritis: in children – 90% of nephrotic syndrome cases; in adults – 80%.

1. Minimal change nephropathy
2. Focal segmental glomerulosclerosis
3. Membranoproliferative glomerulonephritis
4. Membranous nephropathy
5. Proliferative glomerulonephritis: mesangial proliferative glomerulonephritis (IgM)

II. Rapidly progressive glomerulonephritis and antiglomerular basement membrane disease:

1. Antiglomerular basement membrane disease (Goodpasture's syndrome)
2. Idiopathic rapidly progressive glomerulonephritis (including that in vasculites)
3. Rapidly progressive glomerulonephritis in other diseases (systemic lupus erythematosus etc)

III. Glomerulonephrites, manifesting with haematuria:

1. IgA nephropathy

2. Henoch-Shonlein purpura

3. Thin membrane nephropathy (description see below)

This approach seems to be useful from the practical point of view and has a lot of benefits; the only one existing problem is the fact, that one morphological condition (mesangioproliferative glomerulonephritis) is reviewed in 2 different groups; 2 conditions – idiopatic mesangioproliferative glomerulonephritis and that with focal glomeruli affection are not included in these groups.

Renal transplantation: recurrent idiopathic glomerulonephrtis

Several types of idiopathic glomerulonephritis may recur after renal transplantation. These recurrences must be differentiated from glomerular disease that is a consequence of rejection or allograft glomerulopathy, which can lead to de novo histological lesions indistinguishable from FSGS, membranous nephropathy, and MCGN type I, and hence to an overestimate of rate of recurrence. Recurrence of FSGS is commoner in patients whose original disease led to renal failure within 3 years of onset. Proteinuria is often detected within days or weeks of transplantation. Although type II MCGN is often found on biopsy, clinical recurrence and graft losses from this are infrequent. The incidence of recurrent membranous nephropathy is difficult to estimate as this lesion often develops de novo in patients whose original disease was not membranous nephropathy. The possibility of recurrent glomerulonephritis is not a contraindication to renal transplantation.

Thin membrane nephropathy (benign familial haematuria)

Prevalence:

11% of non-transplant renal biopsies

Aethiology: family studies support an autosomal dominant inheritance.

Morphology:

Light microscopy:

- mild mesangial expansion
- mild hypertrophy of the juxtaglomerular apparatus

Electron microscopy:

- decreased width of the glomerular capillary basement membrane - 250 nm (normally 340-450nm); are observed in thin membrane nephropathy.

- in some patients there is marked global thinning of the basement membrane associated with patchy lamellation, electron-lucent flocculation, and subendothelial nodularities. In others, these membrane changes occur intermittently between lengths of near-normal membrane. Immuno- gold studies suggest a reduction in the subepithelial portion of the basement membrane. Unlike some patients with Alport's syndrome, however, Goodpasture's antigen is readily identified within these thin glomerular basement membranes.

Immunofluorescence:

is negative apart from C3 in the arterioles of some patients.

Clinical manifestations

1. Urinary syndrome

- persistent, usually asymptomatic, microscopic, or dipstick discovered haematuria.

- episodes of macroscopic haematuria occasionally occur and raise the possibility of a more sinister diagnosis, such as Alport's syndrome.

2. Hypertension: BP is usually normal

3. Oedemas: are not reported to be present

4. Renal function: typically is normal.

Laboratory and instrumental investigations

Proteinuria: minor proteinuria may be present

Sediment: significant number of dysmorphic red blood cells.

Prognosis

Long-term follow-up suggests that the condition is benign