Glomerulonephritis

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Glomerulonephritis - definition

- Glomerulonephritis (GN) = glomerulopathy due to activation of immune mechanisms mostly (but not always!) with inflammatory changes in glomeruli

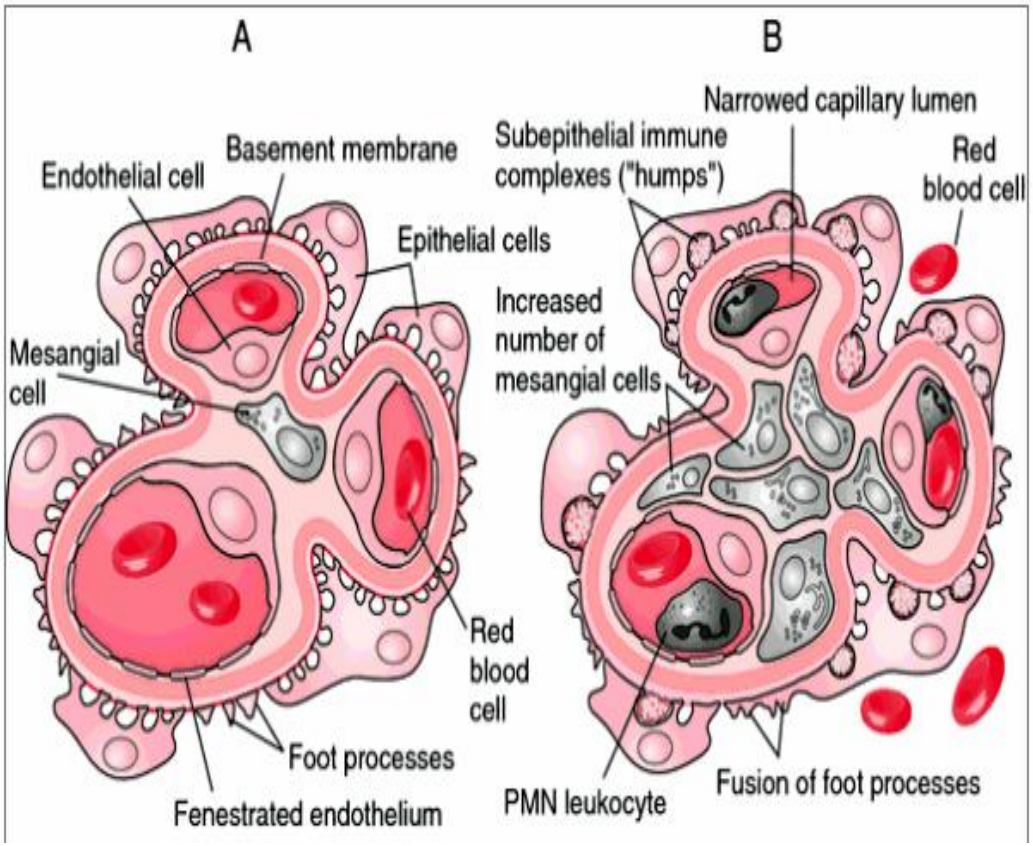
- Etiology: hereditary x acquired

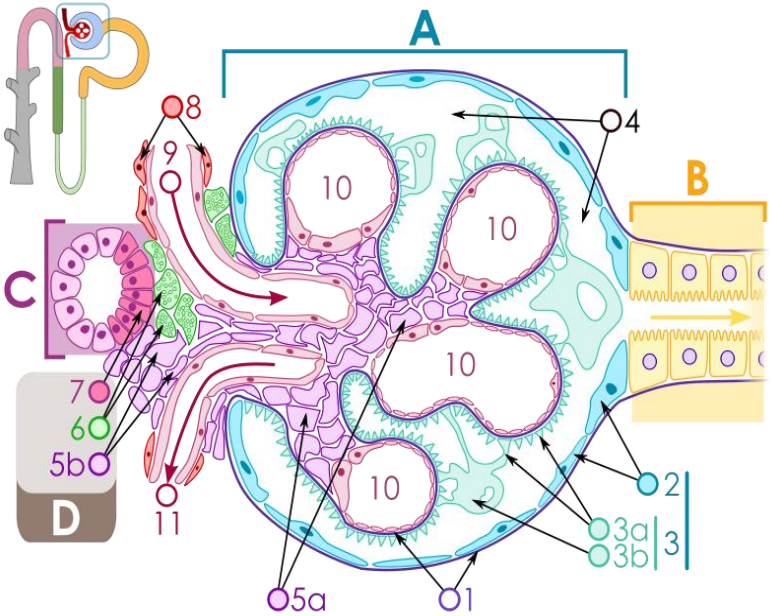
- Mechanisms:
  - deposition of circulating immunocomplexes or external Ag in kidney tissue = immunocomplex GN
  - antibody or cellular response against intrinsick kidney Ag= antirenal GN

Classification – only kidney disease only x systemic disease

Glomerulonephritis according to course

- acute - rapid onset within days to weeks, usually rapid recovery
- subacute - rapidly progressing glomerulonephritis = RPGN (rapid progressive glomerulonephritis) - development over days to weeks or months , high risk for chronic renal failure including ESRD
- chronic - development over months and years
  - progressive character
  - untreated (unfortunately often also treated!) can lead in longer (but also shorter!) time interval to severe functional renal failure including ESRD
- 3 clinical syndromes : nephritic syndrome
  nephrotic syndrome
  HUS


A
B
Endothelial cell
Basement membrane
Epithelial cells
Mesangial cell
Red blood cell
Foot processes
Fenestrated endothelium
Subepithelial immune complexes ("humps")
Narrowed capillary lumen
Red blood cell
Increased number of mesangial cells
PMN leukocyte
Fusion of foot processes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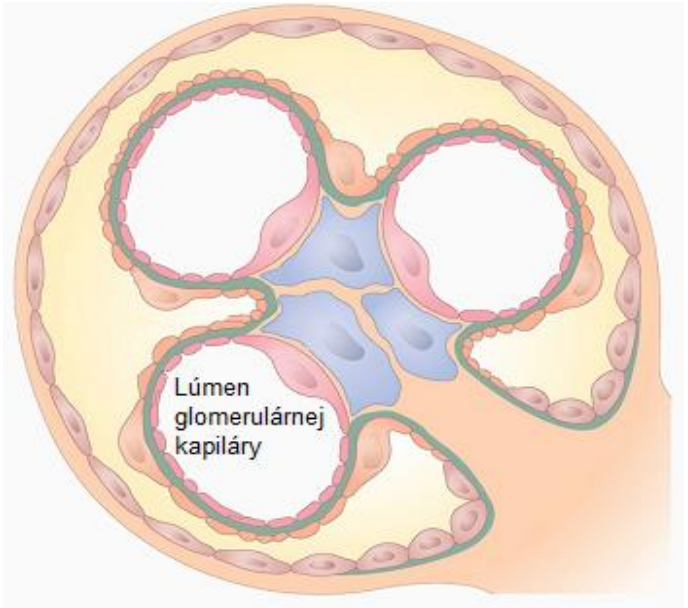

Lúmen glomerulárnej kapiláry

Acute nephritic syndrome

- typical for acute glomerulonephritis
- glomerular type hematuria:

  microscopic / macroscopic
- mild proteinuria: selective /nonselective
- reduced glomerular filtration
- oliguria
- hypertension
- edema

Classification of GN in Children

Table 3. Classification of Glomerulonephritis in Children

Congenital Diseases	Cytomegalovirus, Human Immunodeficiency Virus, Syphilis, Toxoplasmosis
Monogenic diseases	Thin basement membrane nephropathy (*COL4A3, COL4A4*)*
	Alport syndrome, X-linked (*COL4A5*)
	Alport syndrome, autosomal (*COL4A3, COL4A4*)
	Denys-Drash syndrome (*WT1*)
	Frasier syndrome (*WT1*)
	Nail patella syndrome (*LMX1B*)
	Pierson syndrome (*LAMB2*)
	Schimke immuno-osseous dysplasia (*SMARCAL1*)
Primary acquired diseases	Acute postinfectious glomerulonephritis
	Membranoproliferative glomerulonephritis (MPGN)
	C3 glomerulopathy (C3G)
	IgA nephropathy
	Anti–glomerular basement membrane (GBM) disease
Systemic diseases with GN	Infectious glomerulopathies (acute or chronic)
	Systemic lupus erythematosus
	Henoch Schönlein purpura
	Antineutrophil cytoplasmic antibody-associated vasculitis (EGPA, GPA, MPA)
	Goodpasture syndrome

Diagnostics

- GN active sediment- dysmorphic ERY cylinders
- serology - immunology
- renal biopsy:
  light microscopy, immunofluorescence, electron microscopy
- activity and chronicity index

Acute post-infectious glomerulonephritis

- glomerulus as well as the interstitium
- acute immunocomplex GN
- etiology:

  -> bacterial: 80% Streptococcus betahemolyticus
  Staphylococcus aureus, Streptococcus pneumoniae, Staphylococcus albus, Meningococcus, Salmonella typhi, Yersinia, Campylobacter, E. coli

  -> riketsia, fungi, parasites

  -> viruses: EBV, CMV, HSV, VZV, parvovirus B19, parotitis virus, hepatitis B and C virus

Acute post-streptococcal glomerulonephritis

- incidence significantly decreased in recent decades in developed countries
  -> Europe / USA 10-20 cases / 100 thousand population
  -> estimated 50% of inapparent courses
- age groups: 60% children - most often 5-12 years of age
- 10% of patients over 40 years of age
- 5% of patients under 2 years of age
- boys twice as often as girls
- incidence high in developing countries 97%
  - significantly associated with skin infections -pyoderma
- in a temperate climate zone - pharyngitis

Type of infection

- streptococcal infection:
  10% urinary pathology – haematuria
  8% reduced C3 component of the complement

- incidence of haematuria in siblings without clinical symptoms (inapparent AGN)

- scarlet fever, pharyngitis: 1-2% of children develop AGN

- pyoderma: higher incidence of AGN - about 8% AGN

Mechanism of immune response

Immune process - an immune complex type of disease – > IC + complement

3 theories:

- IC in circulation -> glomeruli
- antigen in glomerulus- antibody binding -> IC
- antigen- molecular mimicry-> IC in glomeruli

IC -> complement activation, leukocyte infiltration, mesangial proliferation

- Decrease in GFR->water retention and Na- hyperhydration
- C3 complement component:
  - decrease in 80-90% of cases
  - return to normal for most within 6-8 weeks
  - deposits "HUMPS" in the biopsy material
- C4 complement component is normal

Serological findings in PSAGN

ASLO:

- increase in 10-14 days after URT infection in 70 - 80%
- in pyoderma may not be pathological (increase in 50% cases)
- peak in 3 - 5 weeks, then decline 1 - 6 months

Anti-DNA-se B:

- more than 90% of PSAGN patients after impetigo have elevated titers

Anti-hyaluronidase

Biopsy findings

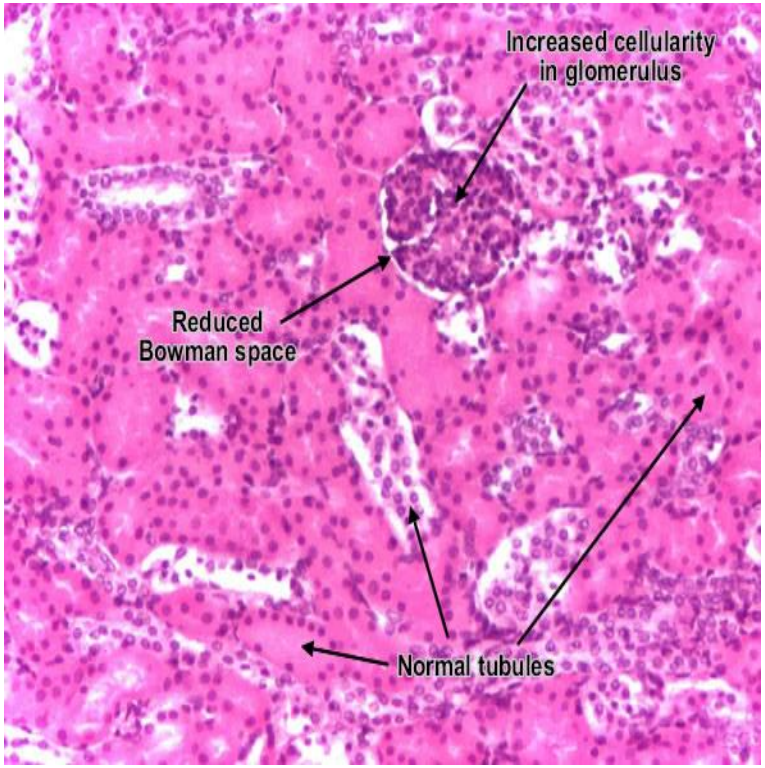
- Light microscopy:
  - "proliferative-exudative nephritis" image
  - intensive endocapillary proliferation and massive accumulation
  - cellular inflammatory infiltration

- Immunofluorescence: deposits of IgG and C3
  -> mesangium granular pattern

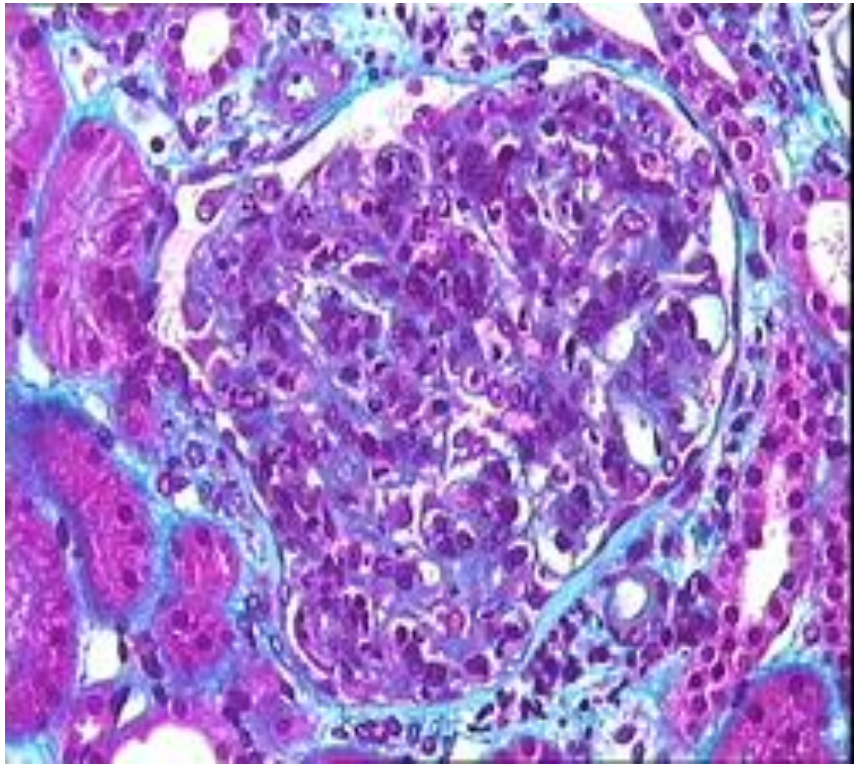
- Electron microscopy:
  Ig and complement deposits located subepithelially -> HUMPS

Acute post-streptococcal GN

Increased cellularity of glomeruli = infiltration with leukocytes, an increased volume of glomerulus leads to narrow the space of the Bowman capsule

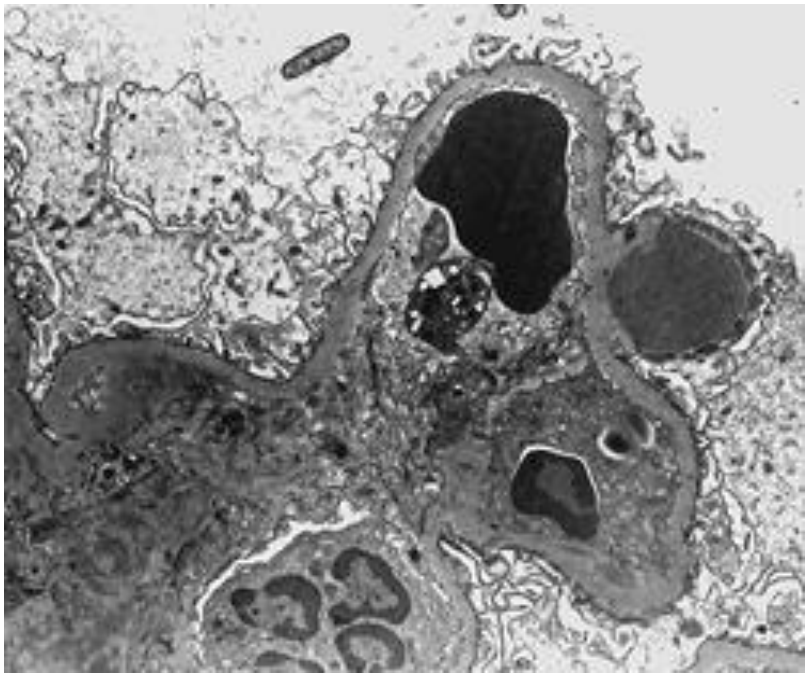


Intense glomerular hypercellularity is evident, not only due to endothelial swelling but by leukocyte infiltration

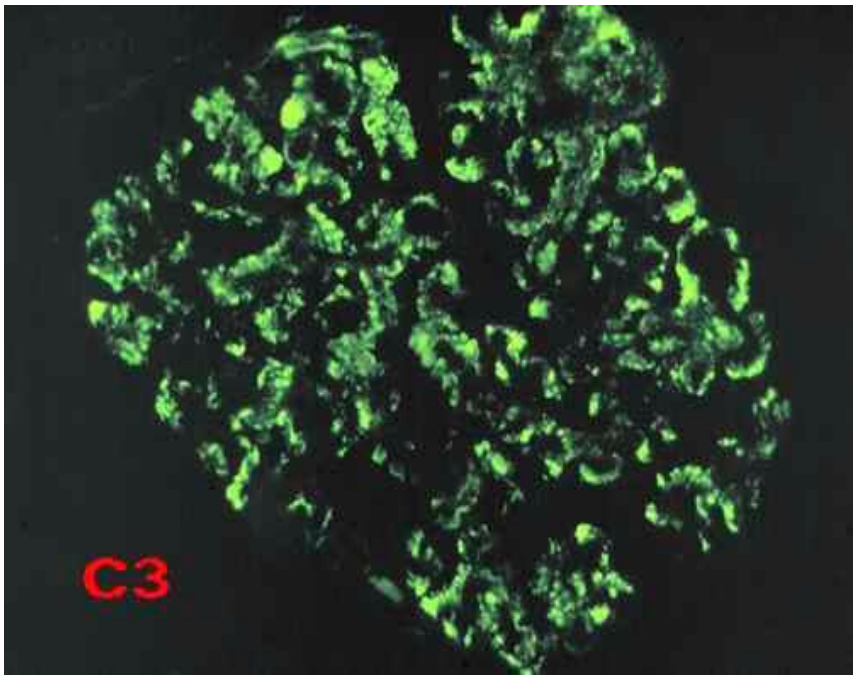


Electron microscopy, IF

Humps -subepithelial density deposits



Deposits of the C3 complement component

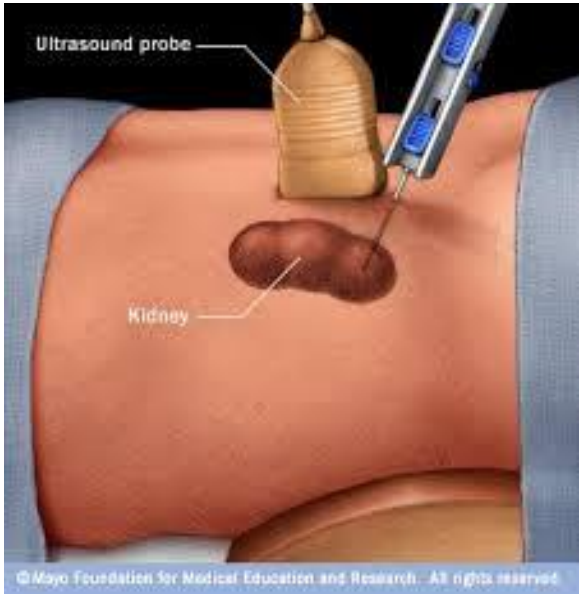


Percutaneous renal biopsy in PSAGN

Indication:

- C3 reduction > 3 months
- nephrotic proteinuria or proteinuria > 6 months
- abnormal creatinine after 6 weeks
- rapid decline in renal function in days-weeks

diagnostic embarrassment - general indications

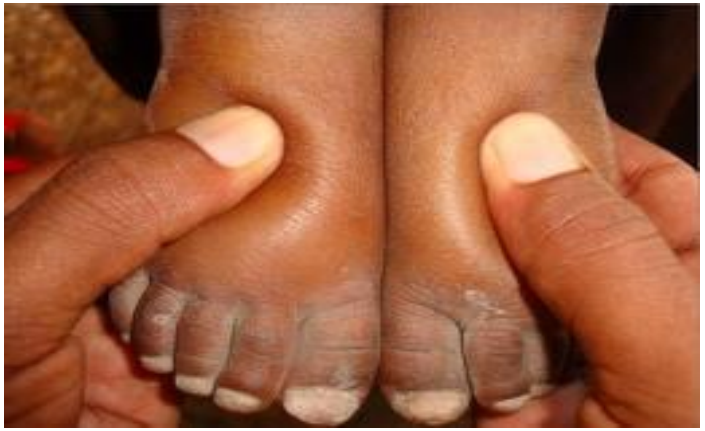


Clinical presentation

- URTI 1-2 weeks ago or pyoderma
  6 weeks ago
- detection of streptococcal infection (cultivation, ASLO, anti-DNA-asa B)
- edema - the skin is tight and stiffer x plastic edema at NS
- hematuria - "coca-cola colored urine", the urine of washed meat
- hypertension
- oliguria, rare anuria
- abdominal pain - capsule tension
- cardiovascular overload
- increase in renal parameters - 20% of patients

-> if creatinine increase > 50% -> check creatinine in 12 hours -> RPGN

- FENa typically <1%



Investigations

- urine + elements: dysmorphic ERY, erythrocyte cylinders
- CRP
- blood count - without conspicuity
- proteinuria - mostly up to 0,5 g / m2 / 24 hours
- ASLO, anti-DNA-asa B
- C3, C4 normal,
- ANA, ENA, ANCA, ds-DNA negative,
- Ig AEGM
- hemoculture
- biochemistry: urea, creatinine, uric acid, P, K
- ASTRUP
- swab neck
- kidney ultrasound

Treatment I

- edema, hypertension -> fluid and salt restriction, diuretics - thiazides, furosemide
- calcium channel blockers, β- blockers, ACEI
- hyperkalemia - conservative treatment
- RPGN, crescent in renal biopsy ->corticoid pulses
- antibiotics - PNC, macrolides
- bed rest - edema, hypertension, macrohematuria
- 6 months less effort, school rest for 6 - 8 weeks
- active treatment of acute GN only with proven RPGN, which can also be caused by streptococcal infection !!

Treatment II

- assessment of hydration status:

  oliguria -> prerenal x renal failure
- restriction of fluid intake:

  perspiration loss 200-400 ml / m2. 24 h + previous hour diuresis + other losses (diarrhea, vomiting)
- diuretics: furosemide test 1- 2 mg/kg
- antihypertensives
- AKI treatment

Prognosis

- most pediatric patients recover completely X in adults the proportion is lower
- hematuria / proteinuria or hypertension - may persist for months
- residual microscopic hematuria does not impair prognosis
- proteinuria and hypertension may impair renal function in the long term
- late sequelae study – Schärer K, Kinderarzt, 24, 1025, 1993:
  - examination of 73 children with a history of AGN at least 6 years from the start
  - proteinuria 6%
  - macrohematuria, microhematuria 10%
  - hypertension 2%
  - hyperazotemia !! 7% !!

Rapidly progressive GN (RPGN)

- rapid deterioration of renal function in days -> weeks
- possibility of rapid progress to chronic renal failure
- symptomatology:

  acute nephritic syndrome - hematuria

  - proteinuria (may be nephrotic)

  presence cylinders in urine

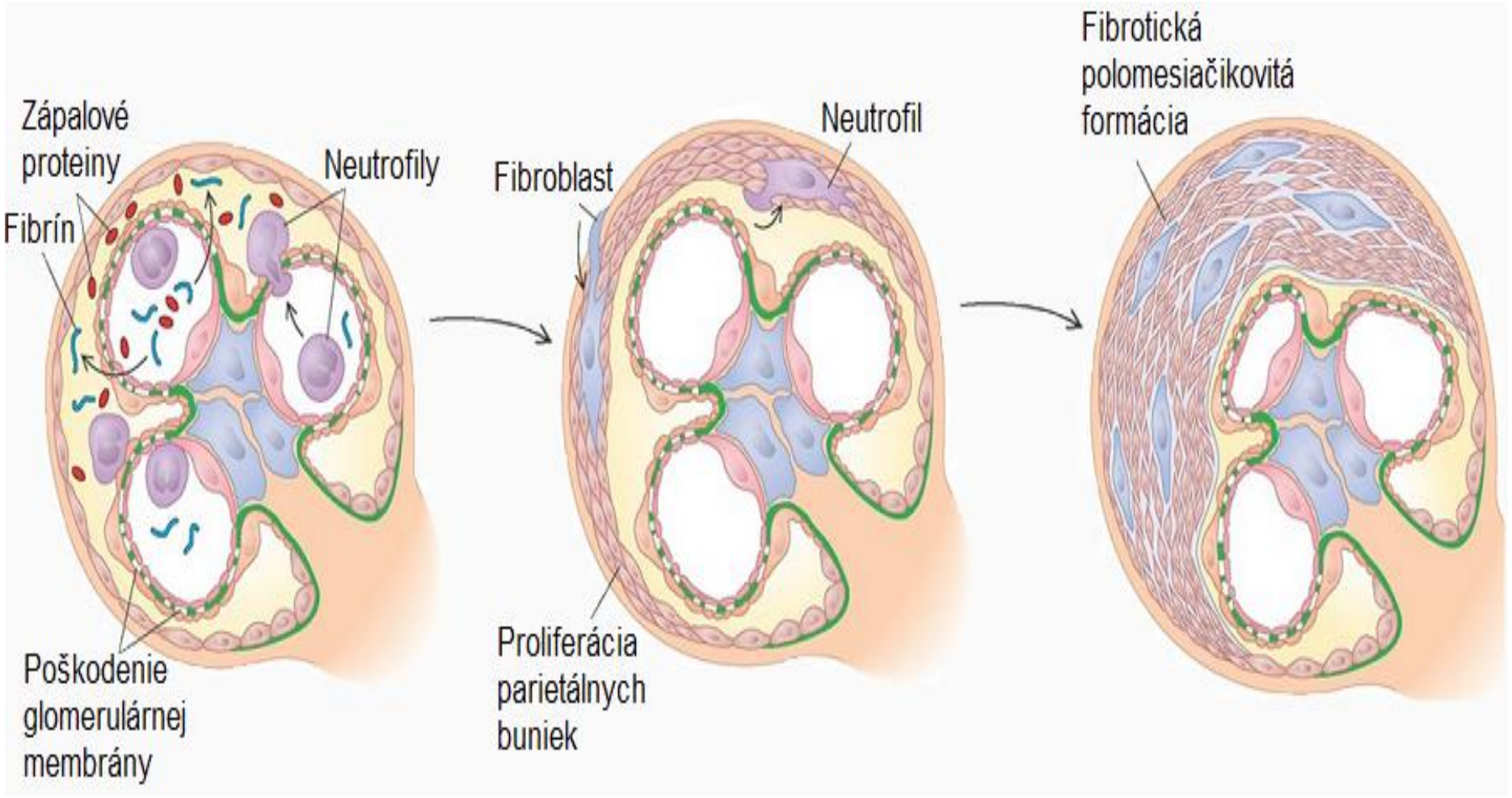
  hypertension

  decrease GFR or oliguria / anuria -> AKI

  edema

RPGN Histological Findings

- extracapillary proliferation - crescent in more than 50% glomeruli
- crescents fill the space of Bowman's capsule -> the answer to damage the glomerulus
- crescents - inflammatory and epithelial cells - *cell crescents* - later organize with fibrin and collagen - *fibrous crescents* - irreversible damage
- the degree of histological involvement corresponds to GFR disorder


Zápalové proteiny
Fibrín
Neutrofily
Poškodenie glomerulárnej membrány
Fibroblast
Neutrofil
Proliferácia parietálnych buniek
Fibrotická polomesiačikovitá formácia

Etiology and classification of RPGN

- with granular deposits - immunocomplex type - 40% of all RPGNs
  - IgA nephropathy
  - nephritis in Henoch-Schönlein purpura
  - nephritis in SLE
  - membranous and membranoproliferative GN
- with antibodies to the cytoplasm of neutrophile
  - ANCA positive RPGN - 40-50% RPGN
    - Wegener's granulomatosis
    - microscopic polyangiitis (MPA)
- with antibodies against basement membrane
  - anti-GBM RPGN- 10 % - Goodpasture syndrome

Diagnostics

- Laboratory examination:
  renal parameters
  blood count + C3, C4, autoantibodies
  urine / 24 hours or sample
- USG
- renal biopsy - light microscopy, immunofluorescence, ELMI

Therapy

- Corticotherapy - pulses, continued p.o.
- Cyclophosphamide - pulses, p.o. (Uromitexan- MESNA)
- Plasmaexchange or immunoadsorption
- Biological therapy (infliximab- anti-TNFa, rituximab- anti CD20, eculizumab- anti C5)

ANCA-associated RPGN

- ANCA-antibodies against neutrophil cytoplasm
- ANCA-associated vasculitis- small and medium caliber vessels
- upper and lower respiratory tract involvement with formation of necrotizing granulomas + RPGN
- histological finding:

  light microscope - severe involvement of glomeruli

  <50% crescent

  IF: negative finding -> pauciimmune GN

Pathogenesis

- primary site of affection - endothelium
- pro-inflammatory stimulus -> cytokine release (TNF alpha), neutrophil- PR-3 and MPO expression -> activation of endothelial cells, neutrophil adherence and their penetration into tissues, release of PR-3 and MPO -> endothelial damage

Wegener granulomatosis

- c-ANCA antibodies positivity against proteinase-3 in neutrophil cytoplasm
- small and medium arteries

Diagnostic criteria:

- upper respiratory tract: ulceration, purulent or haemorrhagic rhinitis
- lower respiratory tract: finding of nodules, infiltrates or cavities on X-ray
- renal involvement: microscopic hematuria with / without leukocyturia up to necrotizing GN - in 75% of patients
- granulomatous inflammation of vessel walls and perivascular area

Microscopic polyangiitis MPA

- positivity of p-ANCA antibodies against myeloperoxidase
- blood vessels of small to medium caliber
- focal segmental necrotizing GN in 90% of patients
- in the airways without formation of granulomas
- symptoms MPA:
  rhinitis, sinusitis, otitis, pneumonia not responding to ATB therapy
- RPGN
- skin manifestations - purpura, nodules, papules
- peripheral neuropathy
- myalgia, arthralgia- arthritis of middle and large joints

Churg-Strauss syndrome Eosinophilic granulomatosis with polyangiitis

- asthma, allergic rhinitis, eosinophilia
- RPGN at 25-50%
- neuropathy
- pulmonary infiltrates
- sinusitis
- therapy:
  systemic steroids, cyclophosphamide, methotrexate, mycophenolate mofetil, azathioprine
  RTX, IVIG, plasmaexchange

RPGN with antibodies against basement membrane

- antibodies against basement membrane of glomeruli – anti-GBM
- cross-reactivity with basement membrane of alveoli - pulmo-renal syndrome - Goodpasture syndrome
- predominantly affects men - smokers
- manifestations: RPGN and pulmonary involvement with bleeding
- histology: high lienar positivity of IgG in IF
- treatment: cyclophosphamide i.v., corticoids i.v., plasmapheresis, immunoadsorption

  biological treatment: infliximab, rituximab, eculizumab
- prognosis: frequent chronic renal insufficiency or failure

Glomerulonephritis in systemic LE

- part of SLE
- systemic immunocomplex hypocomplementary disease
- 90% women, incidence 1: 700, in children 1: 7 000
- creation of antibodies against the cell nucleus DNA
- complement is activated by the classical way - C3 and C4
- autoantibody positivity:
  ANA-antinuclear antibodies
  dsDNA- against DNA
  anti-Sm positivity
  anticardiolipin antibodies
  positive lupus anticoagulans

Criteria for SLE: ACR - fulfill 4 of 11, SLICC criteria - fulfill 4 of 17 criteria - (1 clinical, 1 immunological or lupus nephritis in biopsy)

1. butterfly exanthema
2. photosensitivity
3. discoid rush
4. oral ulceration
5. arthritis
6. serositis: pleural, pericardial
7. renal impairment:
   proteinuri >500 mg/day
   presence of rollers
8. neurological disability:
   convulsions, psychosis

9. haematological disability:
   hemolytic anemia
   leucopenia <4 th.
   lymphopenia <1.5 th.
   thrombocytopenia <100th.
10. ANA positivity
11. immunological symptoms:
   anti-dsDNA positivity
   anti-Sm positivity
   anticardiolipin antibodies
   positive lupus anticoagulans
   positive treponema tests

Lupus nephritis- histology

I.class: normal histological picture
II. class: mesangial glomerulonephritis
III. class: focal and segmental proliferative glomerulonephritis
IV. class: diffuse proliferative glomerulonephritis
V.class: membranous glomerulonephritis
VI. class (most severe): advanced chronic sclerosing glomerulonephritis

Immunofluorescence: IgG, IgA, IgM, C3, C1q

„full house"

ELMI:

polyvalent localization of immunodeposites

Treatment of lupus nephritis

- according to the degree of renal impairment
- class I and II with proteinuria <1 gr/m2.day-> symptomatic therapy - ACEi, ARB

- class II with proteinuria > 1 gr/ m2.day -> corticoids, calcineurin inhibitors

- class III and IV -> loading therapy: corticoid pulses + cyclophosphamide or mycophenolate mofetil
  -> maintenance therapy: mycophenolate m. + low dose corticoids

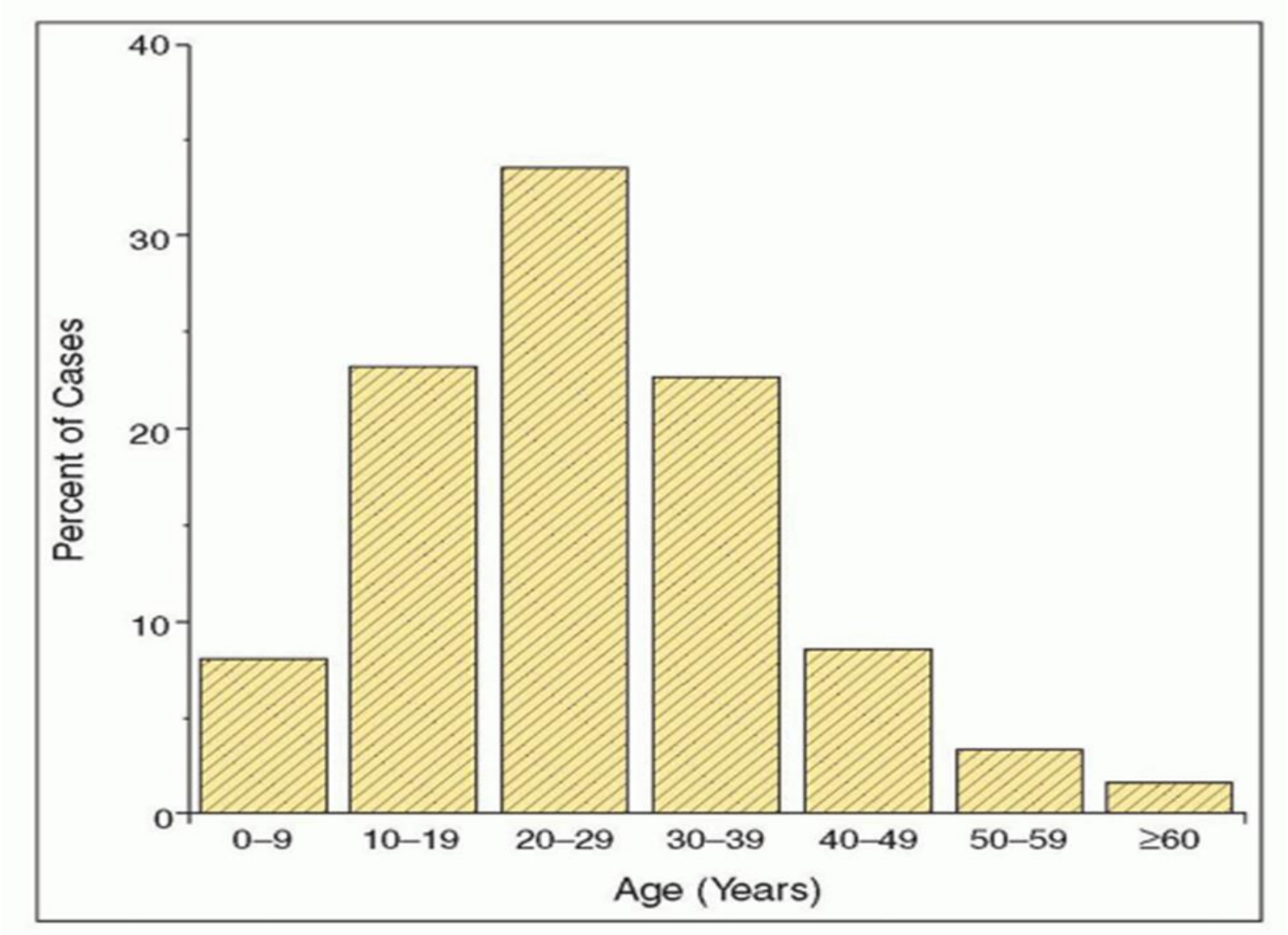
- class V without GFR disorder and nephrotic proteinuria -> ACEi, ARB
  class V with nephrotic proteinuria-> cyclophosphamide,mycophenolate m.,corticoids

- class VI - treatment of extrarenal manifestation

IgA nephropathy (Berger's disease)

- autoimmune diseases
- immunocomplex GN
- manifestations : microscopic hematuria -> RPGN
- IgA mesangioproliferative GN
- the most common primary GN in both children and adults
- incidence most often in the 2nd to 3rd decen
- male to female ratio 2:1
- most common in Asia, rare in blacks
- 20-30% progression to chronic renal failure
- graft recurrence after kidney transplantation

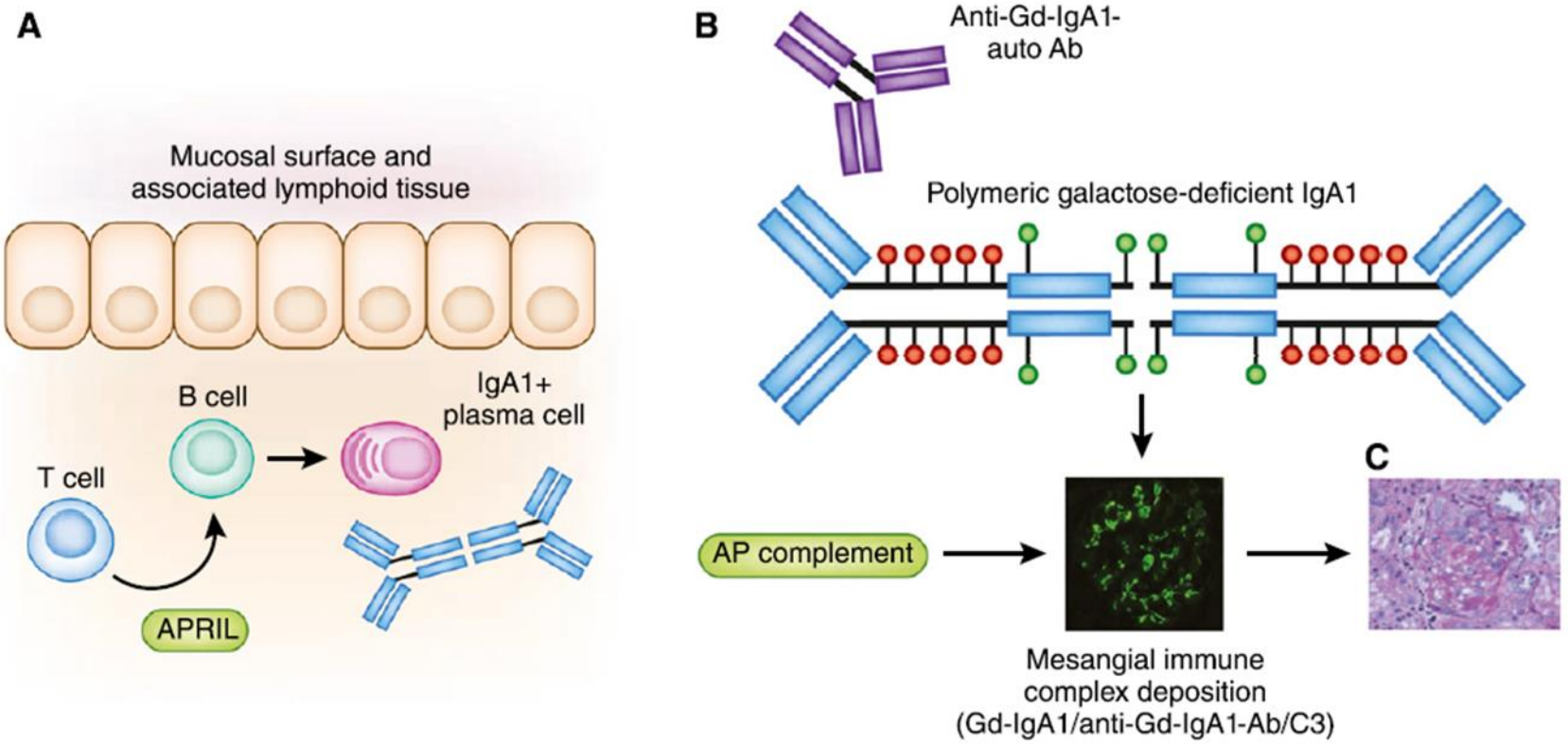
IgA nephropathy (Berger's disease)



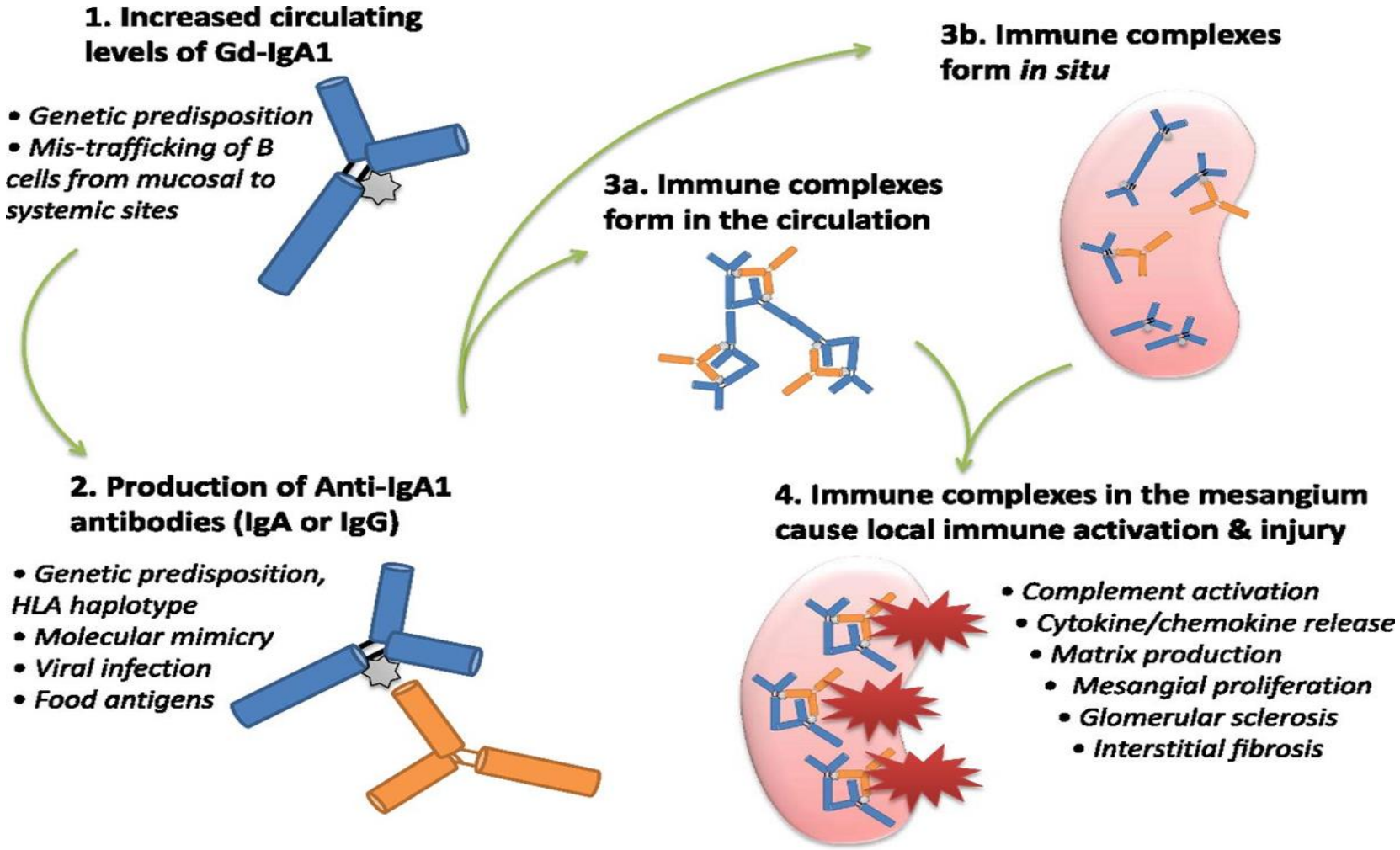
IgA nephropathy- pathogenesis

- genetically determined elevated levels of circulating IgA1 with O-glycosylation deficiency in the hinge region of the IgA1 molecule -> decreased terminal galactose content
- circulating IgG antibodies against deficient IgA1
- formation of IgA1 immunocomplexes
- deposition of IgA1 immunocomplex deposits into mesangium, activation of mesangium cell proliferation and initiation of glomerular damages

IgA nephropathy- pathogenesis



Pathogenesis of IgA nephropathy: a proposed multistep model of IgA nephropathy, demonstrating the interaction of genetics, environmental factors, and both innate and acquired immunity



Symptomatology of IgA nephropathy

- intermittent recurrent hematuria often in relationship with mucosal infections, pain in the lumbar areas, GFR-normal or lower, BP-normal or higher
- microscopic hematuria with / without mild proteinuria, decreased GFR, hypertension
- nephritic syndrome with severe proteinuria
- nephrotic syndrome
- RPGN with edema, hypertension, decreased GFR, oliguria

Oxford classification

Table 8 | Recommended elements in renal biopsy report for a case of IgA nephropathy

Detailed description of the features present on
- Light microscopy
- Immunohistochemistry
- Electron microscopy

Summary of four key pathological features
- Mesangial score $\leqslant$0.5 (M0) or $>$0.5 (M1)
- Segmental glomerulosclerosis absent (S0) or present (S1)
- Endocapillary hypercellularity absent (E0) or present (E1)
- Tubular atrophy/interstitial fibrosis $\leqslant$25% (T0), 26–50% (T1), or $>$50% (T2)

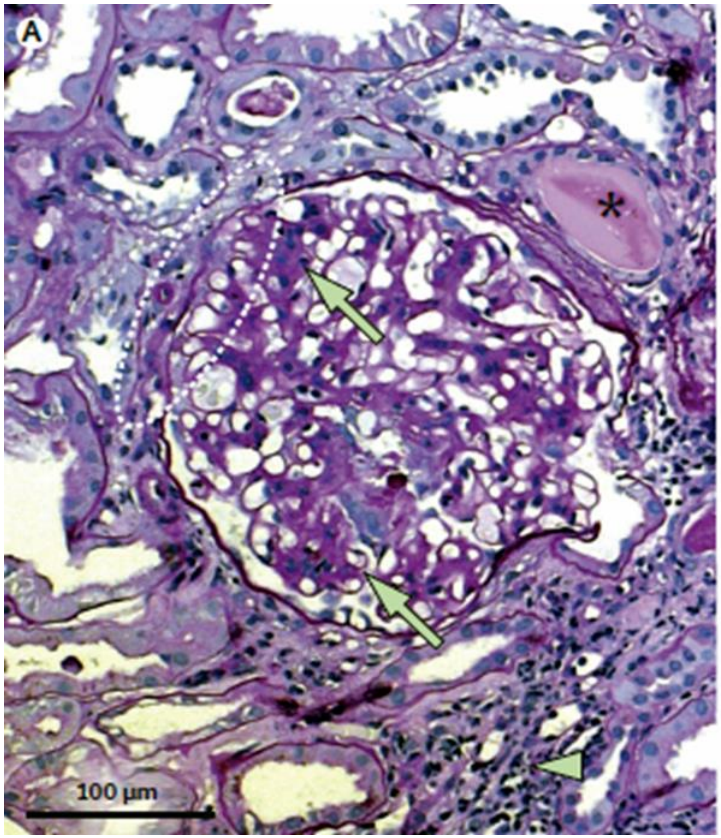
Total number of glomeruli

Number of glomeruli with endocapillary hypercellularity, extracapillary proliferation, global glomerulosclerosis, and segmental glomerulosclerosis

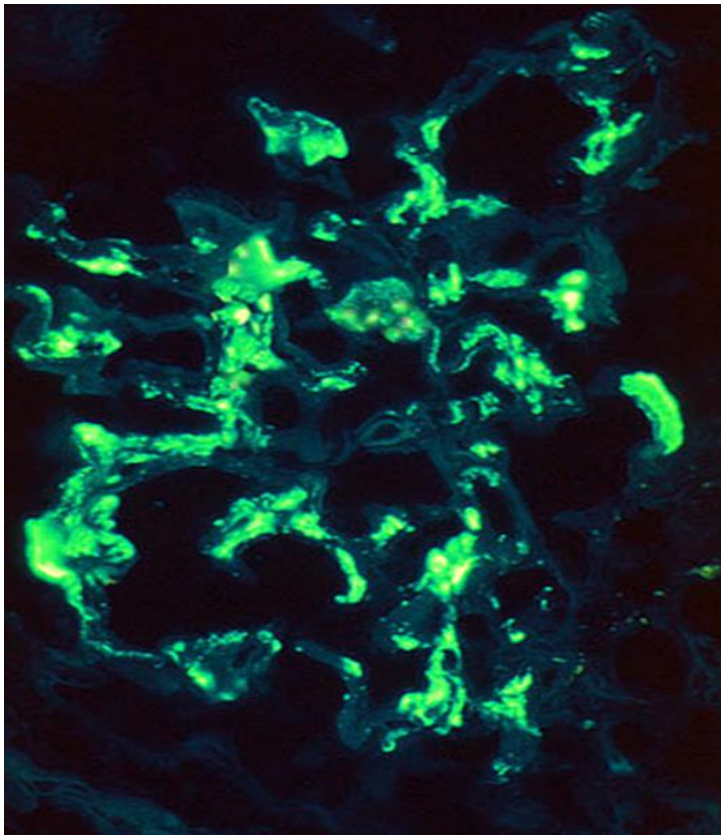
Catran DC et al. Kidney Int. 2009;76:534-545

Histology of IgA nephropathy

Mesangial proliferation, adhesion to Bowman's capsule



Immunofluorescence IgA



Course of IgA nephropathy

- remission
- Iidolent - non-progressive
- progressive
- RPGN
- 50% asymptomatic - lower GFR, hypertension, proteinuria
- 10-30% of ESRD under 10 years, 40% under 20 years
- 50 years - median age of initiation of dialysis

Treatment of IgA nephropathy

- Symptomatic:

  - BP control - antihypertensive therapy
  - reduction of proteinuria - ACEi, angiotensin II ARB blockers
  - fish oil

- Immunosuppressive therapy:
  - glucocorticoids, cyclophosphamide,
  - mycophenolate mofetil?, cyclosporin A?

Treatment strategies:

1) isolated hematuria, proteinuria <500 mg / day, normal GFR
   -> regular follow-up, eventually ACEi, ARB, fish oil

2) persistent proteinuria, normal or slightly reduced GFR ->
   regular follow-up , ACE, ARB, fish oil

3) RPGN -> immunosuppressive therapy

Treatment stragedy Coppo R. JASN. 2016. 28:25-33

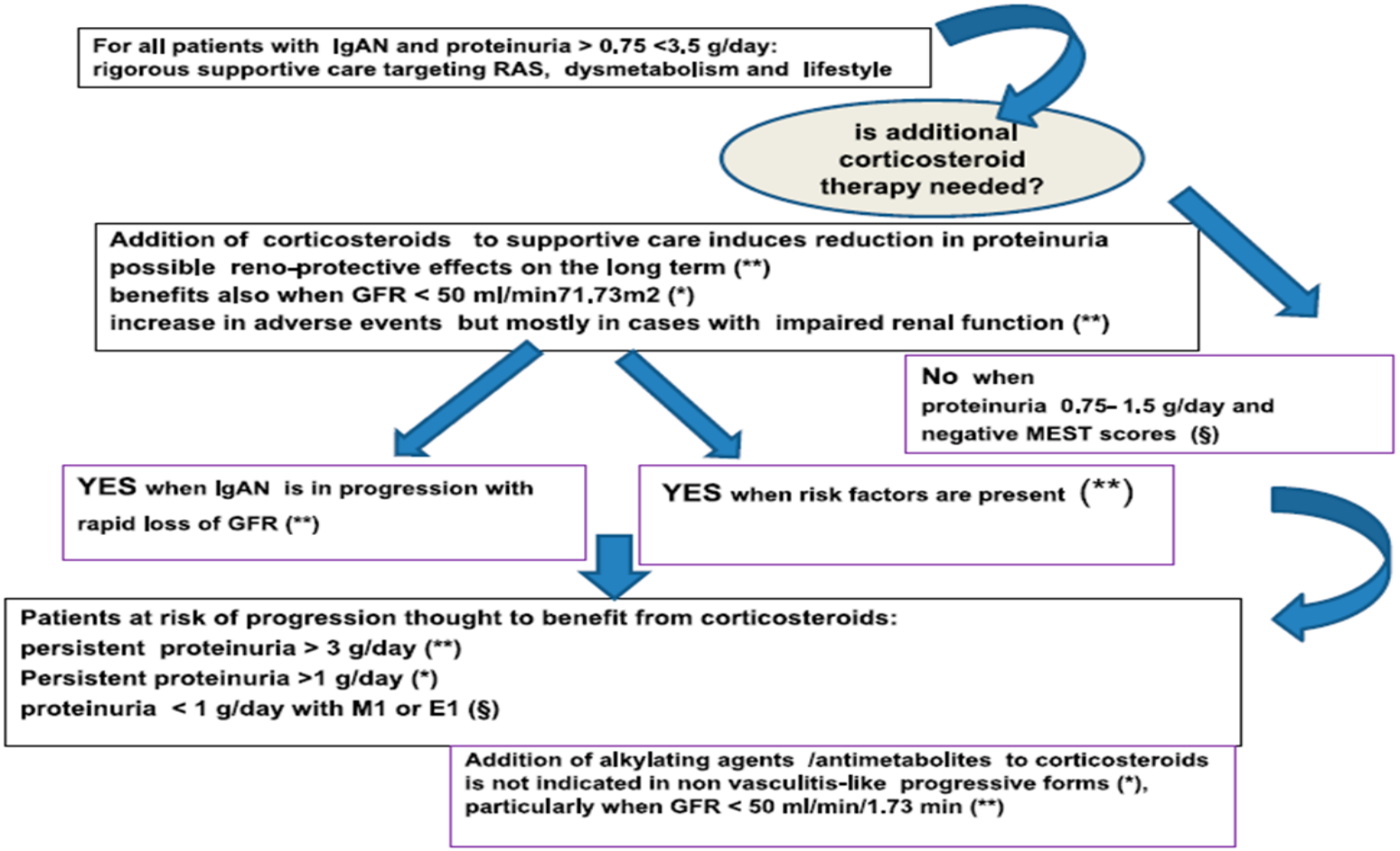


Figure 1. A proposed flow chart for treatment of IgAN on the basis of recent results from RCTs and large retrospective observational studies. RAS, renin-angiotensin system. *Consistent indication. **Strong indication. §Suggestion.

J Am Soc Nephrol 10: 1772–1777, 1999

The Long-Term Outcome of Patients with IgA Nephropathy Treated with Fish Oil in a Controlled Trial

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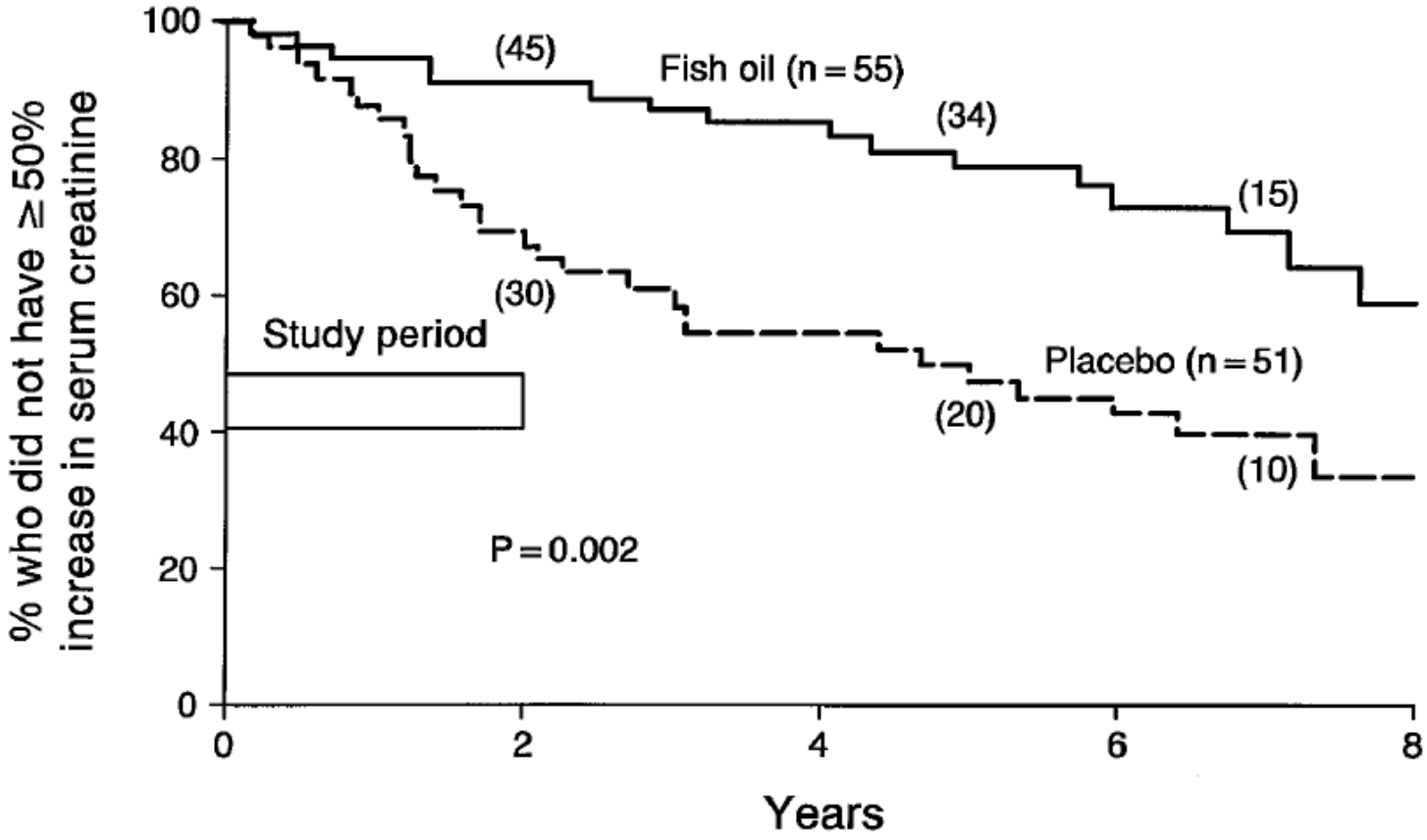
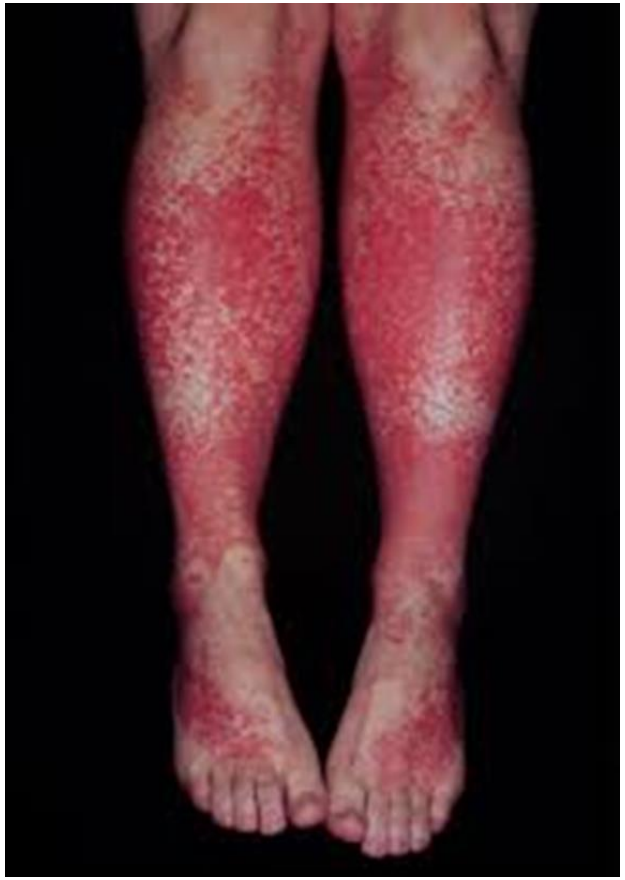


Mesangioproliferative glomerulonephritis in Henoch-Schönlein purpura

- secondary IgA-mesangioproliferative GN
- histologically typical focal segmental proliferation of mesangium
- part of the symptomatology of H-SchP (vasculitis - small vessels):
  - fever
  - anorexia
  - purpura - predilection legs and gluteal area
  - abdominal pain, bloody stools
  - joint pain - knees, ankles
  - edema
- IgA in serum, circulating IgA immunocomplexes
- IgA deposits in the vascular wall and renal mesangium



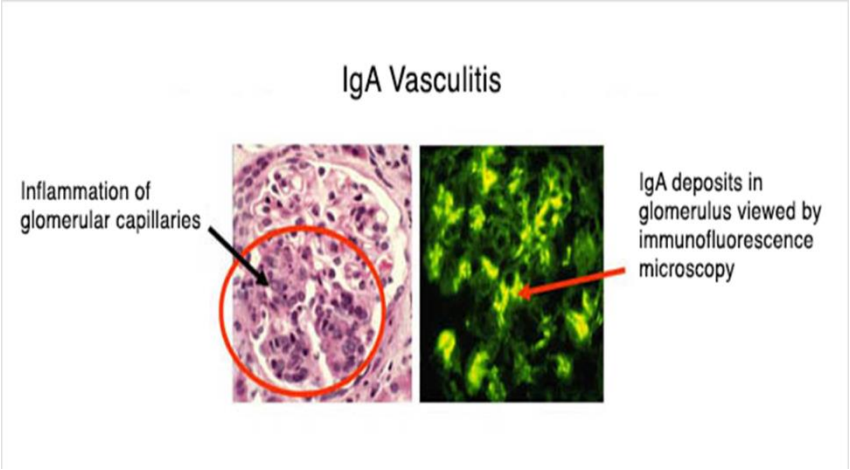
Renal impairment in HSchP

Histological findings:

glomerular demage, mesangial hypercelulization, endocapillary lesions, proliferation, cellular crescent, necroses, mononuclear and neutrophil infiltration

Immunofluorescence:

deposits IgA1,
rarely IgA2, IgG, IgM
C3 and fibrin



Renal impairment in HSchP

Urinary finding:

- before eruption of skin lesions X simultaneously with eruption of skin lesions
- persistent finding up to 6 months after eruption of skin lesions
- microscopic X macroscopic hematuria

- mild to nephrotic proteinuria

- development of hypertension

- occurrence in 50% of children with onset of HSchP
- serious course of 10% of children
- ESRD 2-5%

Management of HSchP

- „self-limited disease ”- mostly supportive treatment
- follow-up : every week for the first month, and 2 weeks for the second month, then and 1 month -> abnormal urine finding
- hospitalization: severe abdominal pain and acute abdomen
  bleeding into the GIT
  more severe renal impairment
- treatment:

  painkillers, antipyretics
  corticoids - nephrotic sy, more than 50% crescent
  - severe abdominal pain, GIT bleeding
  - severe edema, severe edema of the scrotum
  - neurological symptoms

  prednisone 1 mg / kg.day 2-4 weeks

Treatment of severe course HSchP

- intensive immunosuppressive therapy
  methylprednisolone pulses
  cyclophosphamide
  long-term prednisone
  azathioprine, cyclosporine A
- IVIG
- rituximab
- plasmaexchange

Prognosis

complete remission within 8 weeks
5% chronic course
1-2% ESRD

Chronic glomerulonephritis

- low progression - months to years
- indications for biopsy according to the degree of erythrocyturia and proteinuria
- glomeruli impairment: all glomeruli - diffuse GN
  some glomeruli - focal GN
- glomerulus disability:

  all capillary loops - global GN
  some capillary - segmental GN

- cell and mesang mass multiplication: non-proliferative
  proliferative
- localization of proliferation:

  endocapillary
  extracapillary - Bowman capsule -> crescents

Mesangioproliferative GN - MaPGN

- proliferation of mesangial cells and mesangial mass
- mild proportional erythrocyturia and proteinuria
- proteinuria can be nephrotic
- edema and hypertension
- indication of biopsy:

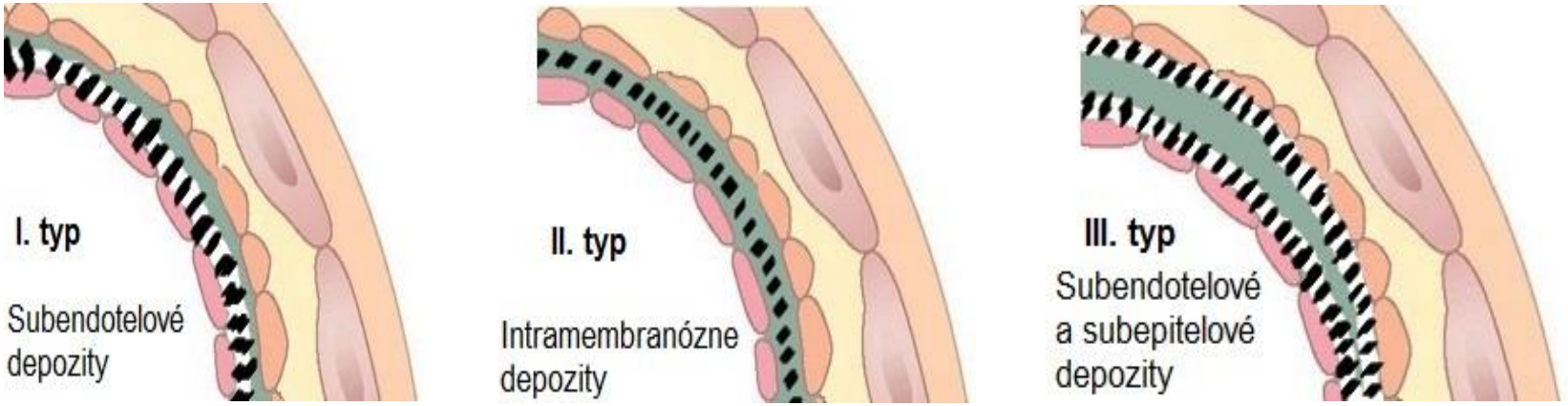
  nephrotic syndrome
  repeated attacks of macroscopic hematuria
  renal impairment

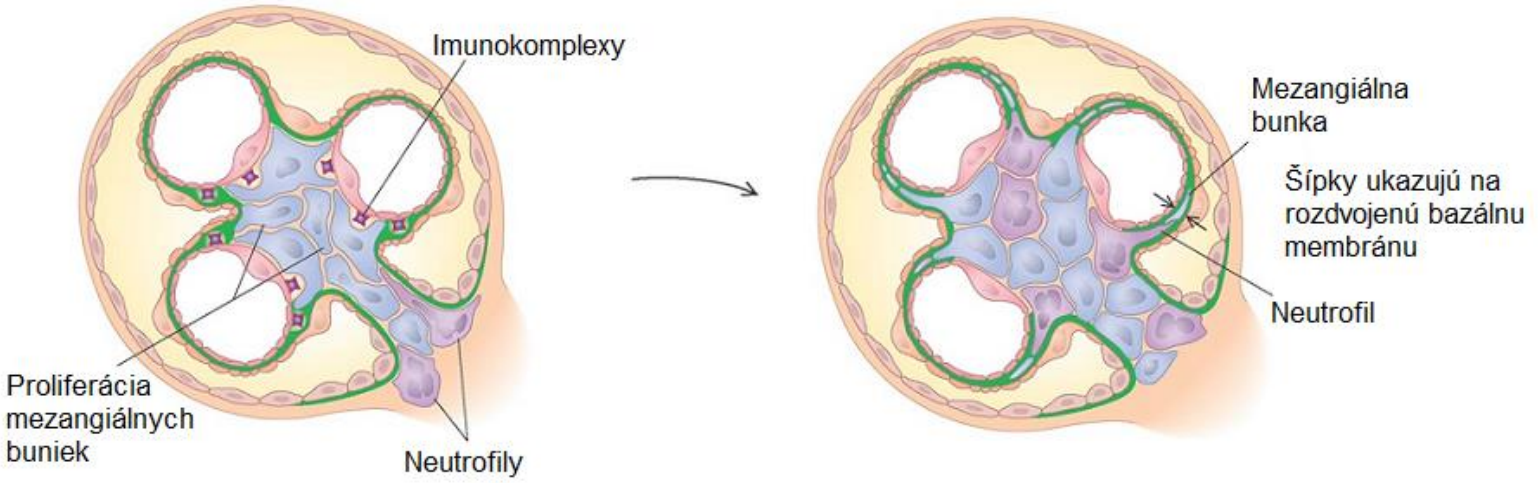
Distribution: IgA- MaPGN
non-IgA MaPGN

Membranoproliferative GN - MPGN

- hypocomplementary GN
- manifestation of 50% of cases in childhood (6-12 years)
- enhancement of mesangium into periphery of capillary loop and thickening of basement membrane, deposition of immunodeposites

- distribution
  type I - subendothelial
  type II - intramembranous = deposite dense disease DDD (C3 glomerulopathy)
  type III- subepithelial

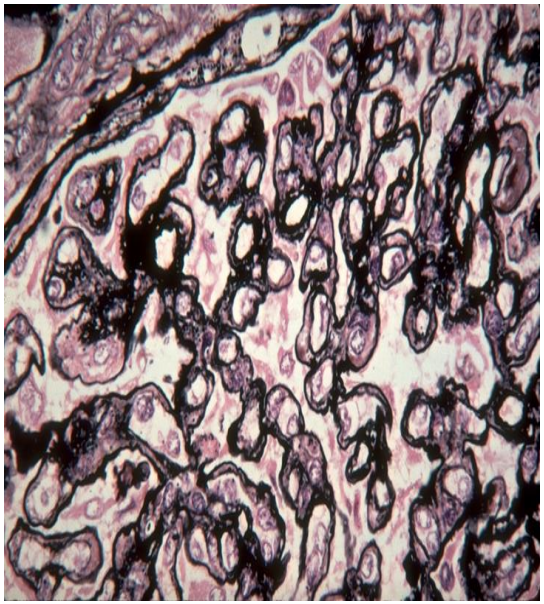

I. typ
Subendotelové depozity
II. typ
Intramembranózne depozity
III. typ
Subendotelové a subepitelové depozity

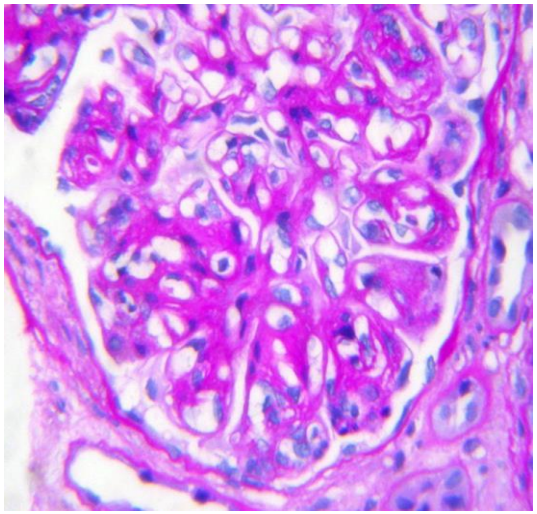

Imunokomplexy
Proliferácia mezangiálnych buniek
Neutrofily
Mezangiálna bunka
Šípky ukazujú na rozdvojenú bazálnu membránu
Neutrofil

C3 glomerulopathy

- dysregulation of alternative complement pathway
- depositing of C3 degradation products (C3d)
  -> endocapillary and extracapillary proliferation
- clinical picture:
  nephritic syndrome
  proportional erythrocyturia and proteinuria
  (non-selective glomerular)
  macroscopic hematuria, hypertension
  permanent reduction of C3
- therapy:
  corticosteroids, eculizumab (anti-C5 antibody),
  antihypertensives

Histological findings





Glomeruli:
- enlarged, increased cellularity
- glomerular infiltration by monocytes and neutrophils
- GBM enhancement at the periphery of the glomerulus
- double line impregnated with silver

Tubules:
- protein and lipid desposity in the epithelium of the canals
- tubular atrophy

Intersticium:
- fibrosis, foam cells
- inflammatory infiltration

Changes in blood vessels:
- sclerotization
- signs of vasculitis

2012

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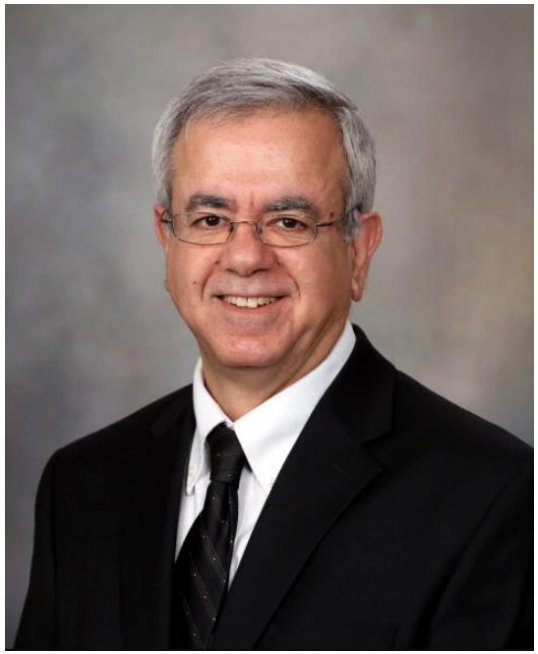
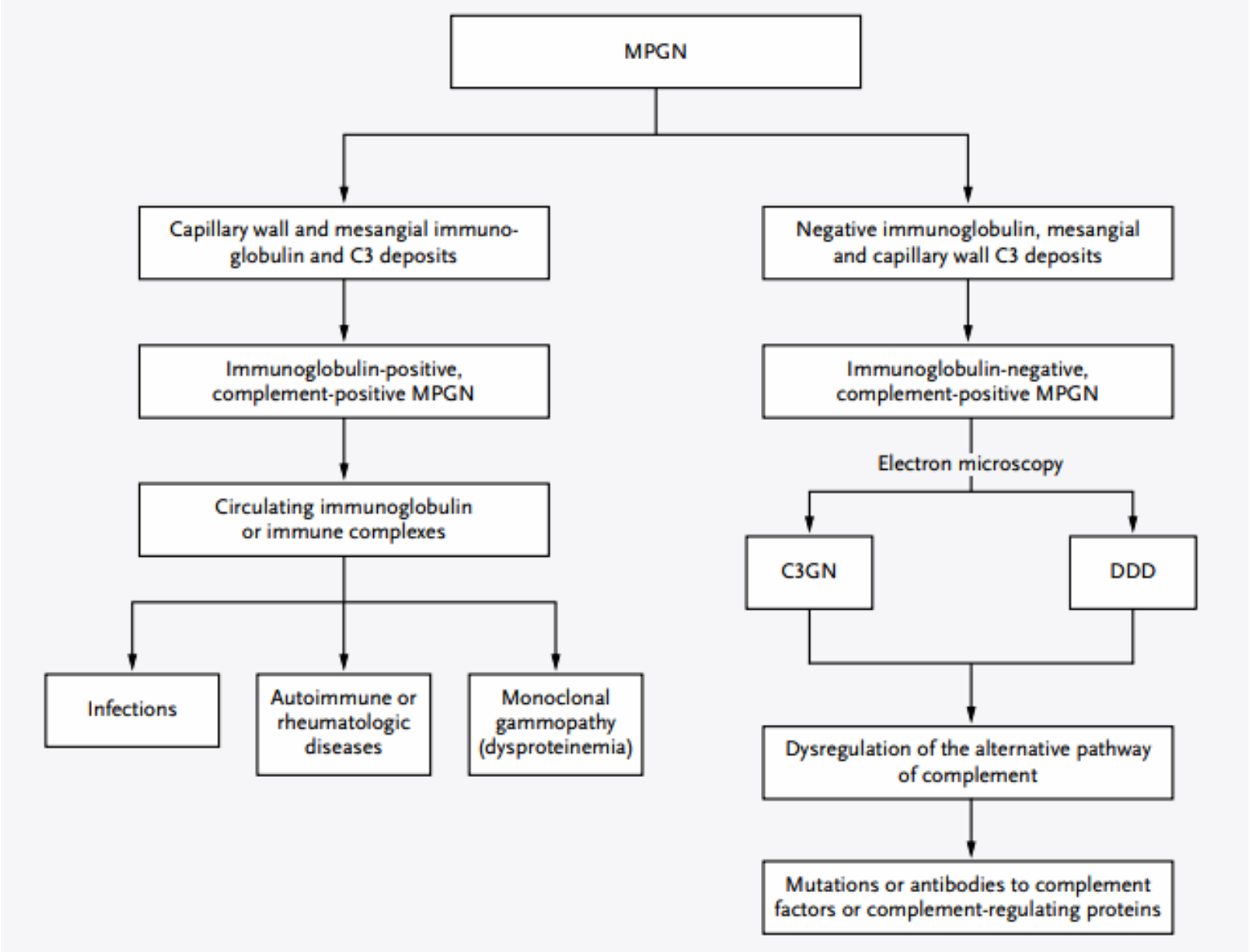
REVIEW ARTICLE

MEDICAL PROGRESS

Membranoproliferative Glomerulonephritis — A New Look at an Old Entity

Sanjeev Sethi, M.D., Ph.D., and Fernando C. Fervenza, M.D., Ph.D.





IMMUNOGLOBULIN POSITIVE

COMPLEMENT POSITIVE

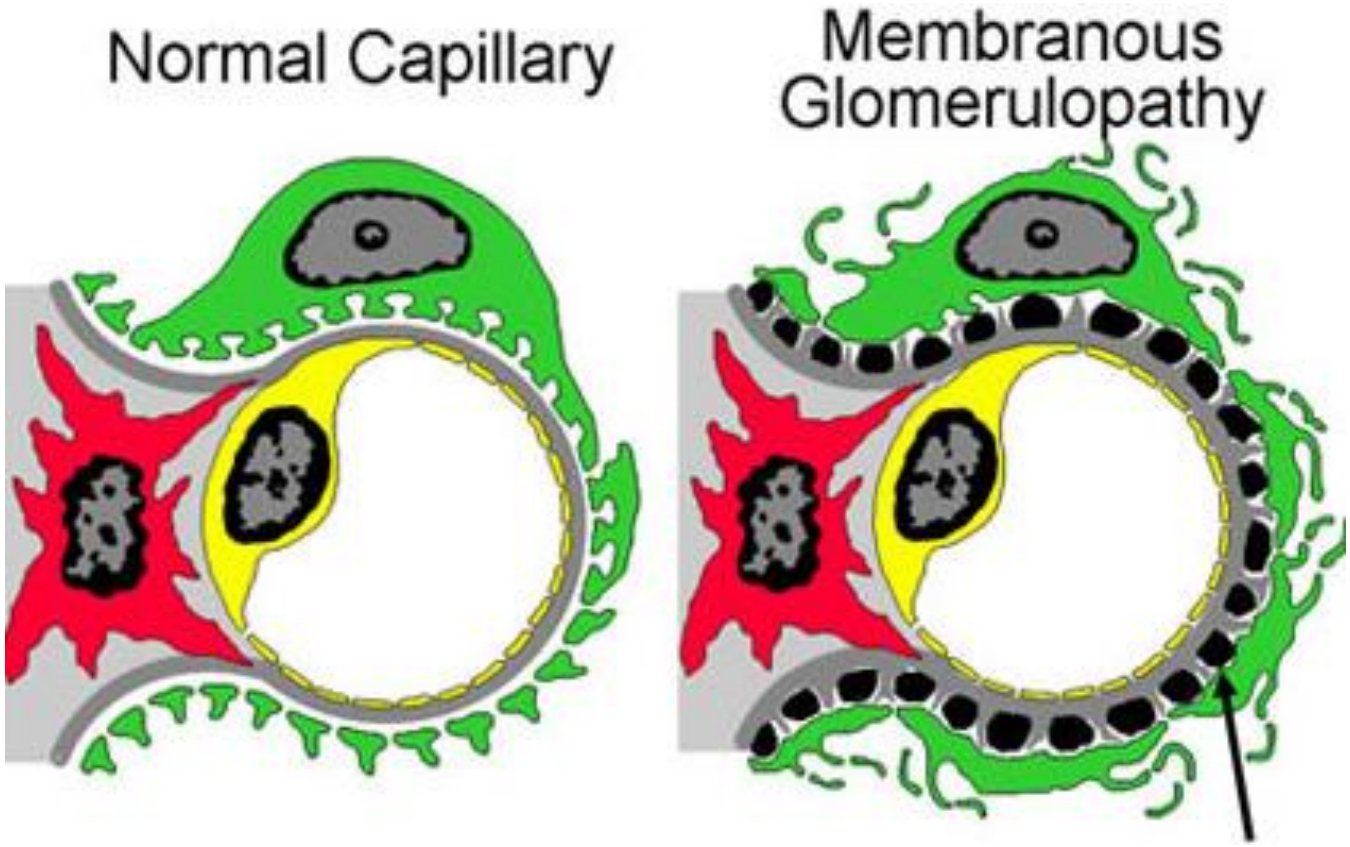
Membranous glomerulonephritis

- rare in childhood
- the most common cause of nephrotic syndrome in adults in the European population

- etiology: - primary (idiopathic)
  - secondary:
    -> infection:
    hepatitis B, syphilis cong.
    -> autoimmune diseases
    -> drugs, neoplasms

Urinary finding: non-selective proteinuria with mild erythrocyturia

Corticoresistant nephrotic syndrome
Hypertension in 20-25% of patients
Possible asymptomatic course
Anti-THSD7A antibodies– in 20% of patients

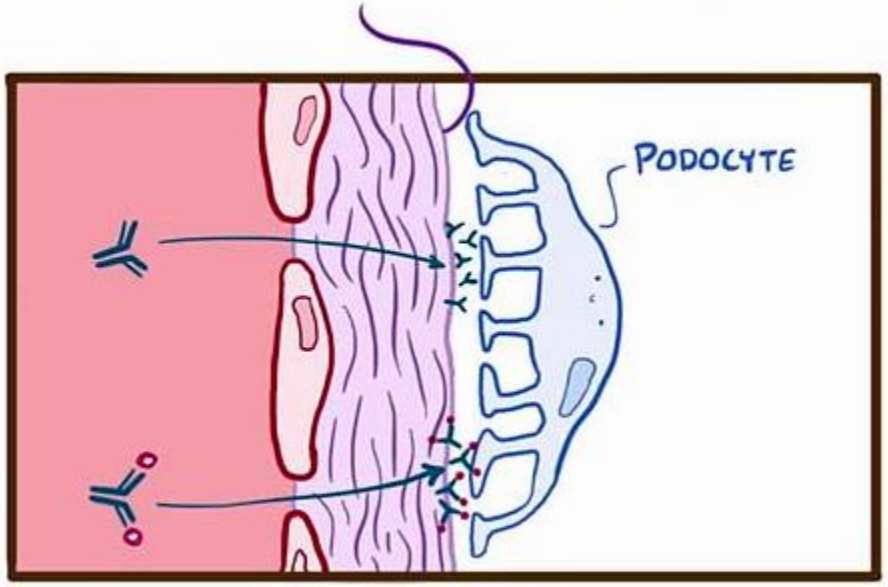

Normal Capillary
Membranous Glomerulopathy

IMMUNE COMPLEXES

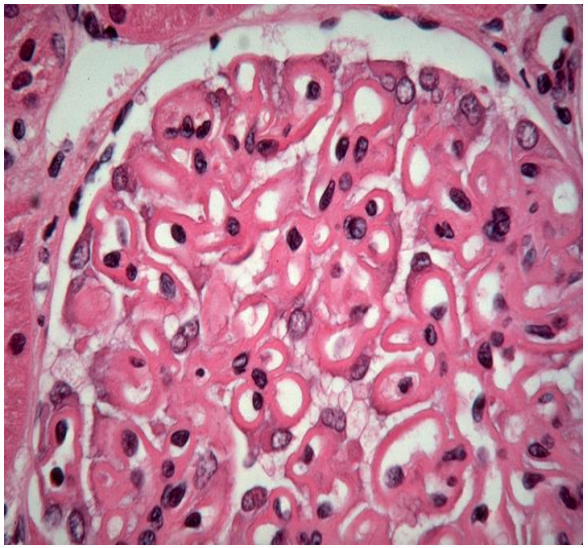
ANTIGEN – ANTIBODY

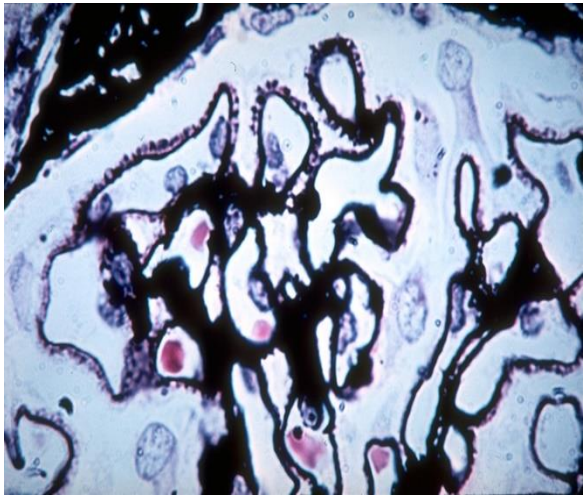
* **AUTOANTIBODIES** targeting **GBM**
  - M-type phospholipase A2 receptor
  - Neutral endopeptidase
* **FORM OUTSIDE KIDNEY** & Carried to **GBM**
  - Cationic bovine serum albumin

FROM COW'S MILK & BEEF PROTEIN → ESCAPES INTESTINAL BARRIER



Histological findings





- normal cellularity of the glomerulus
- thick GBM
- spikes and rings when staining with silver
- various interstitial fibrosis
- interstitial foam cells may or may not be present
- subepithelial localization of deposits between the basement membrane and the podocytes

Diagnostics

- anti PLA2R antibodies indirect immunofluorescence - good sensitivity but semiquantitiative
- ELISA - lower sensitivity, accurate quantification, 100% specificity for membranous GN
- kidney biopsy - PLA2R staining - 30% has negat. antiPLA2R antibodies in serum
- immunological remission

Treatment of MGN

- asymptomatic proteinuria, without hypertension, edema and decrease in GFR
  - > without treatment

- nephrotic proteinuria in primary MGN
  - corticoids, cyclosporin A, mycophenolate mofetil

Prognosis

20% progression to chronic renal failure
Secondary forms - often spontaneous remissions
Dispensarization required

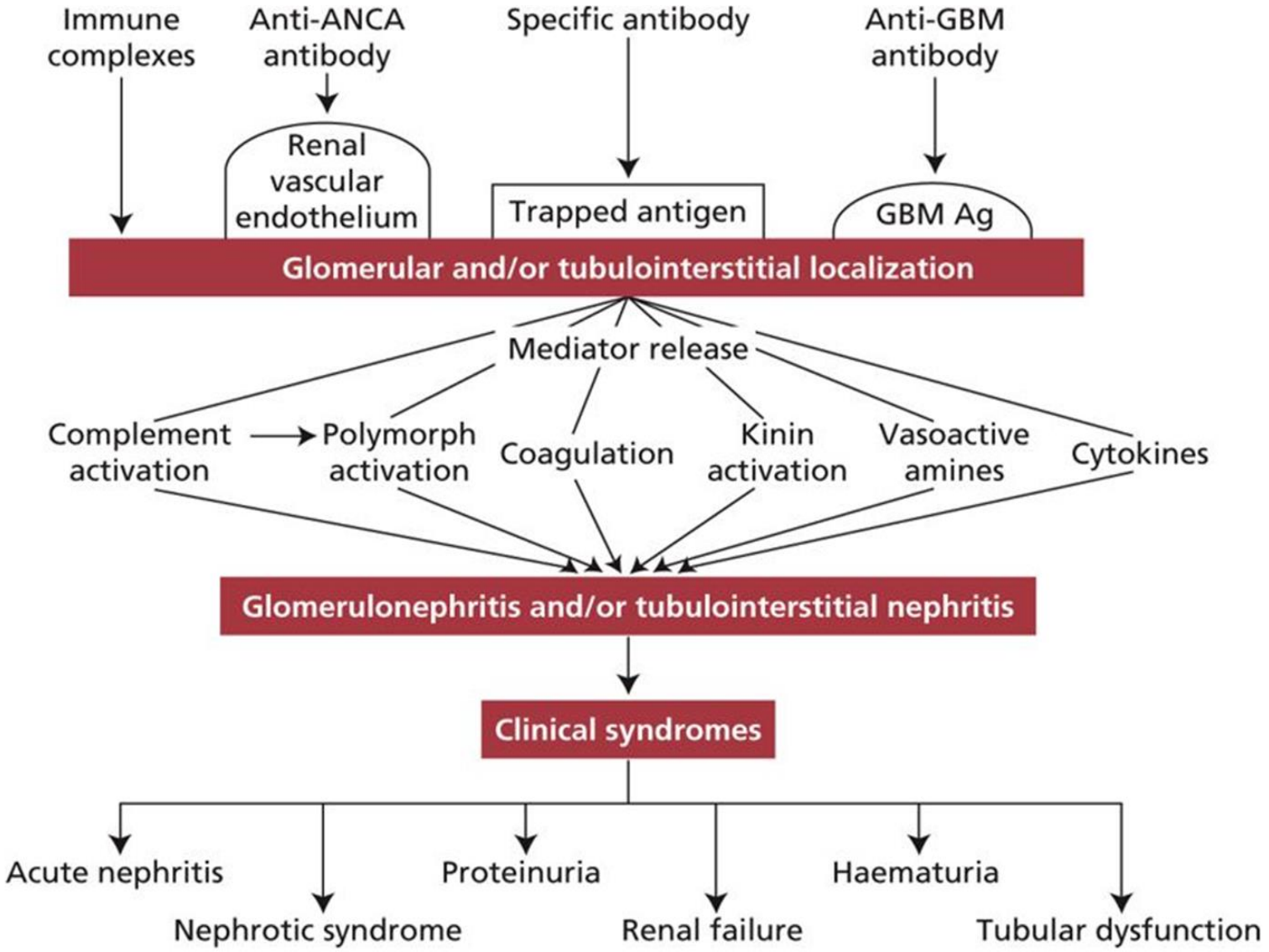
Course

- 20 - 30% spontaneous remission
- 30-40% progression to the ESRD
- Adverse forecasting factors:

  - age > 50 years, male, hypertension, proteinuria, decreased GFR

  - antiPLA2R antibodies – marker of pre-spontaneous remission

Summary


Immune complexes
Anti-ANCA antibody
Specific antibody
Anti-GBM antibody
Renal vascular endothelium
Trapped antigen
GBM Ag
Glomerular and/or tubulointerstitial localization
Mediator release
Complement activation
Polymorph activation
Coagulation
Kinin activation
Vasoactive amines
Cytokines
Glomerulonephritis and/or tubulointerstitial nephritis
Clinical syndromes
Acute nephritis
Nephrotic syndrome
Proteinuria
Renal failure
Haematuria
Tubular dysfunction