PATHOLOGY OF THE KIDNEYS

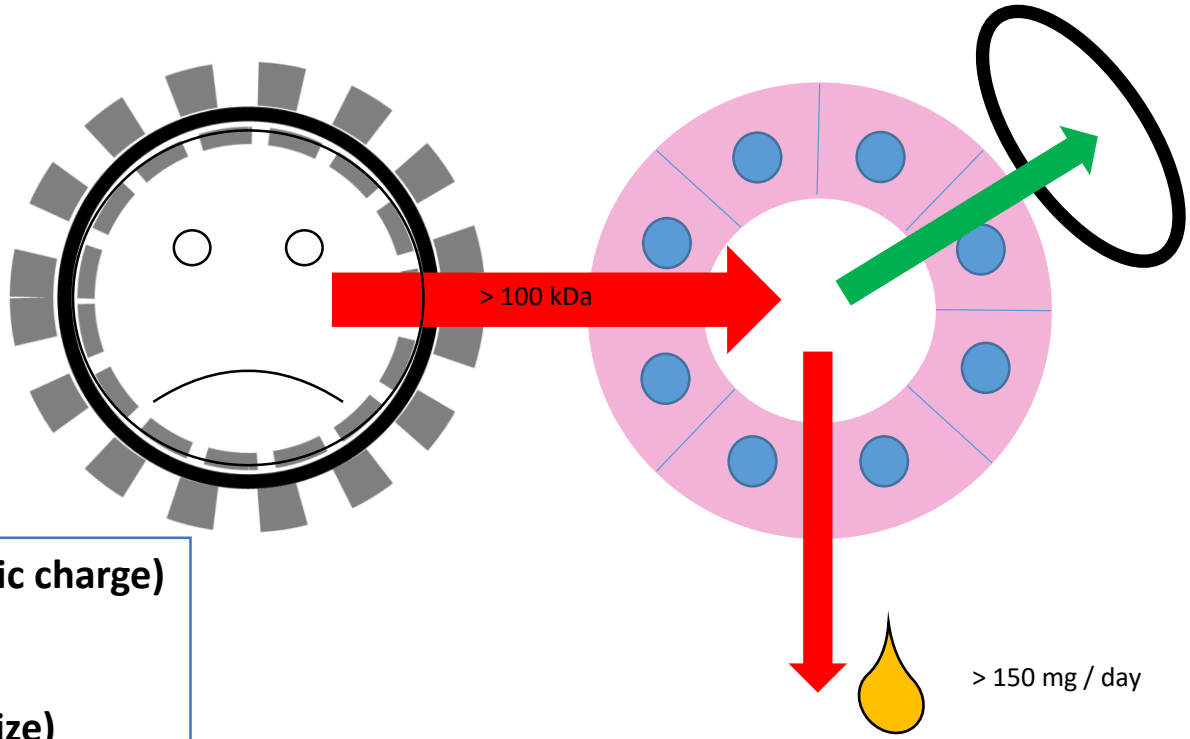
CLINICAL MANIFESTATIONS OF RENAL DISEASES

CLINICAL MANIFESTATIONS OF RENAL DISEASES

- Kidneys don‘t hurt
- Many renal diseases don‘t have any clinical symptoms in the early stages

1) Diseases with isolated/predominant PROTEINURIA
2) Diseases with isolated/predominant HEMATURIA
3) Diseases with a combination of proteinuria and hematuria
4) Renal insufficiency / kidney failure

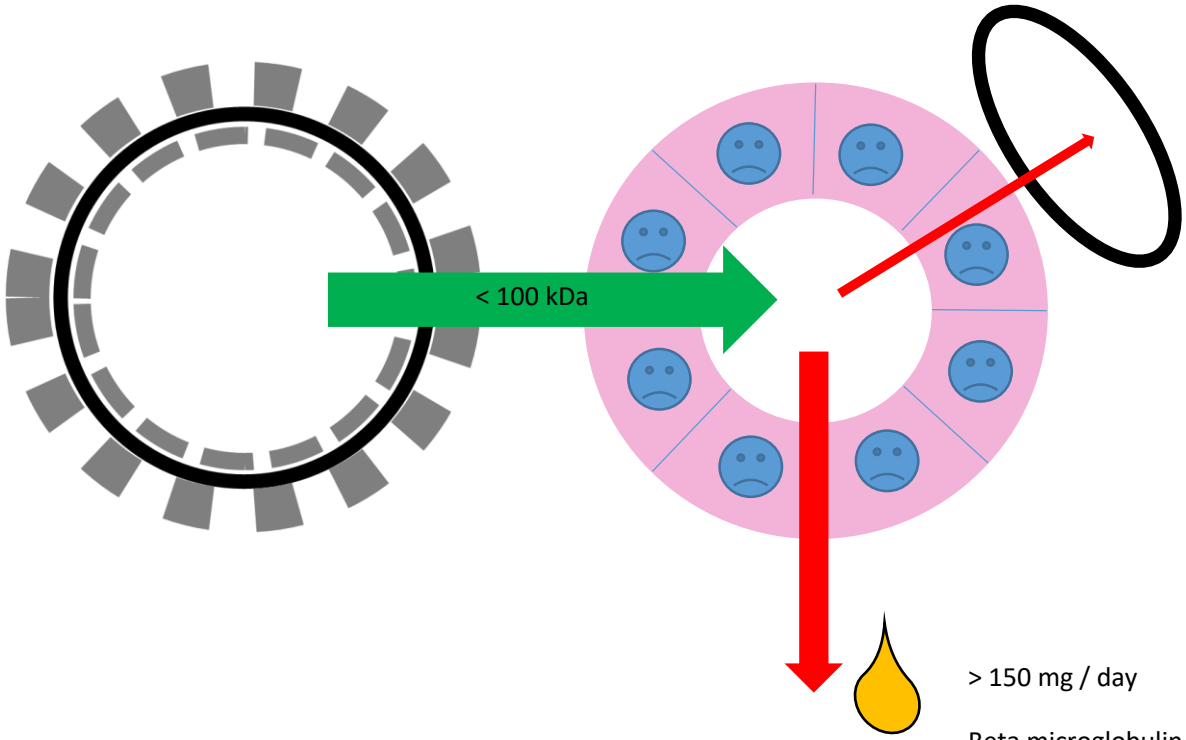
PROTEINURIA glomerular



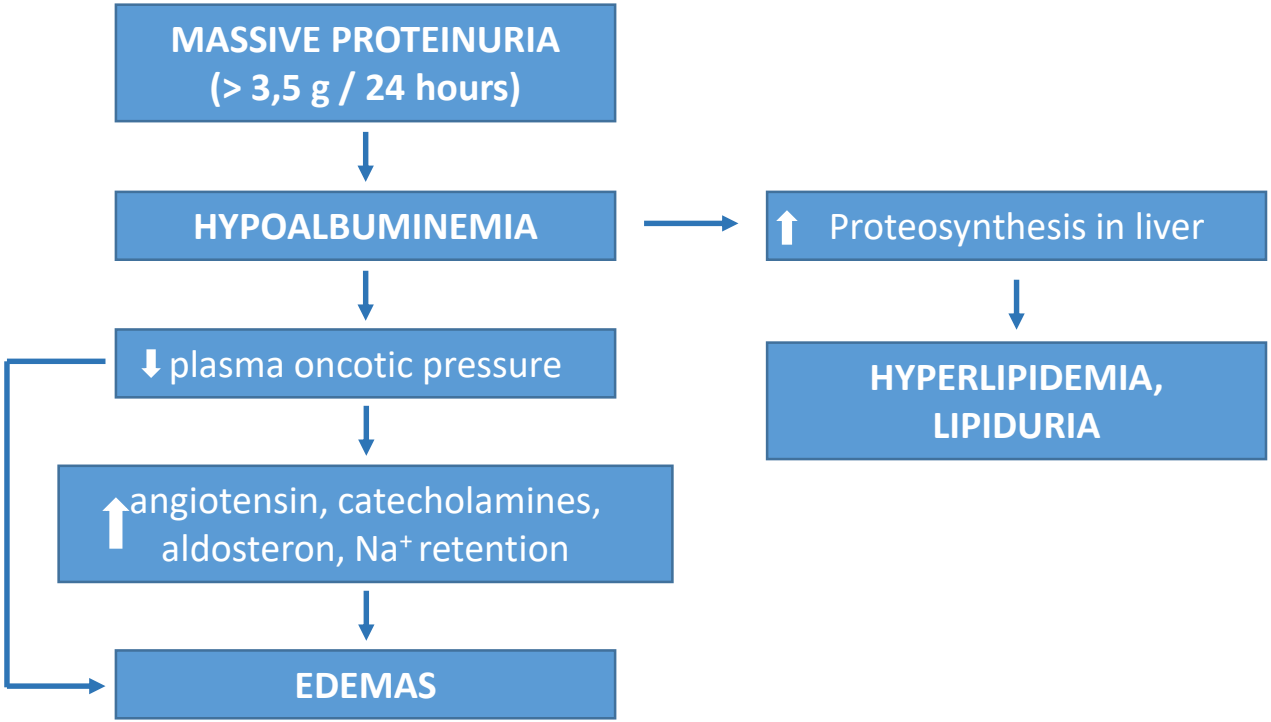
selective (electric charge)
albumin

non-selective (size)
albumin + imunoglobulins

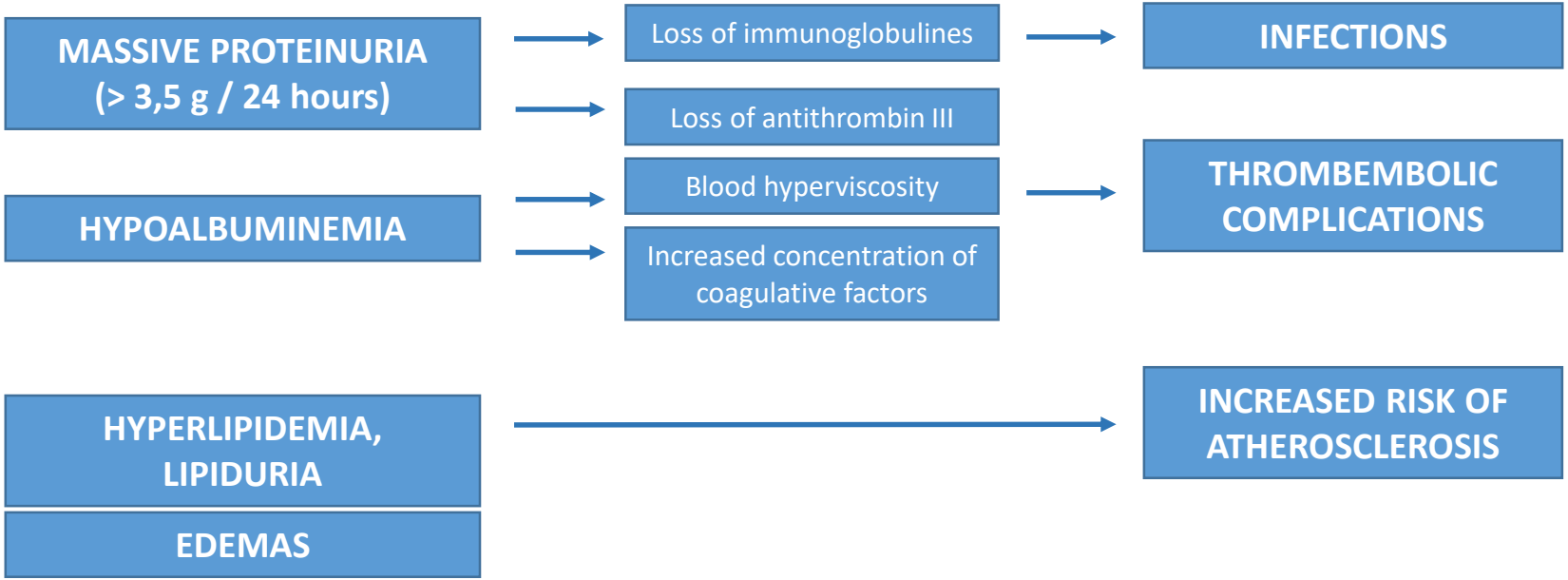
PROTEINURIA tubular



NEPHROTIC SYNDROME



NEPHROTIC SYNDROME



NEPHROTIC SYNDROME

Primary glomerular disorders
- MINIMAL CHANGE DISEASE
- FOCAL-SEGMENTAL GLOMERULOSCLEROSIS
- MEMBRANOUS GLOMERULOPATHY

Secondary glomerular disorders
- DIABETES MELLITUS
- AMYLOIDOSIS
- SYSTEMIC LUPUS ERYTHEMATODES

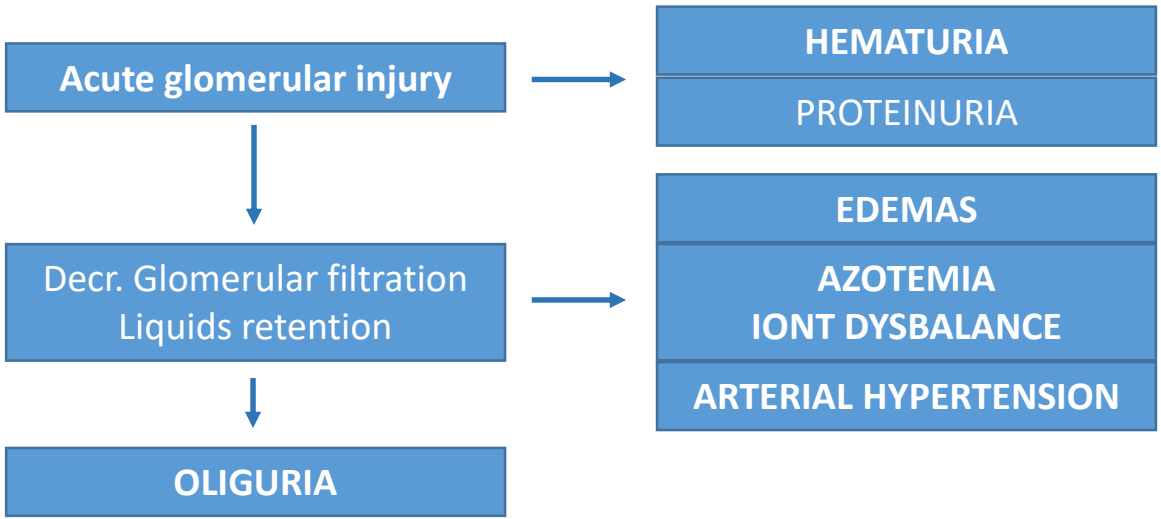
HEMATURIA

- > 10 erythrocytes / 1 µl urine

- MICROSKOPIC – non visible by naked eye
- MACROSKOPIC – urine red to brown

- GLOMERULAR – erythrocytes damaged - acantocytes
- NON-GLOMERULAR – erythrocytes normal, exclude another source of bleeding

NEPHRITIC SYNDROME



NEPHRITIC SYNDROME

- ACUTE (ENDOCAPILLARY) PROLIFERATIVE GLOMERULONEPHRITIS
- RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS
- PROLIFERATIVE GLOMERULONEPHRITIS
- SYSTEMIC LUPUS ERYTHEMATODES

RENAL INSUFFICIENCY / FAILURE

- Marker of renal function: **glomerular filtration (GF)**

OLIGURIA / ANURIA … decreased urine production (< 400 ml … 100 ml / 24 hours)

AZOTEMIA … increased levels of blood nitrogen products of metabolism (**urea, creatinin, uric acid)**

IONTS AND WATER DYSBALANCE

METABOLIC ACIDOSIS

NON SPECIFIC SYMPTOMS … nauzea, headaches…

ACUTE RENAL FAILURE

- develops in hours/days

Prerenal – low kidney perfusion (hypovolemia, shock, heart failure)

Renal – diseases of glomeruli, tubules and interstitium or vessels

Postrenal – urinary tract obstruction

CHRONIC RENAL FAILURE

- long lasting decrease of renal function (glomerular filtration)
  - ***chronic renal insufficiency***
  - ***terminal renal failure (end-stage renal disease)***

- 10-15 % in European and USA population
  - diabetes mellitus (30 %), arter. hypertension (25 %), chron. GN (12 %), TIN (8 %)

CHRONIC RENAL FAILURE

• decreased GF – changes in homeostasis – azotemia, ionts, water, retention of ***uremic toxins*** (fenols…)

• endocrine disorders

• Untreated chronic renal failure - **UREMIC SYNDROME**
and multiorgan failure

fully developed US is rare, patients may have some symptoms

UREMIC SYNDROME (UREMIA)

1. HOMEOSTASIS DISORDERS

- **AZOTEMIA**
- **WATER AND IONTS DYSBALANCE**
- **METABOLIC ACIDOSIS**

2. CLINICAL SIGNS AND COMPLICATIONS

- **CARDIOVASCULAR**
  - Cardiac arrhythmia
  - Fluid retention
  - Arterial hypertension
  - Acceleration of atherosclerosis
  - Fibrinous pericarditis

- **BLOOD**
  - **Coagulation disorders** - platelet dysfunction
  - **Anemia** - a disorder of erythropoietin production

2. CLINICAL SIGNS AND COMPLICATIONS

- **IMMUNITY**
  - **T cell response disorder**
  - **Fibrinous inflammation of the mucous membranes of the GIT** *(Treitz colitis)*

- **NEUROLOGICAL**
  - **Uremic encephalopathy**
  - **Peripheral neuropathy**

- **BONE DISEASE**
  - Elevated phosphate levels (with decreased GF) and decreased levels of vitamin D (activated in the kidneys), leading to hypocalcaemia, cause **secondary hyperparathyroidism**
  - **Fibrous osteodystrophy** - osteoclastic bone resorption and fibrosis of the medullary spaces
  - **Osteomalacia** - bone demineralization

GLOMERULAR DISEASES

glomerulonephritis

glomerulopathy

GLOMERULAR INJURY MECHANISMS

- VASCULAR, HEMODYNAMIC
- METABOLIC DISORDERS
- IMMUNOLOGICAL DISORDERS
- SYSTEMIC DISEASES
- TUMORS
- HEREDITARY DISORDERS

IMMUNE-RELATED glomerular injury

IMMUNOCOMPLEX = antigen + bound antibody

Immunocomplexes deposited in glomerulus = DEPOSITS

1) CIRCULATING IC

Antibody bounded to antigen in circulation

- Bacterial / viral antigens
- Tumor antigens
- Endogenous antigens

IMMUNE-RELATED glomerular injury

IMMUNOCOMPLEX = antigen + bound antibody

Immunocomplexes deposited in glomerulus = DEPOSITS

2) IN SITU FORMED IC

antigen localised in kidney, where circulating antibody is bounded

- Circulating antigen deposited in kidney
- Antigen is a structure of kidney

IMMUNE-RELATED glomerular injury

AUTOANTIBODIES

1) **ANCA – anti neutrophil cytoplasm**
   (myeloperoxidase, proteinase-3)
   „*pauciimmune glomerulonephritis“*

2) **Against complement factors**
   (C3b convertase, H factor…)

NON-IMMUNE glomerular injury

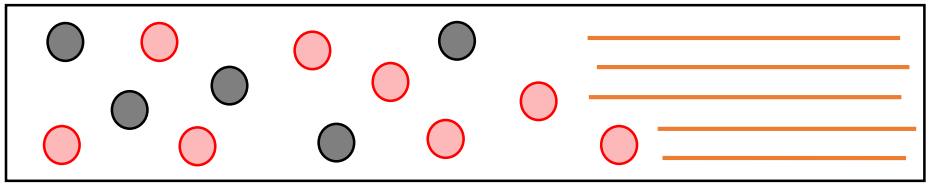
PODOCYTE INJURY - PODOCYTOPATHY

- Genetic disorders
- Acquired injury

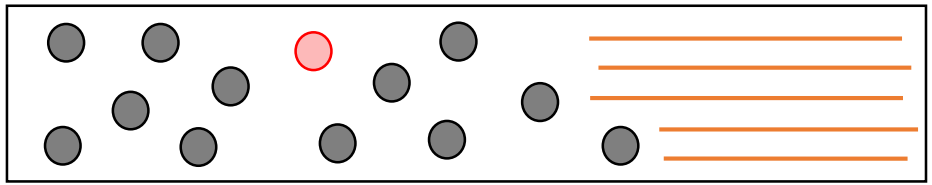
- Injury – adaptive change ***effusion of pedicels***
- Desquamation and compensatory hypertrophy of remaining podocytes

- Podocyte injury = **proteinuria**

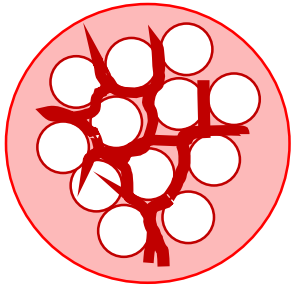
GENERAL HISTOLOGIC CHANGES IN GLOMERULAR DISEASES

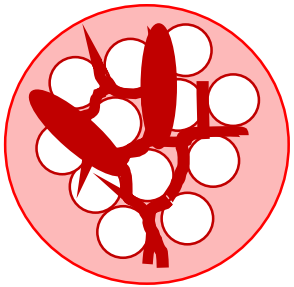


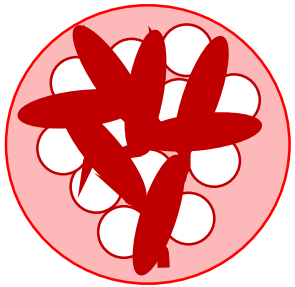
FOCAL



DIFUSE







SEGMENTAL

GLOBAL

GENERAL HISTOLOGIC CHANGES IN GLOMERULAR DISEASES

INCREASED CELLULARITY

- MESANGIAL PROLIFERATION
- ENDOCAPILLARY PROLIFERATION
- EXTRACAPILLARY PROLIFERATION

BASAL MEMBRANE THICKENING

HYALINISATION, SCLEROTISATION

- (FOCAL) SEGMENTAL
- GLOBAL

IMMUNOFLUORESCENCE

MESANGIAL POSITIVITY

PERIPHERAL POSITIVITY - GRANULAR

PERIPHERAL POSITIVITY - LINEAR

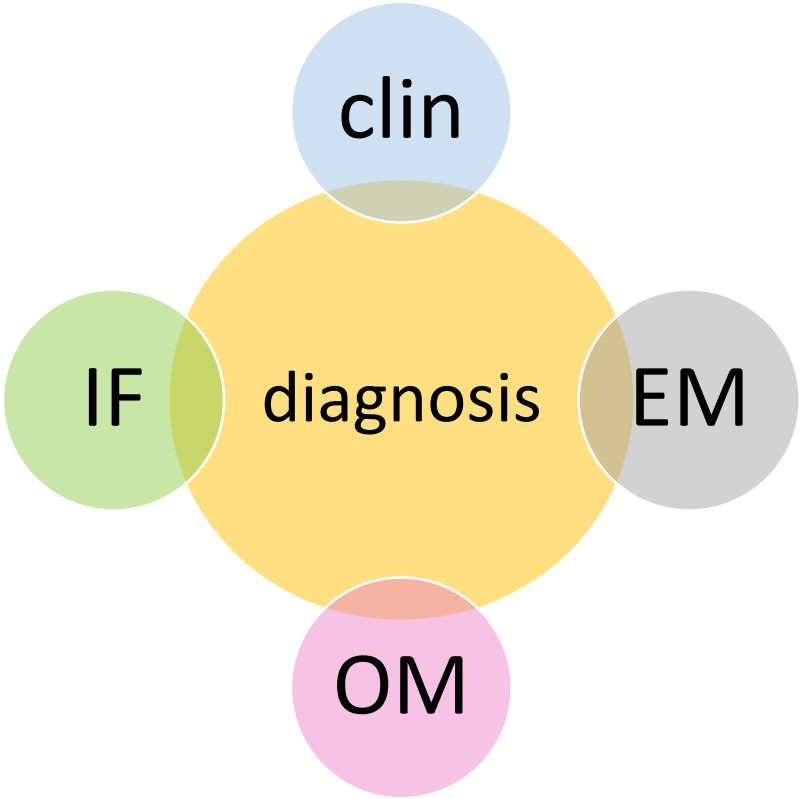
ELMI – DEPOSITS LOCALISATION

SUBENDOTHELIAL

INTRAMEMBRANOUS

SUBEPITHELIAL

MESANGIAL



1) one morphologic pattern can occur in different diseases

2) one disease can have different morphology

3) one clinic syndrome may have different morphology

synthesis of various examinations and information is necessary

CLASSIFICATION OF GLOMERULONEPHRITIS

- **ACUTE GN (WITH NEPHRITIC SYNDROME)**
  - Acute proliferative GN (postinfectious GN)
  - Rapidly progressive GN – RPGN (GN with crescents)
  - membranoproliferative glomerulonephritis
- **GN/GP WITH NEPHROTIC SYNDROME**
  - minimal change disease
  - focal-segmental glomerulosclerosis (FSGS)
  - membranous glomerulopathy
  - amyloidosis
  - diabetes mellitus
- **GN/GP WITH ISOLATED HEMATURIA**
  - IgA nephropathy (mesangioproliferative GN)
  - Alport syndrome + thin membrane syndrome
- **GN IN SYSTEMIC DISEASES**
  - systemic lupus erythematodes

WHO CLASSIFICATION

- primary GN/GP
- GN in systemic diseases
- GN in systemic vasculitides
- GN hereditary
- GN in metabolic disorders
- chronic sclerosing GN

other classifications…

- morphology
- acute / chronic
- primary / secondary

GN with NEPHRITIC SYNDROME

- Proliferative GN – increased glomerular cellularity
- Mesangial proliferation, narrowing of capillary loops, (crescents formation)

- ACUTE GLOMERULONEPHRITIS / POSTINFECTIOUS GN
- MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS
- RAPIDLY PROGRESSIVE GLOMERULONEPHRITIDES

ACUTE PROLIFERATIVE GLOMERULONEPHRITIS
POST-SREPTOCOCCAL GN, POST-INFECTIOUS GN, ENDOCAPILLARY GN

- Bacterial infection outside the kidneys
- Immunocomplex GN
  - Deposition of circulating immunocomplexes (bacterial antigen + antibody)
  - Deposition of bacterial antigens in glomerulus and IC forming in situ
- Immunocomplexes activate complement

ACUTE PROLIFERATIVE GLOMERULONEPHRITIS
POST-SREPTOCOCCAL GN, POST-INFECTIOUS GN, ENDOCAPILLARY GN

Classic form

- typical patient: child 7-14
- 1-2 weeks after streptococcal infection (pharyngitis, skin infection…)
- Variable clinical symptoms
  - Asymptomatic
  - Isolated microscopic hematuria
  - Fully developer nephritic syndrome: hematuria, proteinuria, hypertension, edemas
  - Kidney failure
- Symptomatic therapy, benign course with full recovery

ACUTE PROLIFERATIVE GLOMERULONEPHRITIS
POST-SREPTOCOCCAL GN, POST-INFECTIOUS GN, ENDOCAPILLARY GN

Recent form

- patient: elderly adult
- Staphylococcus infection
- Variable clinical manifestation
  - Fluid retention – heart failure
- Not so benign course – complete recovery only in < 40 %

ACUTE PROLIFERATIVE GLOMERULONEPHRITIS
POST-SREPTOCOCCAL GN, POST-INFECTIOUS GN, ENDOCAPILLARY GN

- IMMUNOCOMPLEXES (Ig+antigen)
- granular deposits
- mezangium + capillaries
- IgG, C3

ACUTE PROLIFERATIVE GLOMERULONEPHRITIS

POST-SREPTOCOCCAL GN, POST-INFECTIOUS GN, ENDOCAPILLARY GN

- hypercellular glomeruli
- proliferation of mesangial cells
- endothelial swelling
- leukocytes, monocytes in capillaries
- (crescents)
- erytrocytar casts in tubules

ACUTE PROLIFERATIVE GLOMERULONEPHRITIS
POST-SREPTOCOCCAL GN, POST-INFECTIOUS GN, ENDOCAPILLARY GN

- subepithelial deposits – „humps“

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS
MESANGIOCAPILLARY GN, LOBULAR GN

1) **MPGN with IMMUNOCOMPLEX deposites**
   activation of complement (classical pathway) by immunocomplexes
   - **Idiopatic**
   - **Secondary**
     infections (HCV, IE), autoimmune diseases (SLE), tumors (CLL, lymphomas, ca)

2) **MPGN with COMPLEMENT deposites, without immunocomplexes**
   Complement activated by alternatice pathway (autoantibodies against C3 convertase = C3 nephritic factor, factor H defects)
   - **C3 nephropathy**
   - **Dense deposit disease**

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS
MESANGIOCAPILLARY GN, LOBULAR GN

- chronic immunocomplex GN
- adolescents and young adults
- the most common secondary glomerulonephritis
- clinic presentation: variable – nephritic syndrome / combinated proteinuria and hematuria / nephrotic syndrome / RPGN
- slow progression, 50 % of patients develop chronic renal failure in 10 years

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS
MESANGIOCAPILLARY GN, LOBULAR GN

Imunocomplex MPGN

- deposits in capilaries and mesangium
- IgG + C3

DDD + C3 nephropathy

- Granular or linear deposits in capilaries and mesangium
- C3

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS
MESANGIOCAPILLARY GN, LOBULAR GN

- enlarged hypercellular glomeruli
- mesangial proliferation
- endocapillary proliferation (endotelium, leukocytes)
- capillary tuft lobulisation
- thickening of capillaries
- double contoured GBM

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

GN WITH CRESCENTS, EXTRACAPILLARY GN, RPGN

- rapid loss of renal function, progression in renal failure
- **nephritic syndrome**
- **crescent formation:** cellular – fibrous
- therapy: plasmaferesis, corticoides

1. **Pauciimmune GN**
   - ANCA associated, idiopatic
   - Wegener granulomatosis
   - microscopic polyangiitis
2. **Anti-GBM**
   - limited renal injury
   - Goodpasture syndrome (+ lung)
3. **Immunocomplex GN**
   - postinfectious GN
   - IgA nephropathy
   - lupus nephritis

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

GN WITH CRESCENTS, EXTRACAPILLARY GN, RPGN

Pauciimmune GN

- no antiGBM antibodies, no immunocomplexes, but circulating ANCA antibodies
- Involvement of various tissues/organs: kidney, lungs, skin, …
- **Type of vasculitis – capillaritis**
  1) **Granulomatosis with polyangiitis (formerly Wegener granulomatosis)**
  2) **Microscopic polyangiitis**
  3) **Polyangiitis with eosinophilia (Churg-Strauss syndrome)**

Anti-GBM

- autoantibodies against α3 chain of collagen IV in GBM
- in some patients cross reactivity with alveolar BM – lung involvement (haemorrhagia, hemoptysis - Goodpasture syndrome)

Immunocomplex GN

- RPGN as a complication

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

GN WITH CRESCENTS, EXTRACAPILLARY GN, RPGN

Pauciimmune GN

- no deposites

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

GN WITH CRESCENTS, EXTRACAPILLARY GN, RPGN

Anti GBM glomerulonephritis

- linear positivity of capillaries
- IgG

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

GN WITH CRESCENTS, EXTRACAPILLARY GN, RPGN

- necrosis of glomerular capillaries
- crescents formation

GN with NEPHROTIC SYNDROME

- Often non-proliferative disorders
- Injury of podocytes

CHILDREN

- MINIMAL CHANGE DISEASE
- FOCAL SEGMENTAL GLOMERULOSCLEROSIS
- OTHER…

ADULTS

- DIABETES MELLITUS
- AMYLOIDOSIS
- FOCAL SEGMENTAL GLOMERULOSCLEROSIS
- MEMBRANOUS GLOMERULOPATHY
- OTHER…

MINIMAL CHANGE DISEASE
LIPOID NEPHROSIS, MINIMAL CHANGE NEPHROTIC SYNDROME

- no clear ethiology
  - Unknown circulationg factor
  - immune mechanisms, tumors, drugs
- Injury of podocytes, loss of polyanion

- typical patient: child 1-6 years
- **nephrotic syndrome: severe proteinuria (selective – albumin), edema, hypercholesterolemia, hyperlipidemie**
- renal function normal, blood pressure normal
- therapy: corticoides (corticosensitive, corticodependent, corticoresistent)
- excellent prognosis

MINIMAL CHANGE DISEASE

LIPOID NEPHROSIS, MINIMAL CHANGE NEPHROTIC SYNDROME

IF negative

no immunocomplexes

MINIMAL CHANGE DISEASE

LIPOID NEPHROSIS, MINIMAL CHANGE NEPHROTIC SYNDROME

- **normal morphology of glomeruli**

MINIMAL CHANGE DISEASE

LIPOID NEPHROSIS, MINIMAL CHANGE NEPHROTIC SYNDROME

- diffuse effacement of podocyte foot processes (pedicels)

FOCAL SEGMENTAL GLOMERULOSCLEROSIS
FSGS

- variable age
- **nephrotic syndrome,** proteinuria (nonselective)
- often also hematuria, hypertension
- corticoresistant NS
- in 50 % chronic renal failure develops in 10 years

FOCAL SEGMENTAL GLOMERULOSCLEROSIS
FSGS

- **Idiopatic FSGS**
  - Unknown toxick factor causing podocyte injury
- **Hereditary FSGS**
  - mutations of slit membrane proteins (podocin, nephrin…)
- **FSGS in advanced kidney disease with glomerular overload**
  - Loss of > 70 % nephrons
  - Congenital disorders, reflux …
- Viral infections – HIV, CMV, EBV, Toxic – heroin, kokain

FOCAL SEGMENTAL GLOMERULOSCLEROSIS

FSGS

- changes are focal – segmental
- sclerosis of capillary tuft, collaps of capillaries
- adhesions to Bowman capsule
- increased mesangial matrix
- progressive global sclerosis of glomeruli and tubulointersitital fibrosis

FOCAL SEGMENTAL GLOMERULOSCLEROSIS

FSGS

- **diffuse effacement of foot processes**
- **detachment of foot processes from GBM**
- **increased mesangial matrix**
- **collaps of capillaries**

MEMBRANOUS GLOMERULOPATHY

MEMBRANOUS GN, MEMBRANOUS NEPHROPATHY

- chronic immunocomplex GN

1) **PRIMARY (75 %)**
   - **autoimmune** process with antibodies against podocyte surface antigenes (phospholipase A2 receptors: **PLA2R**)
2) **SECONDARY**
   - DRUGS – nonsteroid antiinflammatory drugs, penicilamin
   - MALIGNANT TUMOR – lung carcinoma, melanoma
   - SYSTEMIC LUPUS ERYTHEMATODES
   - INFECTIONS – chronic hepatitis (B, C), syfilis, schistosomissis, malaria
   - AUTOIMMUNE DISEASES - thyroiditis

MEMBRANOUS GLOMERULOPATHY

MEMBRANOUS GN, MEMBRANOUS NEPHROPATHY

- adult patients
- **nephrotic syndrome,** nonselective proteinuria
- secondary ethiology must be excluded
- variable course, some patients - chronic proteinuria, some slow progression to renal failure

MEMBRANOUS GLOMERULOPATHY

MEMBRANOUS GN, MEMBRANOUS NEPHROPATHY

- **granular deposites IgG, C3 in capillaries**

MEMBRANOUS GLOMERULOPATHY

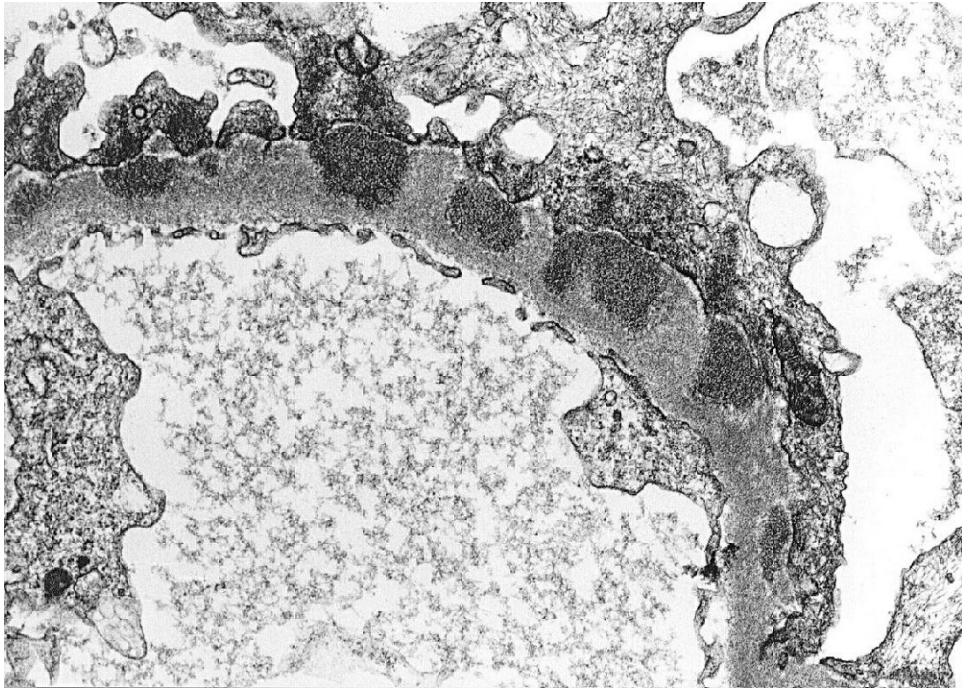
MEMBRANOUS GN, MEMBRANOUS NEPHROPATHY

- **diffuse thickening of capillaries**
- **silver impregnation – „spikes“**

MEMBRANOUS GLOMERULOPATHY

MEMBRANOUS GN, MEMBRANOUS NEPHROPATHY

- **foot processes effacement**
- **deposites SUBEPITHELIAL in GBM**



MEMBRANOUS vs. MEMBRANOPROLIFERATIVE

Membranous

1) PLA2R (IK)
2) Secondary* (IK)

Membranoproliferative

1) C3 nephropathy (no IK)
2) Secondary* (IK)

*Secondary GN (IK)

- Tumor
- Infection
- Autoimmunity

DIABETIC NEPHROPATHY

- Kindey involvement in 40 % diabetis patients
- The most common cause of kidney failure
- Structural changes in all kidney compartments

- biochemical alterations of GBM, incr. colagen IV, decr. heparansulphate, oxygen radicals
- Glycosylation of proteins
- Hemodynamic factors

DIABETIC NEPHROPATHY

- non-nephrotic proteinuria (microalbuminuria, macroalbuminuria)
- nephrotic syndrome
- hypertension, acceleration of vascular injury of kidneys
- progression to chronic renal failure

DIABETIC NEPHROPATHY

1) GLOMERULAR LESIONS
   - GBM thickening
   - diffuse mesangial sclerosis
   - nodular glomerular sclerosis
2) VASCULAR LESIONS
   - arteriolosklerosis – both afferent and efferent arterioles are involved
3) INTERSTITIAL LESIONS
   - pyelonephritis
   - necrotising papilitis

DIABETIC NEPHROPATHY

thickening of GBM

DIABETIC NEPHROPATHY

- diffuse mesangial glomerulosclerosis – increase of mesangial matrix
- nodular mesangial glomerulosclerosis – Kimmelstiel-Wilson
- arteriolosclerosis of both hilar arterioles
- sclerosis of glomeruli and tubulointerstitial fibrosis

AMYLOIDOSIS

- usually AL and AA amyloid
- deposition of amyloid in glomerulus (mesangium, capillary wall), arterioles, interstitium, TBM
- proteinuria – nephrotic syndrome
- diagnosis: kongo red histochemistry, immunohistochemistry, immunofluorescence (native material – frozen sections)

GN with HEMATURIA

IgA NEPHROPATHY
MESANGIOPROLIFERATIVE GN, BERGER'S DISEASE

- The **most common** type of GN worldwide (40 % adults with GN)
- The cause is outside the kidneys – autoimmunite process
- Autoantibodies against **abnormally glycosylated IgA** molecules
- Complexes IgG-IgA or IgA-IgA (large molecules difficult to degrade in the liver)
- Deposition of immunocomplexes in mesangium with its proliferation
- More common in celiac sprue and liver diseases

IgA NEPHROPATHY

MESANGIOPROLIFERATIVE GN, BERGER‘S DISEASE

- children and young adults most commonly
- typical sign: macroscopic hematuria afters infection of respiratory or digestive tract lasting several days
- may be slight proteinuria, nephritic syndrome, nephrotic syndrome
- in up to 40 % patients slow progression to chronic renal failure in 20 years

IgA NEPHROPATHY

MESANGIOPROLIFERATIVE GN, BERGER‘S DISEASE

MESANGIAL deposits

IgA

IgA NEPHROPATHY

MESANGIOPROLIFERATIVE GN, BERGER‘S DISEASE

- **variable morphology**
- **typicaly: proliferation of mesangium (cells + matrix)**

IgA NEPHROPATHY

MESANGIOPROLIFERATIVE GN, BERGER‘S DISEASE

- **electrondense deposits in mesangium**

HENOCH-SCHÖNLEIN PURPURA

- Vasculitis with IgA deposits in vessels and glomerules
- young children

1) skin haemorrhage – purpura
2) GIT disorders (stomachache, vomiting, hemorrhage into intestines)
3) joints pain
4) renal injury – hematuria / nephritic sy / nephrotic sy / RPGN

- overall good prognosis

- **morphology is identical to IgA nephropathy**

ALPORT SYNDROME

HEREDITARY NEPHRITIS

- 1927 Alport – men in one family had progressive nephropathy and deafness
- 1970‘ – discovered a cause – mutation of genes encoding collagen IV
- clasical signs: hematuria, mild proteinuria and progression to renal failure, the first signs in age 5-20 years
- associated disorders: hearing, vision
- aprox. 300 various mutations of collagen IV
- therapy – hemodialysis, transplantation

ALPORT SYNDROME

HEREDITARY NEPHRITIS

mutation COL4A5 – X-linked (80 %), mutation COL4A3, COL4A4 - autosomal …
defective chains of collagen are produced, quick degradation

ALPORT SYNDROME

HEREDITARY NEPHRITIS

- at the beginnig there are no morphologic changes in kidney
- later in course glomeruli besomes focal or global sclerotic, interstitial fibrosis is associated

ALPORT SYNDROME

HEREDITARY NEPHRITIS

- **variable thickness of GBM, thin and thickened parts alternate**
- **lamination of GBM - „basket weave“ appearance**

THIN MEMBRANE SYMDROME

BENIGN FAMILIAR HEMATURIA

- familiar asymptomatic hematuria
- renal functions are normal, good prognosis
- X-linked Alport asymptomatis female carriers, other rare colagen IV mutations
- normal histology, negative immunofluorescence
- EM: thinning of GBM 100-250 nm (normally in adults 300-400 nm)

SYSTEMIC LUPUS ERYTHEMATODES

- multisystem autoimunite disease
- variable clinical manifestation
- renal manifestations in 50-70 % cases
- more often women
- diagnostic critera (clinical and laboratory)
- autoantibodies: ANA (antinuclear antibodies … DNA, RNA, proteins)
- immunocomplex deposition (DNA + anti-DNA) in mesangium and GBM
- hematuria, proteinuria, nephrotic syndrome

SYSTEMIC LUPUS ERYTHEMATODES

class I	minimal mesangial LN	5 %
class II	mesangial proliferative LN	20 %
class III	focal (active/inactive) LN	20 %
class IV	diffuse (active/inactive) LN	40 %
class V	membranous LN	15 %
class VI	sclerosing LN	

SYSTEMIC LUPUS ERYTHEMATODES

- **mesangial and peripheral positivity**
- **IgG, IgA, IgM, C3, C1q**
- **„full – house“ positivity**

SYSTEMIC LUPUS ERYTHEMATODES

Cl. 1 – normal histology

Cl. 2 – mesangial hypercellularity

Cl. 3 – focal endocapillary or extracapillary GN (active/inactive), with/without mesangial lesion

Cl. 4 – diffuse endocapillary or extracapillary GN (active/inactive), with/without mesangial lesion, wire loops

Cl. 5. – thickening of capillaries

Cl. 6. – > 90 % glomeruli with global sclerosis

SYSTEMIC LUPUS ERYTHEMATODES

- **polyvalent deposits SUBENDOTHELIAL, MESANGIAL, SUBEPITHELIAL**

VASCULAR DISEASES

- Renal vessels don‘t have collaterals: any occlusion leads to ischemia of supplied tissue area
- Relationship between kidneys and arterial hypertension
  - Renal diseases are common cause of arterial hypertension
  - Arterial hypertension leads to significant vessels damage and involve renal function
- Renal vessels are often involved in systemic diseases (vasculitis)

Hypertensive angiopathy
(hypertensive or age-related nephrosclerosis)

- Formerly „benign nephrosclerosis“

1) Arteriolar injury

   endothelial injury – insudation of plasmatic proteins to the arteriolar wall eosinophil insudates **– hyaline arteriolosclerosis**

   arteriolar stenosis – ischemia of glomerulus – glomerulosclerosis – atrophy of tubules and interstitial fibrosis

2) Arteriar injury

   changes analogous to atherosclerosis (fibrous thickening of intima – stenosis) ischemia

Kidney injury in Malignant hypertension

- Formerly „malignant nephrosclerosis“
- Associated with malignant hypertension (> 200/120 mm Hg)

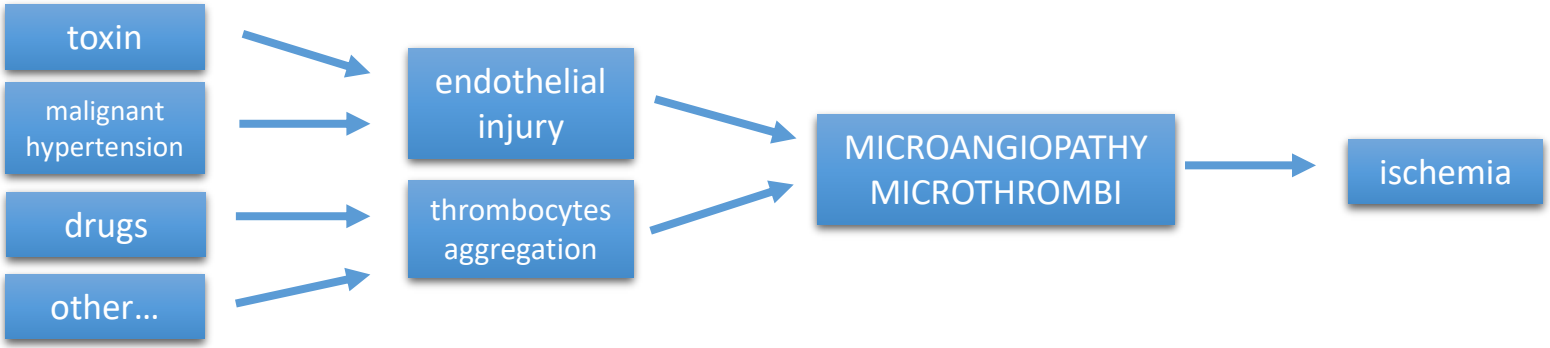
1) Arteriolar injury
   severe endothelial injury – **thrombosis**
   fibrinoid necrosis of arteriols
   changes may progress to glomerulus
   ischemia of renal parenchyma
   - healing leads to concentric fibrosis of arteriols (onion skin) – **hyperplastic arteriolosclerosis**
2) Arteriar injury
   intimal edema
   - healing leads to intimal fibrosis

Hypertensive angiopathy – clinic symptoms

- **„benign nephrosclerosis“**
  - No clin. signs, slow decrease of renal function – chronic ren. insufficiency
- **„malignant nephrosclerosis“**
  - Acute renal failure
  - Microangiopathy – hemolytic anemia, trombocytopenia
  - Severe complications – cerebral hemorrhage, retinopathy, myocardial infarction…
  - Chronic changes - proteinuria, hematuria, renal insufficiency
- Both categories need therapy!

THROMBOTIC MICROANGIOPATHIES

- thrombosis in capillaries and arterioles
- microangiopathic haemolytic anemia
- thrombocytopenia
- (renal failure, neurologic signs)



1. HEMOLYTIC-UREMIC SYNDROME

- mikroangiopathic haemolytic anemia + acute renal failure

1) Typical HUS (childhood) … D+ HUS

- after infection E. coli O157:H7 producing *verotoxin* (diarrhea)

2) Atypical HUS (adults)

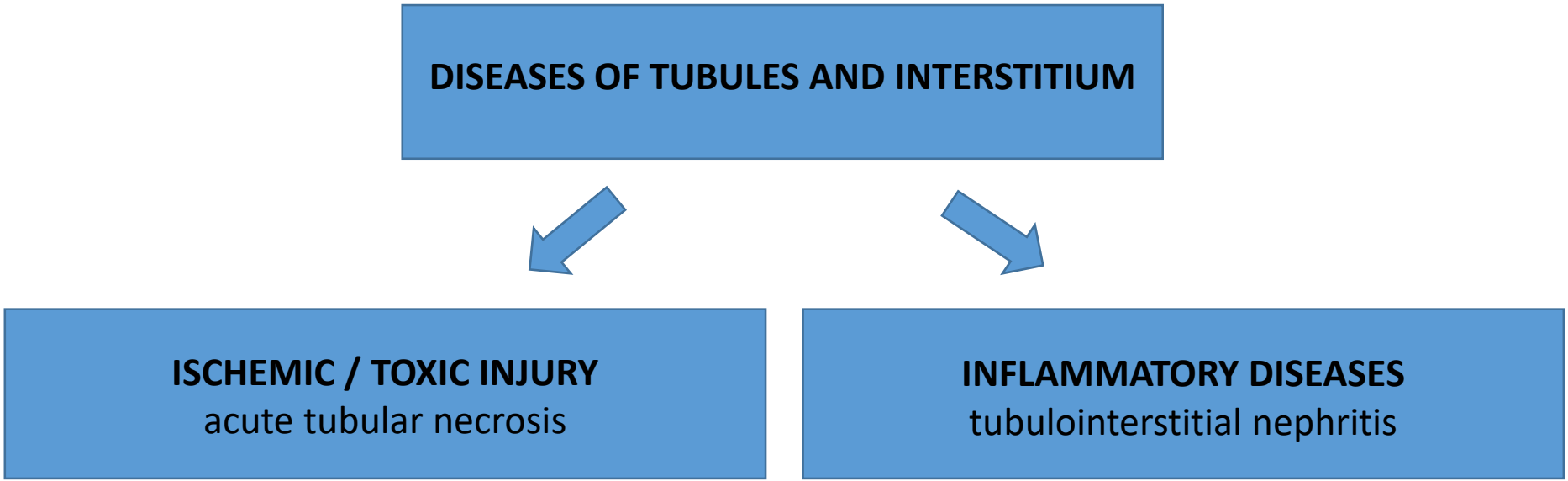
- infection (E. coli, Shigella, virus), chemotherapy, SLE

2. THROMBOTIC THROMBOCYTOPENIC PURPURA

- fever, microangiopathic haemolytic anemia, thrombocytopenia, ***neurologic disorders***, renal disorders
- morphology similar to HUS

- etio: autoimmune/drug-induced, defective degradation of von Willebrand factor multimers – increased aggregation of thrombocytes

TUBULOINTERSTITIAL DISEASES


DISEASES OF TUBULES AND INTERSTITIUM
ISCHEMIC / TOXIC INJURY
acute tubular necrosis
INFLAMMATORY DISEASES
tubulointerstitial nephritis

ISCHEMIC / TOXIC INJURY
acute tubular necrosis

the most common cause of **acute renal failure**

with adequate therapy fully **reversible** disorder

Ethiology

1) **ischemia**
   - inadequate blood supply of kidneys
     - microangiopathy (malignant hypertension, HUS, TTP, DIC, …)
     - hypotension, shock (kardiogenic, hypovolemic, septic, trauma…)
     - ***„shock kidney***“
2) **direct toxic injury**
   - drugs (gentamycin, sulfonamides, metotrexat, CyA…)
   - heavy metals (Hg, Pb, Cr), organic solvents (tetrachlormetan), etylenglykol
   - myoglobin, hemoglobin
   - toxins (phaloidin)
3) **acute tubulointerstitial nephritis = inflammation**
   - hypersensitive reaction after drugs (antibiotics)
4) **urinary tract obstruction**

Macro

- swelling of kidneys, pale cortex, hyperemic medulla, (cortical necrosis)

Micro

- proximal and distal tubules

  - loss of brush border, lowering of epithelial cells, necrosis and desquamation

  - granular casts in distal nephron (= necrotic epithelia, proteins, ery)

- interstitial edema + inflammatory cells (PM)

Clinical course

- acute renal failure
- after some time - restoration of renal functions

1) **initial stadium**
   - inadequate perfusion of kidneys, mild oliguria
2) **oliguric stadium**
   - oliguria; < 400 ml/den), water and salts retention
   - uremia, hyperkalemia, MAC
   - dialysis !
3) **polyuric stadium**
   - regeneration of epithelial cells, insufficient concentration function of tubules
   - 3 l/day, Na, K

INFLAMMATORY DISEASES
tubulointerstitial nephritis

group of heterogenous diseases

inflammation in interstitium + tubular injury

acute / chronic

Ethiology

- **infection** (acute bacterial pyelonephritis, chronic pyelonephritis, viral infestions…)
- **toxic injury** (drugs, metals)
- **metabolic disorders** (urate nephropathy, nephrocalcinosis, oxalate nephropathy…)
- **physical causes** (obstruction, RT…)
- **tumors** (multiple myeloma…)
- **immnite reactions** (rejection…)
- **vascular diseases**

	acute TIN	chronic TIN
interstitium	edém neutrofily, eosinofily lymfocyty, makrofágy plazmocyty	fibrosis lymphocytes, macrophges plasma cells
tubules	dystrophy → necrosis	atrophy
glomeruli	no changes	collapsed capillary tufts periglomerular fibrosis
vessels	no changes	arteriosclerosis arteriolosclerosis

Acute pyelonephritis

ascendent

E. Coli, Proteus, Klebsiella, Enterobacter …
CMV, poliomavirus, adenovirus

hematogenous

complication of pyemia (infectious endocarditis …)
Staphylococcus, E. Coli, mycosis...

Acute pyelonephritis – clinic

- obstruction of urinary tract, VUR, anamnesis of cathetrisation, diabetes, immunodeficit
- abrupt onset
- pain in costovertebral angle
- dysuria, polakisuria
- fever, malaise
- urinanalysis: pyuria (+ leukocytar casts), bakteriuria, hematuria

- frequent recurrences $\rightarrow$ chronic form
- healing – postpyelonephritic scars (fibrosis, chronic onflammation)

Acute pyelonephritis – complications

- **necrosis of papils**
  - in diabetes, coagulative necrosis, dystrophic calcification
- **pyonephros**
  - accumulation of pus in renal pelvis or uteter
  - urinary tract obstruction
- **perinephric abscesus**
  - propagation of purulent inflammation over the capsula in perirenal fat
- **sepsis**

Chronic pyelonephritis

- chronic inflammation and fibrosis of interstitium
- tubular atrophy – thyroidisation
- periglomerular fibrosis, collaps of tufts→sclerosis
- renovascular hypertension
- CHRI, end-stage kidney

Chronic pyelonephritis

REFLUX NEPHROPATHY	CHRONIC OBSTRUCTIVE PYELONEPHRITIS
• children, result of infections in congenital VUR • unilateral / bilateral	• recurrent infections in obstruction of urinary tract • urine stagnation leads to renal parenchyma atrophy

TIN inducted by drugs and toxins

1) acute renal failure (ATN)
2) acute tubulointerstitial nephritis – hypersensitive nephritis
3) chronic tubular injury – CHRI

Acute drug induced interstitial nephritis

- sulfonamids, methicilin, ampicilin, rifampicin, thiazid, NSAID, allopurinol
- 2 weeks after application
- fever, eosinophilia, skin exantema
- renal injury (hematuria, proteinuria, incr. kreatinin, ARI)

- interstitial edema, inflamatory cells with **eosinophils**

Analgetic nephropathy

- chronic renal injury in excessive intake of some analgetics
- chronic tubulointerstitial nephritis + necrosis of papils
- may progress to renal failure
- „fenacetin nephropathy“

Urate nephropathy

1) **acute urate nephropathy**
   - precipitation of urate crystals in tubules – obstruction – ARI
2) **chronic urate nephropathy**
   - in chronic hyperurikemia
   - deposition of urate crystals in tubules and interstitium – tofus formation
   - *tofus* = giant-cell reaction, chronic inflammation, fibrosis
   - atrophy and fibrosis of cortex
   - slow progression to renal failure
3) **urolithiasis**

Renal injury in multiple myeloma

1) myeloma kidney
2) amyloidosis - AL
3) light chain deposition disease
4) nephrocalcinosis (hypercalciuria), urolithiasis

Renal injury in multiple myeloma

- Bence-Jones protein in tubules
  - toxic for tubular epithelial cells
  - obstruction of tubules by casts
  - giant cell reaction and fibrosis around tubules
- makro – pale smooth surface
- symptoms: acute renal failure or slow progression in chronic renal failure