# Nephropathology

V. Žampachová
I. ÚP

# Anatomical remarks

- Vessels - 90% of blood flow through the cortex
- Afferent arteriole → glomerular capillaries → efferent arteriole → peritubular capillary plexus (from superficial glomeruli) or vasa recta for medulla (from juxtamedullary glomeruli)
- terminal arteries
- glomerular damage commonly leads to damage of peritubular blood flow – risk of ischemia

# Possible clinical signs

- Weight gain, edema – fluid retention
- Thirst – chronic renal failure, DM
- Fatigue – acute/chronic renal failure (RF)
- Fever – urinary tract infection (UTI)
- Headache – hypertension, RF
- Hematuria – UTI, glomerulonephritis, tumor, stone
- Polyuria – DM, tubular disorders

Renal diseases commonly clinically silent!

# Clinical features

- Diminished renal reserve – GFR ~ 50% of normal
- Renal insufficiency - GFR 20-50% of normal
- Azotemia – increase of blood urea and creatinine due to decreased glomerular filtration (20-30%), or extrarenal cause
- Uraemia - azotemia together with several clinical and biochemical abnormities: metabolic, endocrine, …
  - uremic gastroenteritis/colitis + IS dysregulation, malnutrition;
  - hypertension, fibrinous pericarditis, AS acceleration, arrythmias
  - pneumonia, pleuritis
  - dermatitis, itching
  - renal osteodystrophy, osteoporosis, muscle loss
  - peripheral neuropathy,

# Clinical features

- Renal failure - GFR less than 20-25%, oedema, uraemia; causes: *prerenal, postrenal, renal (vascular, glomerular, tubulointerstitial);* acute r.f. (oliguria→anuria) chronic r.f.
- End-stage renal disease - GFR less than 5% of norm
- Anuria <100ml/24hrs

# Clinical features

- Nephritic syndrome due to acute glomerular disease; hematuria + mild proteinuria + hypertension; oliguria + azotemia + mineral dysbalance
- Rapidly progressive glomerulonephritis – very rapid (days - a few weeks) nephritic syndrome
- Nephrotic syndrome: usually chronic gl. dis., severe proteinuria (>3,5 g/d) + hypoalbuminemia/oedema + hyperlipidemia + lipiduria; possible ↑ infections (IgG loss); hypercoagulative state – loss of coagulation proteins, ↑ blood viscosity
-

# Clinical presentations

- Acute renal failure – progressive oliguria to anuria, azotemia, metabolic acidosis;
  - prerenal – renal – postrenal
  - with according therapy usually return to function
- Chronic renal failure - prolongated symptoms of uremia, anemia, nausea
  - chronic uremia in irreversible damage
  - most commonly due to DM, hypertension, AS

# Clinical features

- Asymptomatic hematuria and/or proteinuria – commonly mild glomerular lesion
- Polyuria + nocturia + electrolyte disorders – renal tubular defects
- Bacteriuria + pyuria – urinary tract infection (UTI)
- Renal colic + hematuria - nephrolithiasis

# Renal diseases

- congenital anomalies
- glomerular diseases
- vascular diseases
- tubulointerstitial diseases
- tumors

# Congenital anomalies

- 10% of all people
- hereditary or acquired developmental defect
- decreased volume of renal tissue (e.g. agenesis)
- disorders of differentiation (dysplasia)
- anatomical abnormalities (ectopy)
- metabolic disorders (cystinuria)

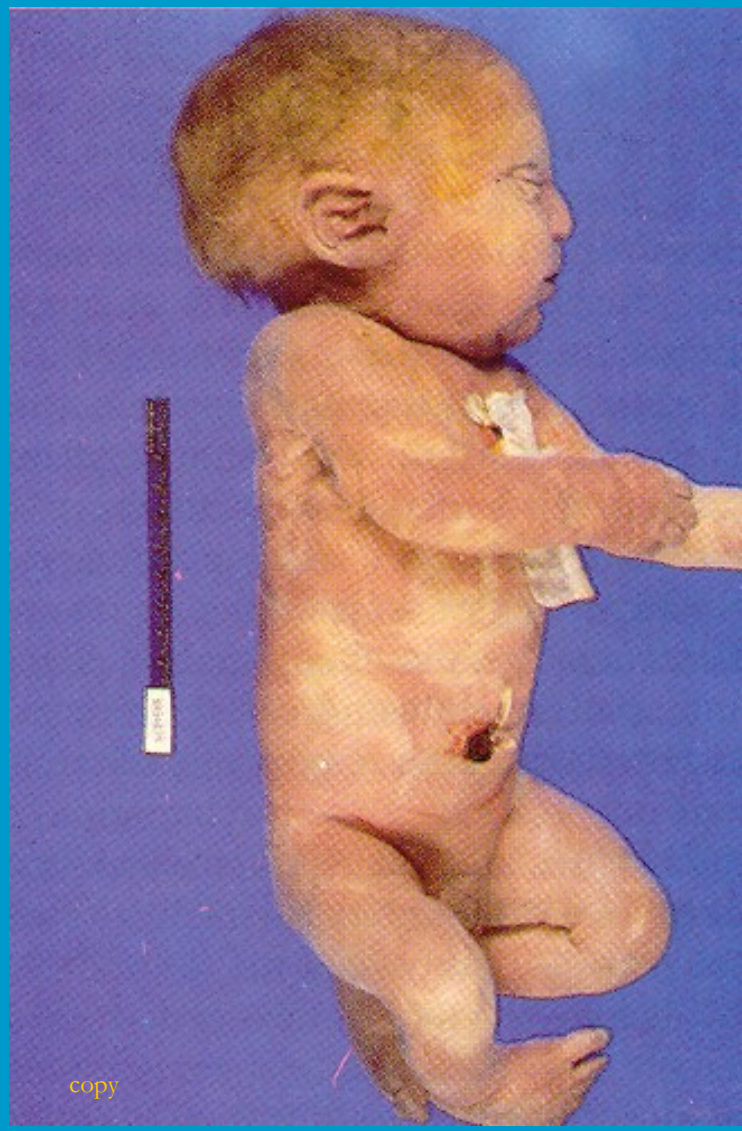
# Agenesis

- Bilateral agenesis – 1:6000, incompatible with independent life, usually stillborn, accompanied by characteristic appearance (Potter's syndrome), commonly associated with other congenital defects
- Unilateral agenesis – infrequent, the opposite kidney enlarged by compensatory hypertrophy

# Oligohydramnion (Potter´s syndrome)

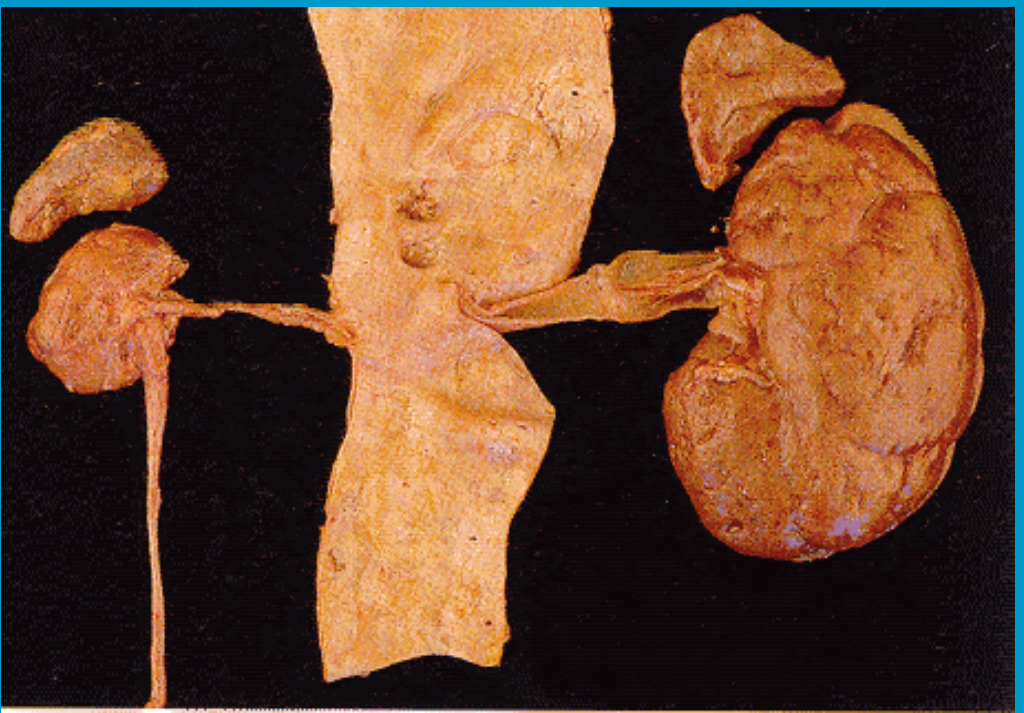
decreased amount of amniotic fluid (placental abnormities, renal **agenesis or malformation)**

flat face, lung hypoplasia, limb deformities, ...



# Hypoplasia

- Abnormally small kidneys (x atrophy)
- reduced number of lobes and pyramids



# Renal ectopy

- Abnormal site, usually in pelvis, due to migration stop of the *metanephros*
- *A. renalis* - from lower aorta or *a. ilica communis*
- Short ureter

# Ren migrans, ren mobilis

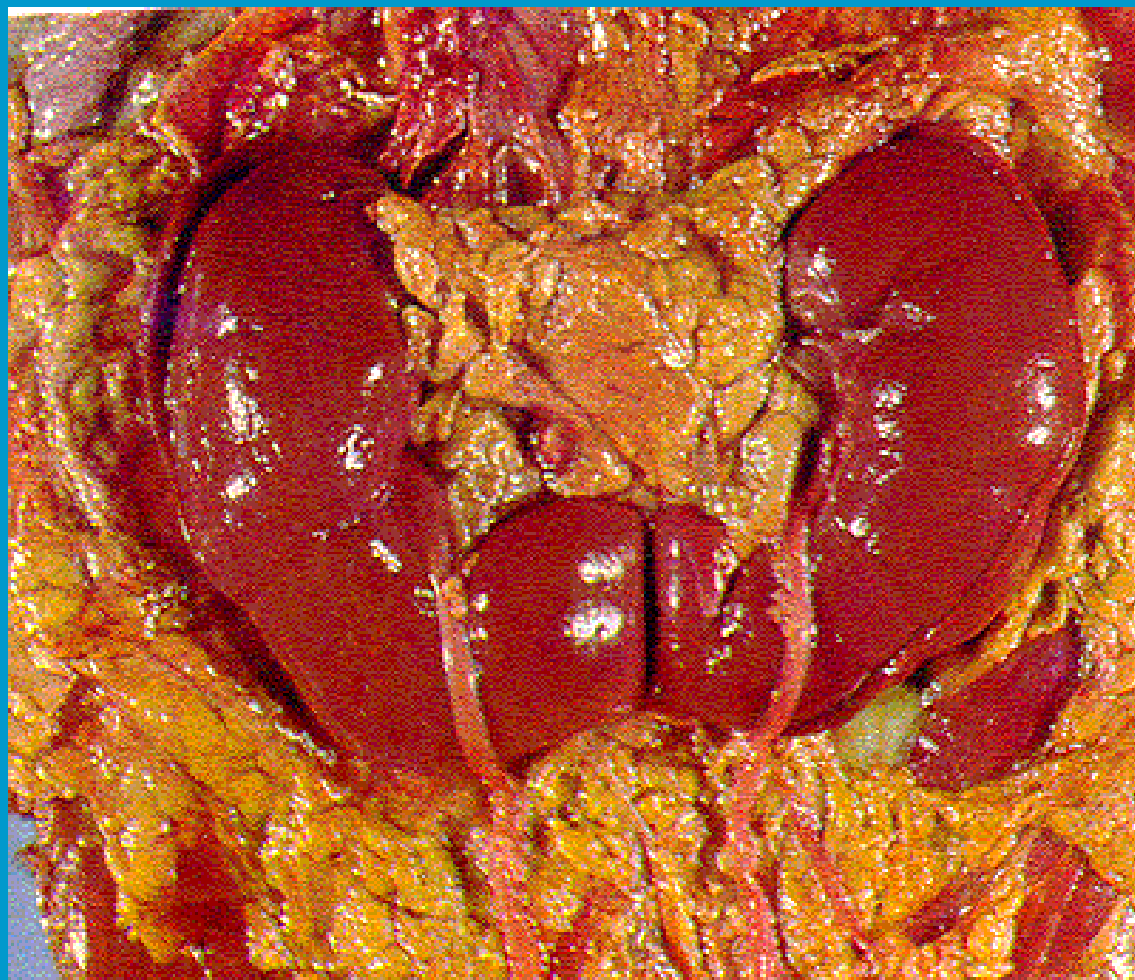
- Not a malformation, normal *a. renalis*
- Secondary renal descensus, usually due to loss of adipous capsule
- Long ureter, risk of obstruction and infection

# Other inborn defects

- **Tuberous sclerosis**
  - AD, 1:5800; multiple benigh proliferations/tumors in the brain, heart, kidney
  - in 50 % kidney lesions incl. cysts (→CHRI), angiomyolipomas, hamartomas, rare carcinomas
- **Sy von Hippel – Lindau**
  - AD, multiorgan disorders (eyes, CNS, pancreas, kidney – tumors benign / malignant; common kidney cysts, possible → ca)

# Horseshoe kidney

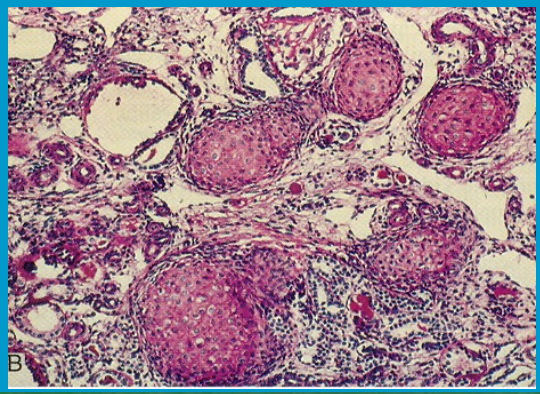
- Renal pole fusion
- Ureteral obstruction



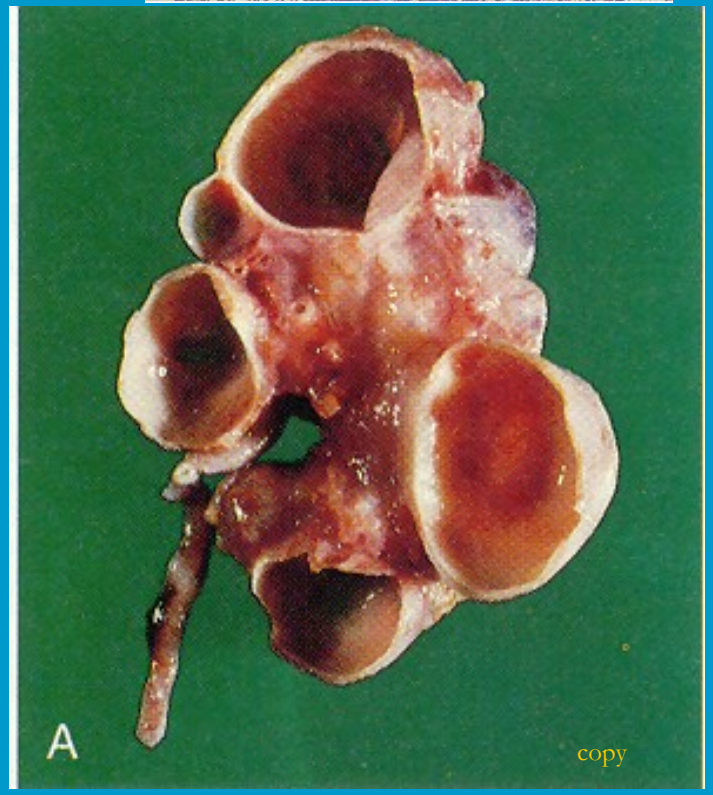
# Cystic renal disease

- Hereditary, congenital nonhereditary, acquired
- Pathogenesis: primary defect of tubular epithelial cells and their growth, resulting in tubular dilatation
- Secondary tubular obstruction (oxalate crystals etc.)
- Multiple or solitary
- Affects the whole kidney, or mostly cortex or medulla

# Cystic dysplasia

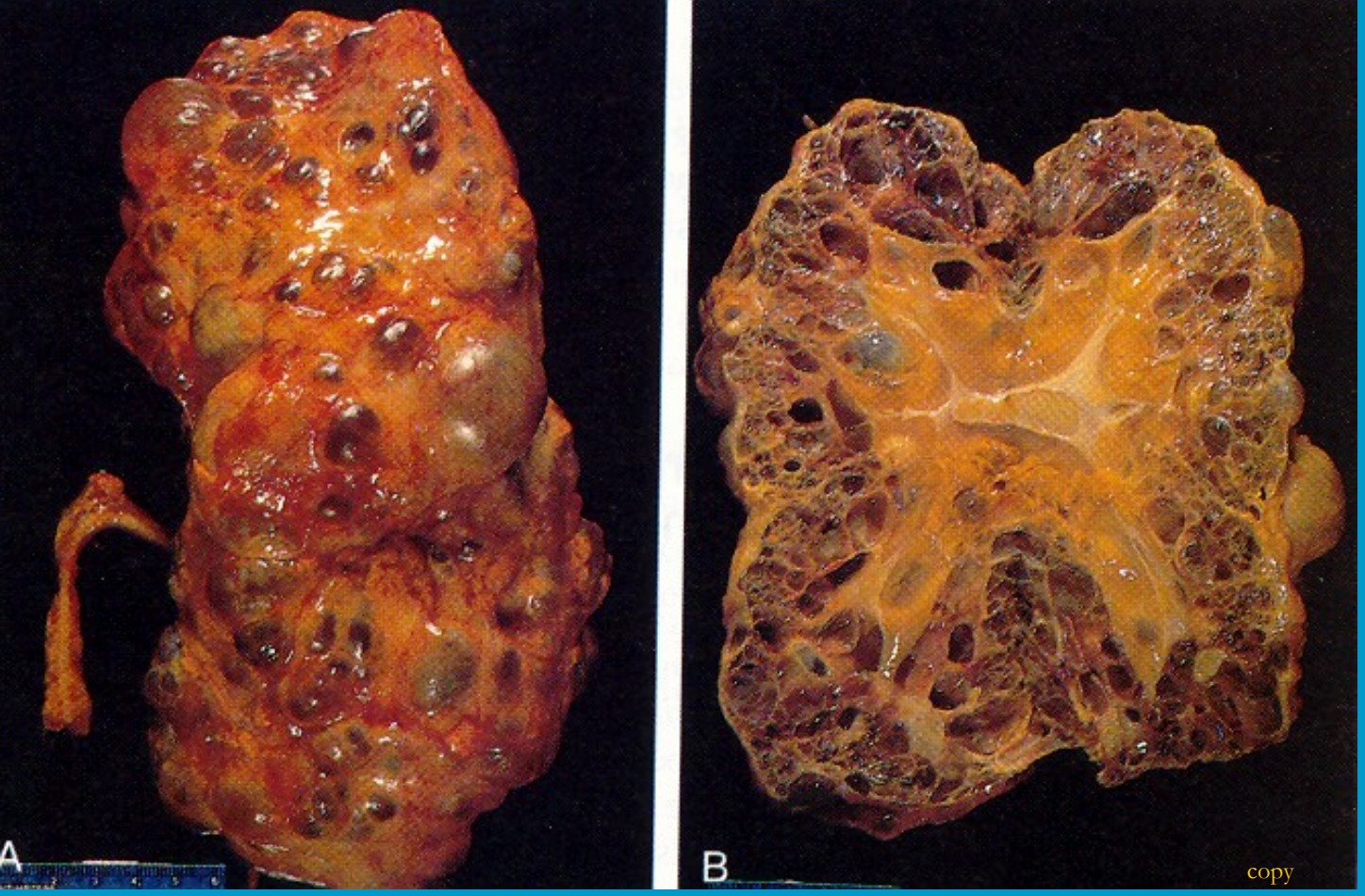



- Uni- or bilateral
- Enlarged multicystic kidney
- Cysts mm-cm.
- Islands of undifferentiated mesenchyme, immature tubules
- Commonly cartilage
- Bilateral - renal insufficiency



# Polycystic kidney - autosomal recessive

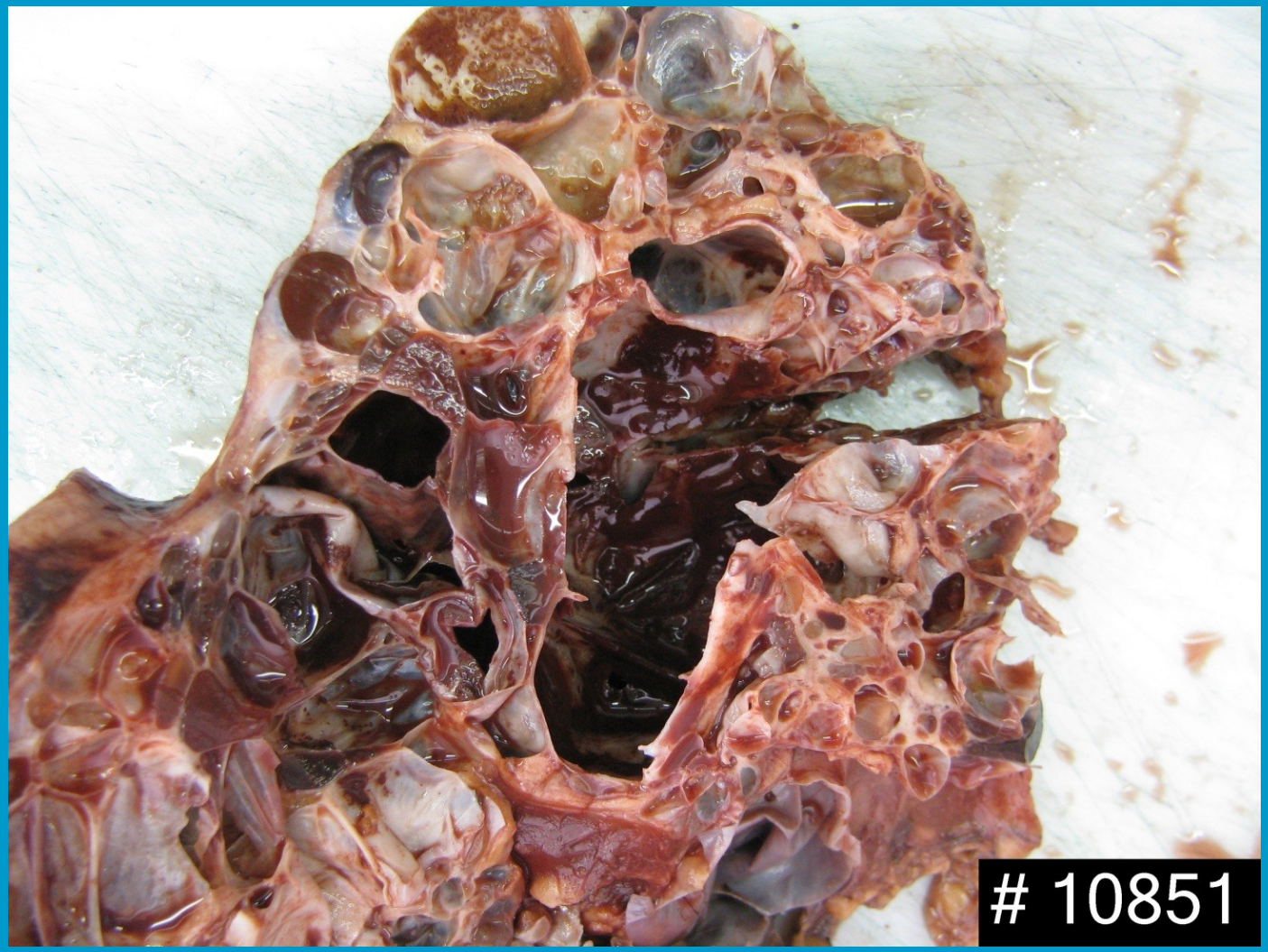
- Infants
- Enlarged kidney at birth, smooth surface, microcystic
- Radial elongated cysts and channels
- Congenital hepatic fibrosis
- RF in childhood




**Adult polycystic kidney disease (APKD)**

Autosomal-dominant, liver cysts, berry aneurysms. 1:500-1:1000. Pain, hematuria, UTI, stones, hypertension, slow progression, chronic RF at 40-60 yrs. ↑risk of ca

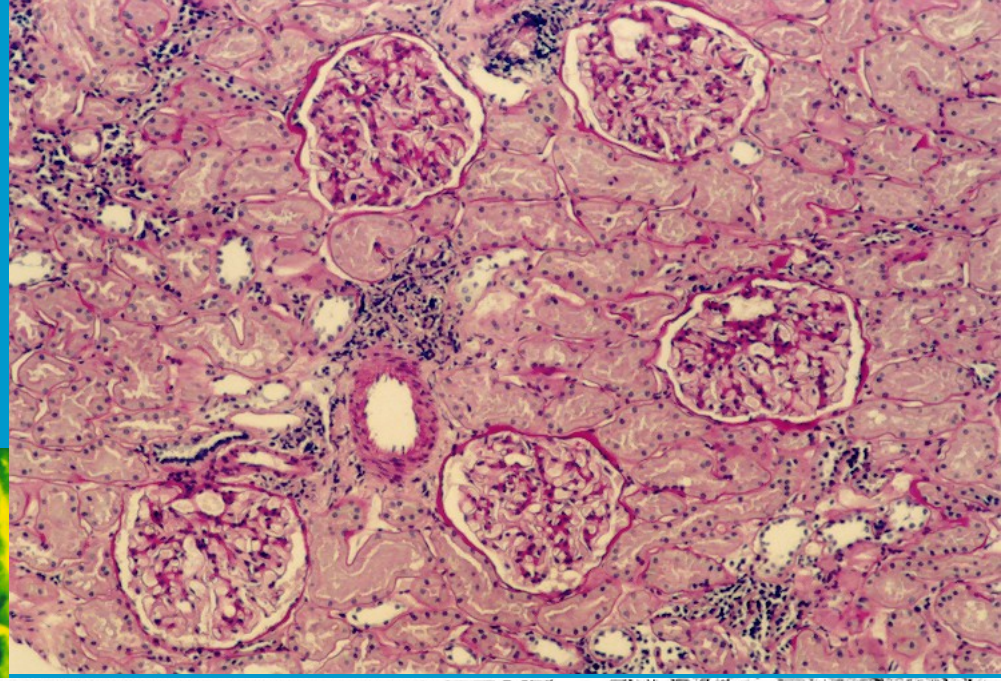
# Adult polycystic kidney

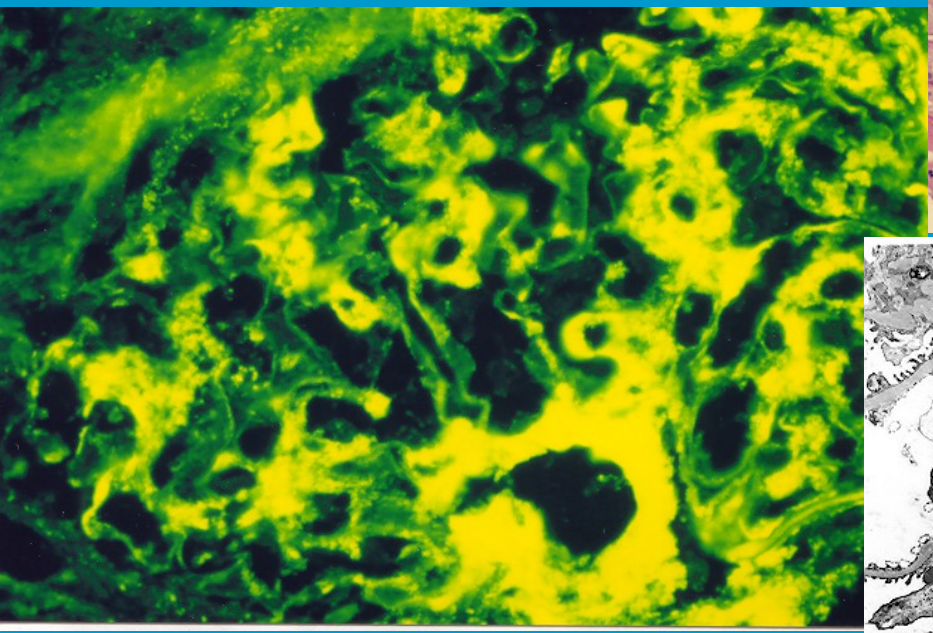


# Simple cyst

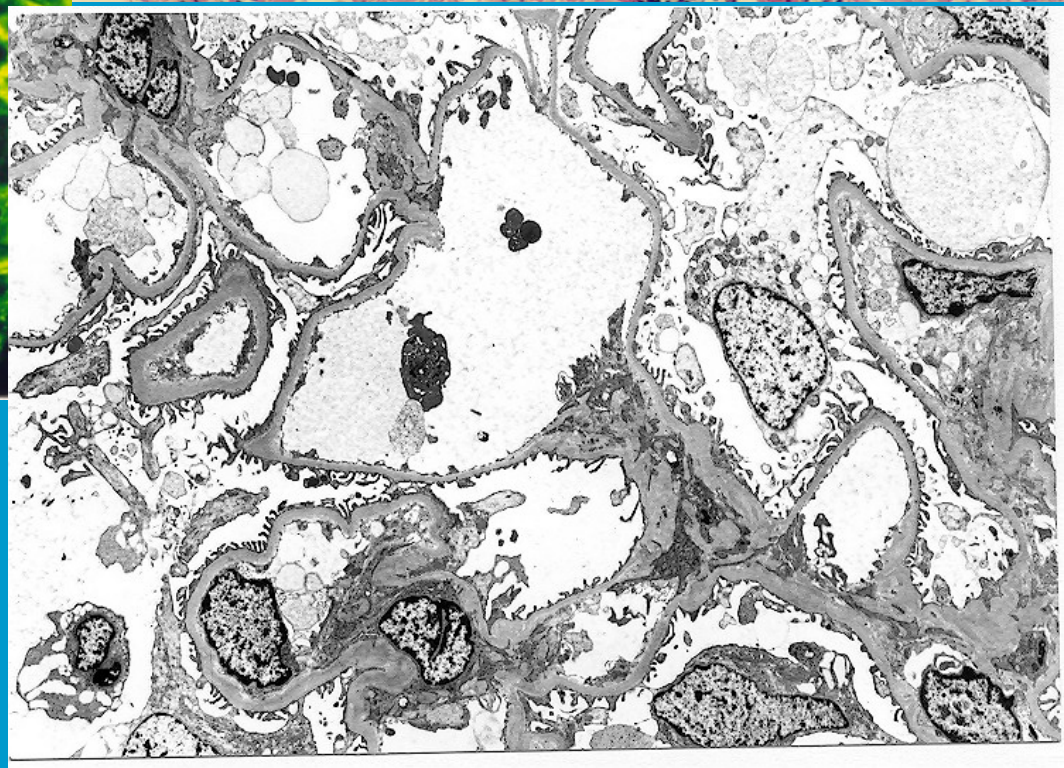
- Single or multiple
- Up to 10 cm
- Haemorrhage posible
- Differential diagnosis x cystic tumors
- „Complicated“ cyst – with regressive changes, diff. dg. x ca

# Renal biopsy



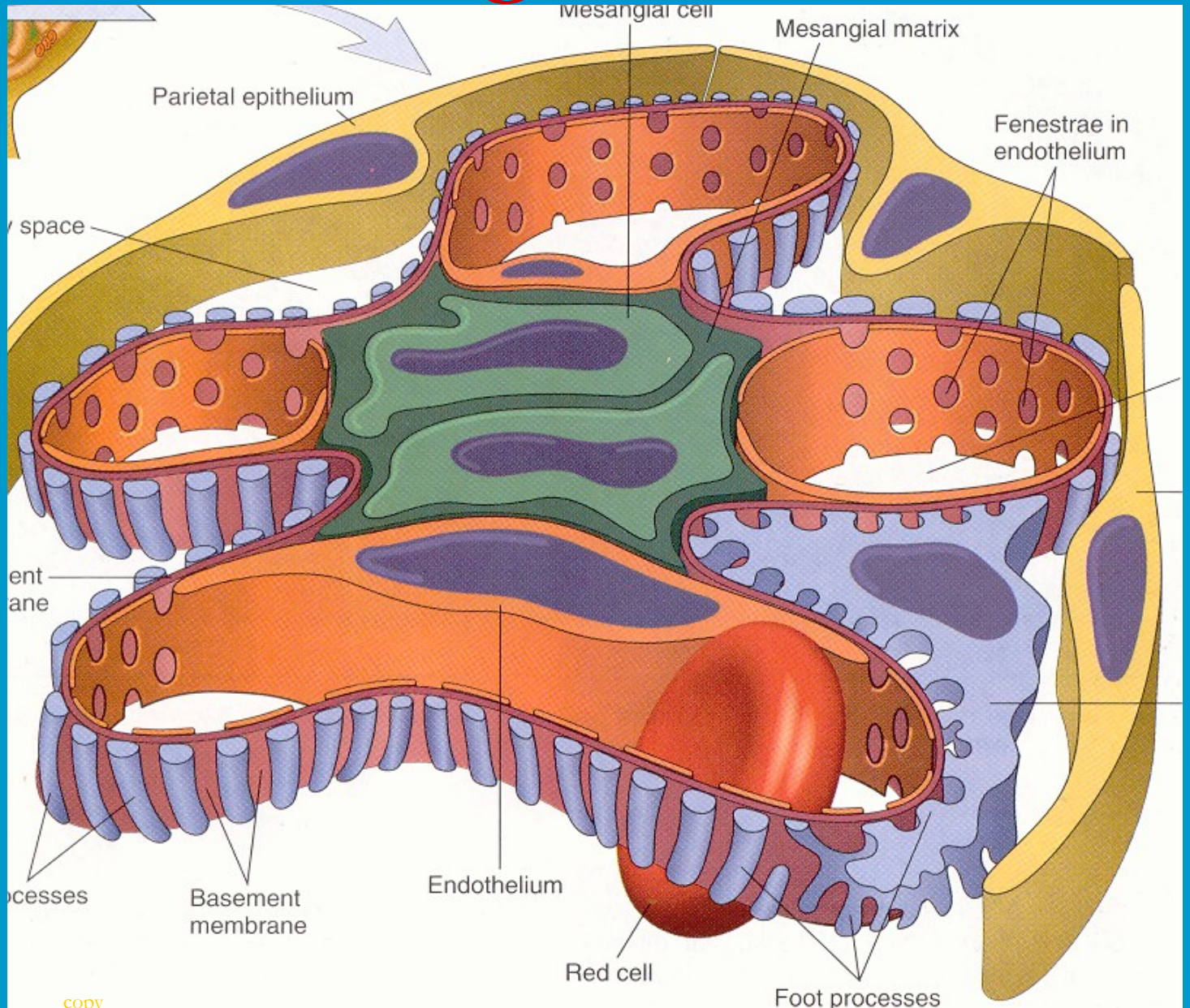


Direct immunofluorescence

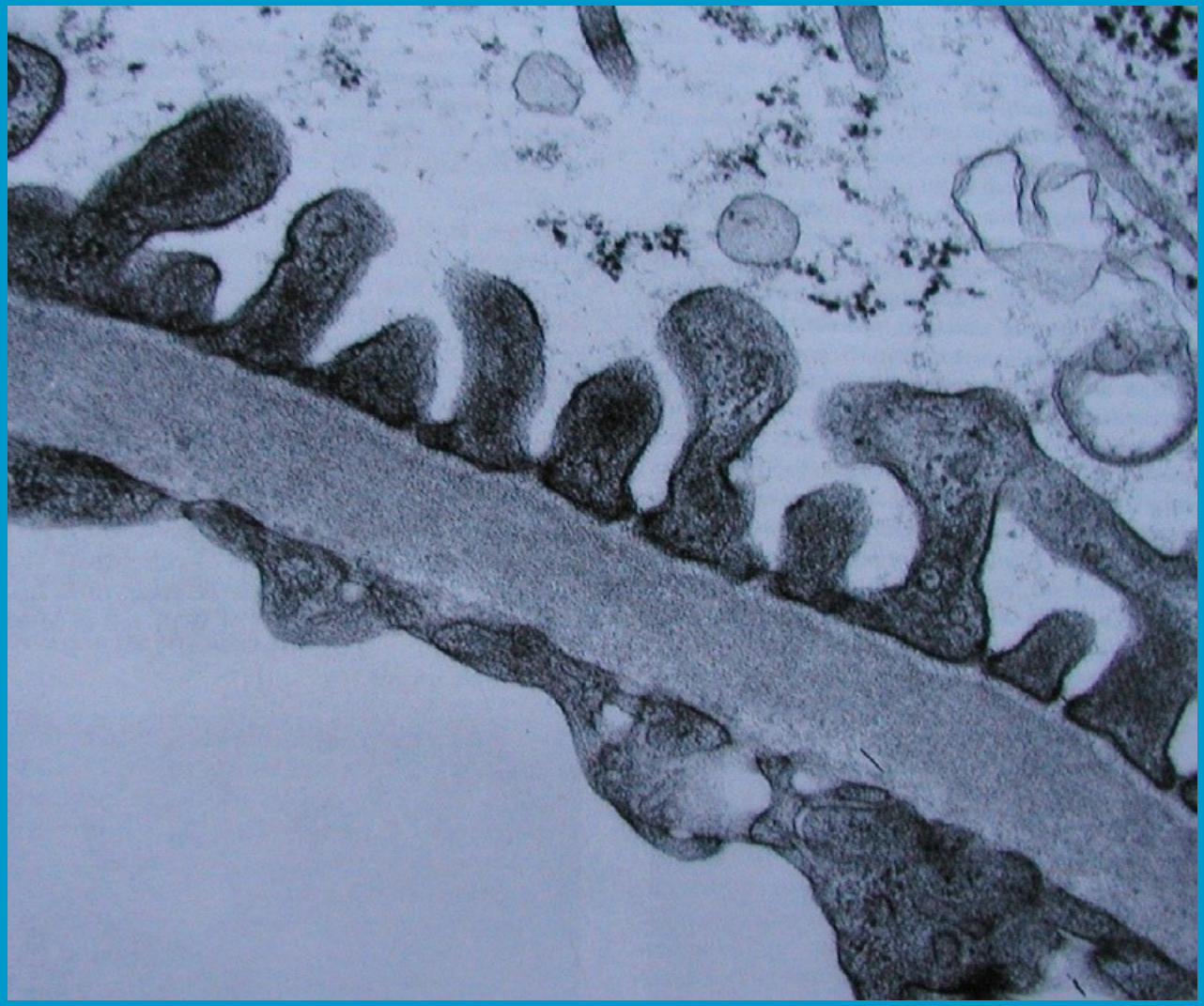


Electron microscopy

# Normal glomerulus



# Glomerular filtration barrier



# Glomerular diseases

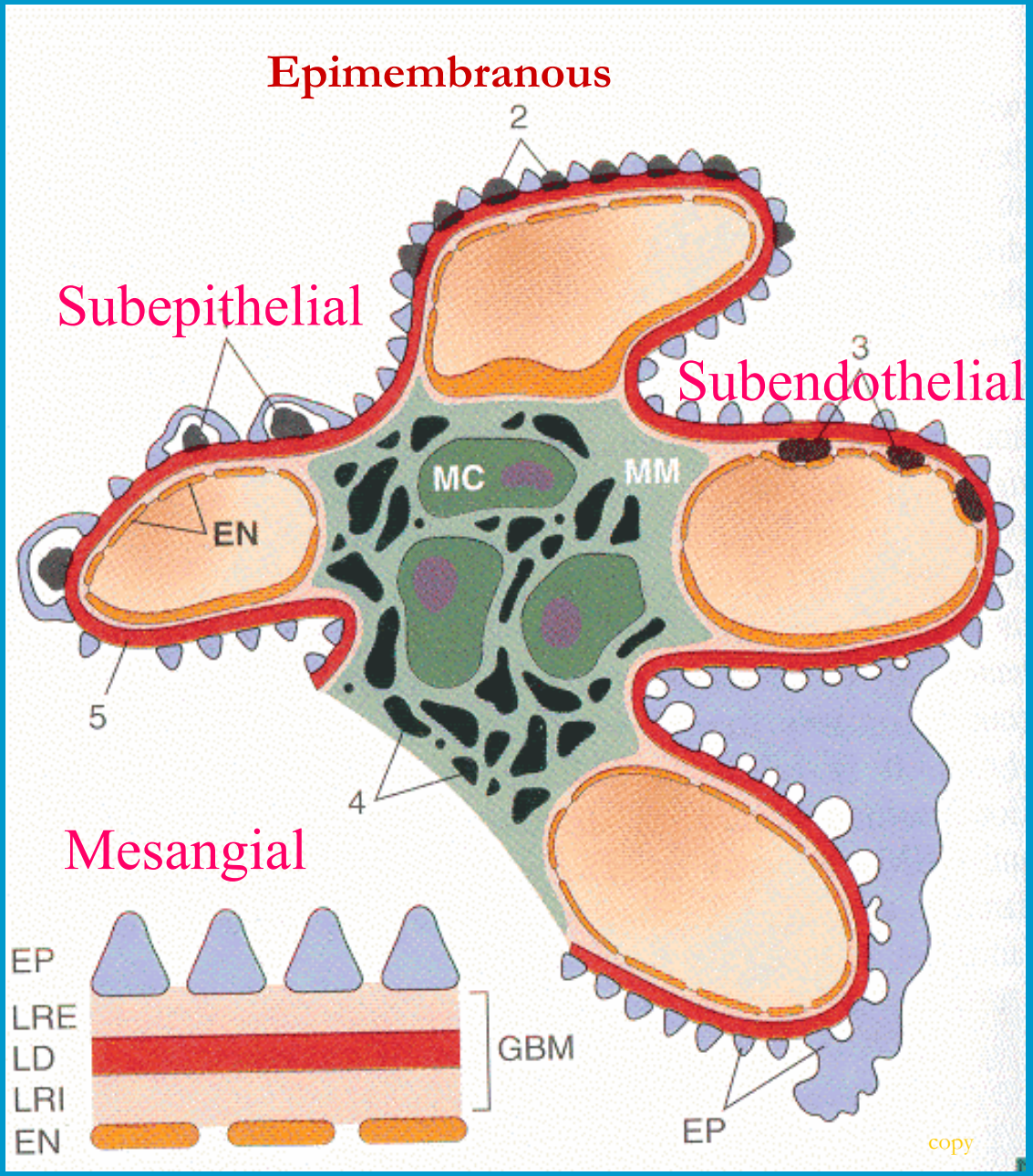
- Classification by aetiology and mechanisms of injury (primary x secondary; immunological x non-immunological)
- Histological classification (patterns of injury – proliferative, membranous change, membrano-proliferative, crescentic, hyalinisation + sclerosis)
- One disease may have variable morphology/pattern (SLE)
- One pattern may be seen in variable disorders

# Glomerular diseases

Immune mediated lesions

- circulating immune complexes
- in situ immune complexes
- anti-GBM antibodies
- autoantibodies (ANCA)

# IC localisation



# Glomerular diseases

Non-immune mediated lesions

vascular

- hemodynamic factors
- hypertension
- ischemia

# Patterns of glomerular injury

- **Proliferative** – increased glomerular cellularity, combination of endogenous proliferation and exogen. infiltration
- **Membranous change** – thickening of loops due to BM expansion + IC deposition
- **Membrano-proliferative**
- **Crescentic** – florid prolif. of cells in Bowman‘s capsule + infiltration, later fibrotic changes
- **Hyalinisation** – extracellular/intramural amorphous material w. plasmatic proteins + lipids, PAS+, silver impregnation -
- **Sclerosis** – extracellular collagenous matrix, membranes, PAS+, impregn. +

# Glomerular injury distribution

- **Diffuse** – almost all glomeruli affected (> 50-80%)
- **Focal** – only some glomeruli
- **Global** – affecting the whole glomerulus
- **Segmental** – affecting only part of the glomerulus

# Clinical presentations

- Nephritic syndrome – acute gl. damage, rapid start, hematuria, variable proteinuria, oliguria, edema, hypertension, azotemia, mineral dysbalance
- Nephrotic syndrome - heavy proteinuria > 3,5 g/daily, generalised edema, hypoalbuminemia, hyperlipidemia, lipiduria; hypercoagulative state (loss of coagulation proteins, increase in blood viscosity)

# Glomerular diseases

- Nephritic syndrome, rapidly progressive GN: inflammation +/- endothelial damage; ↑ gl. cellularity
- usually immune mediated
  - Immune complex deposition (acute proliferative GN, SLE)
  - Antibodies x glomerular basement membrane (Goodpasture sy)
  - Systemic noninfectious vasculitis: autoantibodies p-ANCA, c-ANCA; (polyangiitis with granuloma)
  - immune mediated abnormalities of complement system regulation (C3)

# Glomerular diseases

- Nephrotic syndrome: malfunction/leakage of barrier-filtration system - ↑ increased permeability

Capillary wall: thickening by in situ IC deposits (membranous glomerulopathy; primary, sec.), abnormal substances (DM, amyloid)

Epithelial cells: loss of normal structure (detachment + loss of podocytes, compensatory hypetrophy of remaining cells, fusion of foot processes in minimal change disease; disruption in focal segmental glomerulosclerosis)

# Other clinical presentations

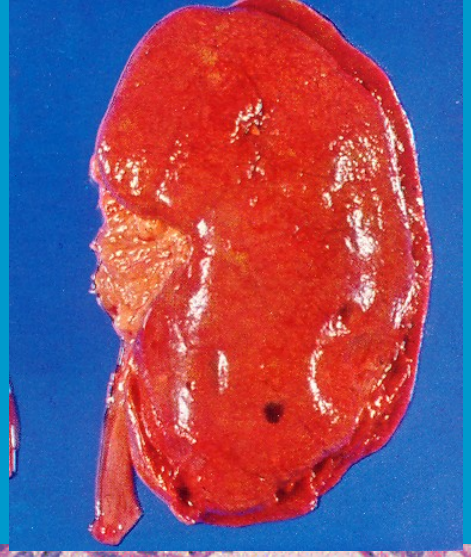
- Isolated proteinuria
  - sometimes asymptomatic
  - glomerular – damage to filtration membrane
    - selective – proteins w. low-middle molecular weight (albumin)
    - nonselective – more damage, high weight proteins – Ig
  - tubular
    - problem in tubular resorption of LMW proteins
- Isolated hematuria
  - microscopic x macroscopic

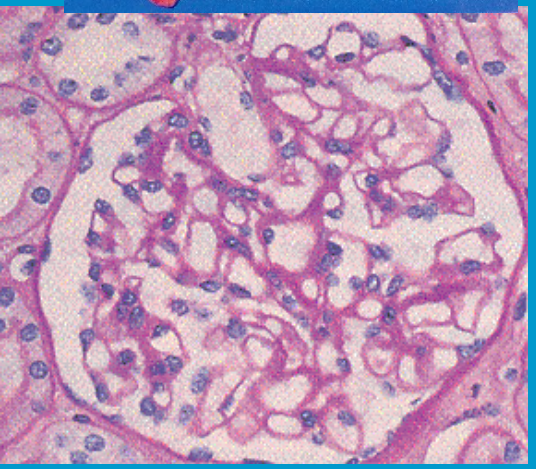
# Progression in glomerular disease

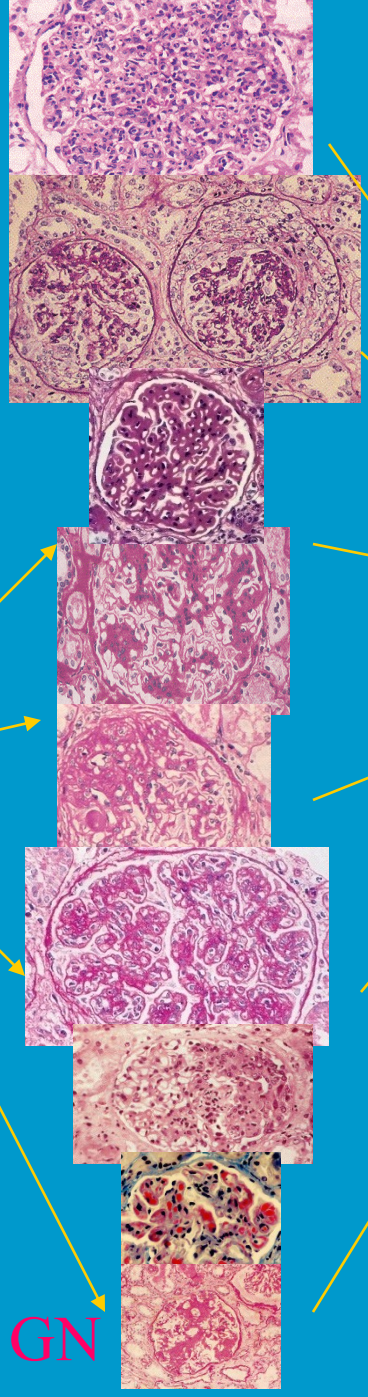
- ↓ GFR (30-50% of normal) → independent progression to RF – ablation nephropathy
- Focal segmental glomerulosclerosis – adaptation – compensatory glomerular hypertrophy (glomerular + systemic hypertension → proteinuria → mesangial proliferation + matrix accumulation → sclerosis)
- Tubulointerstitial fibrosis – proteinuria + ischemia → tubular damage + interstitial inflammation

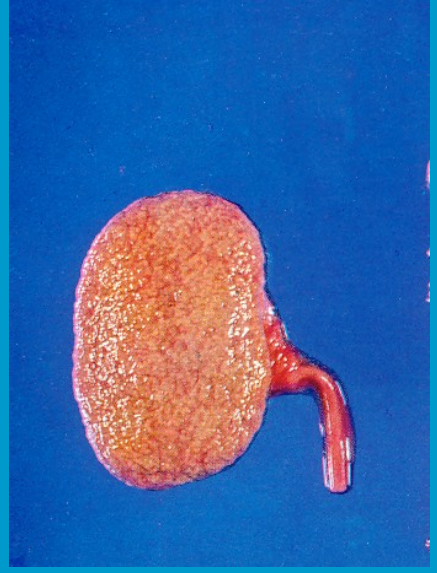
# GLOMERULAR DISEASES

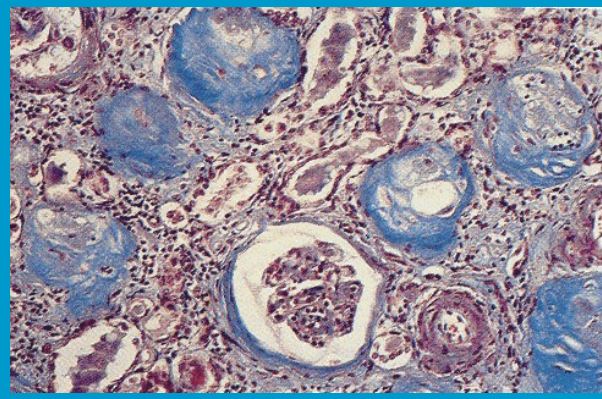
- PRIMARY GLOMERULAR DISEASE: kidney as a main affected organ, other clinical signs due to impaired renal function (i.e. minimal change disease)
- SECONDARY GLOMERULAR DISEASE: renal injury only a part of systemic disease affecting multiple organs (lung, joints, skin), i.e. SLE, infections (hepatitis C), vascular disorders (vasculitis, HT), tumors, inborn disorders











Normal kidney

GN

Chronic sclerosing GN

# Glomerulopathy

- One histological type may have variable clinical presentation, i.e. membranoproliferative lesion may present as glomerulonephritis with nephritic sy, glomerulopathy with nephrotic sy, or isolated hematuria

# Glomerulopathy with:

- Proteinuria or nephrotic syndrome
- Isolated or predominant hematuria
- Hematuria + proteinuria combined w. renal failure
- Glomerulopathy due to vascular diseases
- Glomerulopathy in systemic lupus
- Chronic glomerulopathy

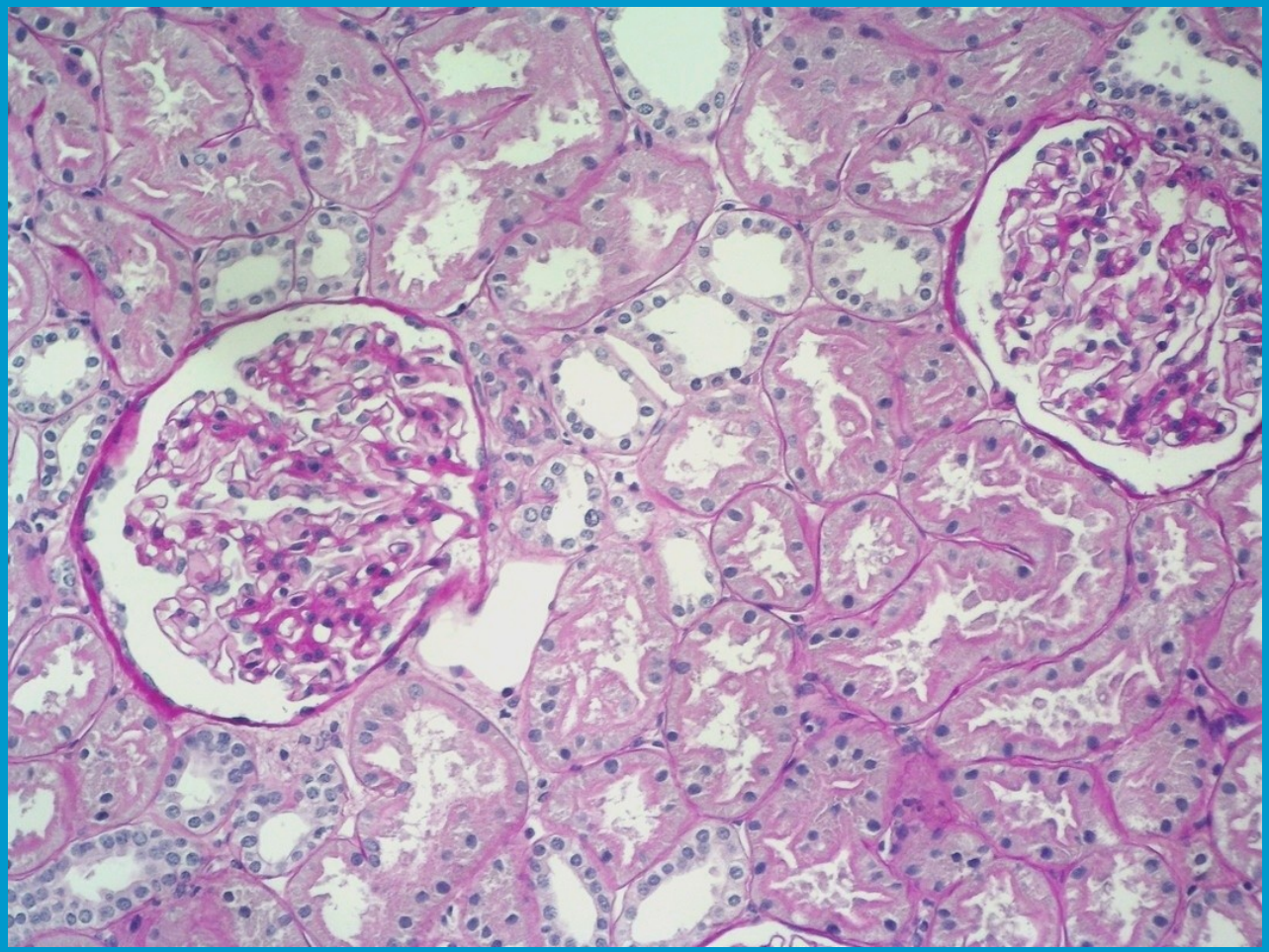
# Glomerulopathy with proteinuria or nephrotic syndrome

- Minimal glomerular change disease
- Focal segmental glomerulosclerosis
- Membranous glomerulopathy
- Amyloidosis
- Diabetic nephropathy

# Minimal change disease

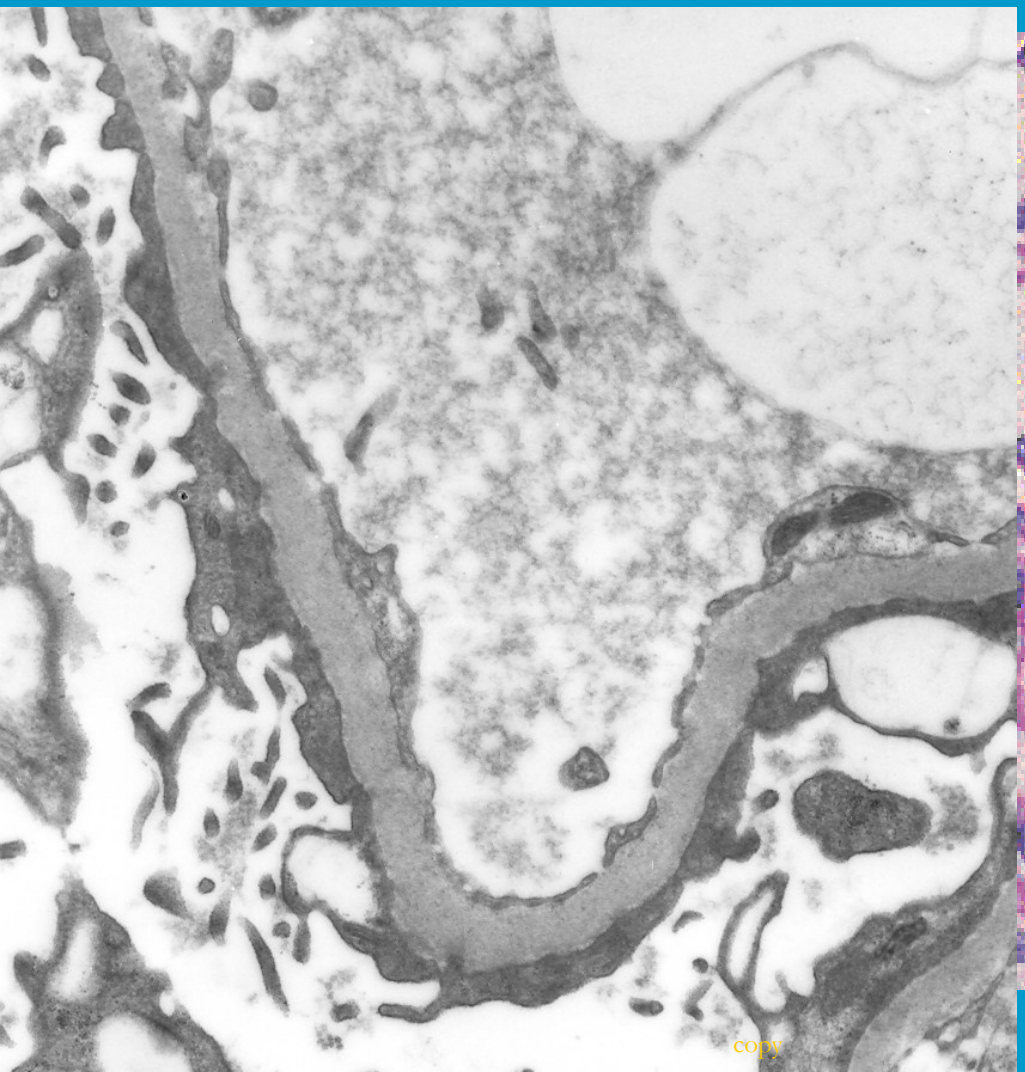
- Most common cause of nephrotic sy in children
- heavy selective proteinuria - albuminuria
- mostly in children ≤ 5 yrs
- in adults commonly associated w. NSAID, ML
- Light microscopy + IMF normal
- Genetic predisposition + immunological basis (association with respiratory infection, atopy, Hodgkin lymphoma)
- Epithelial cell injury – effaced foot processes
- Steroid therapy, good prognosis in children, in adults necessity of biopsy – dif. dg.

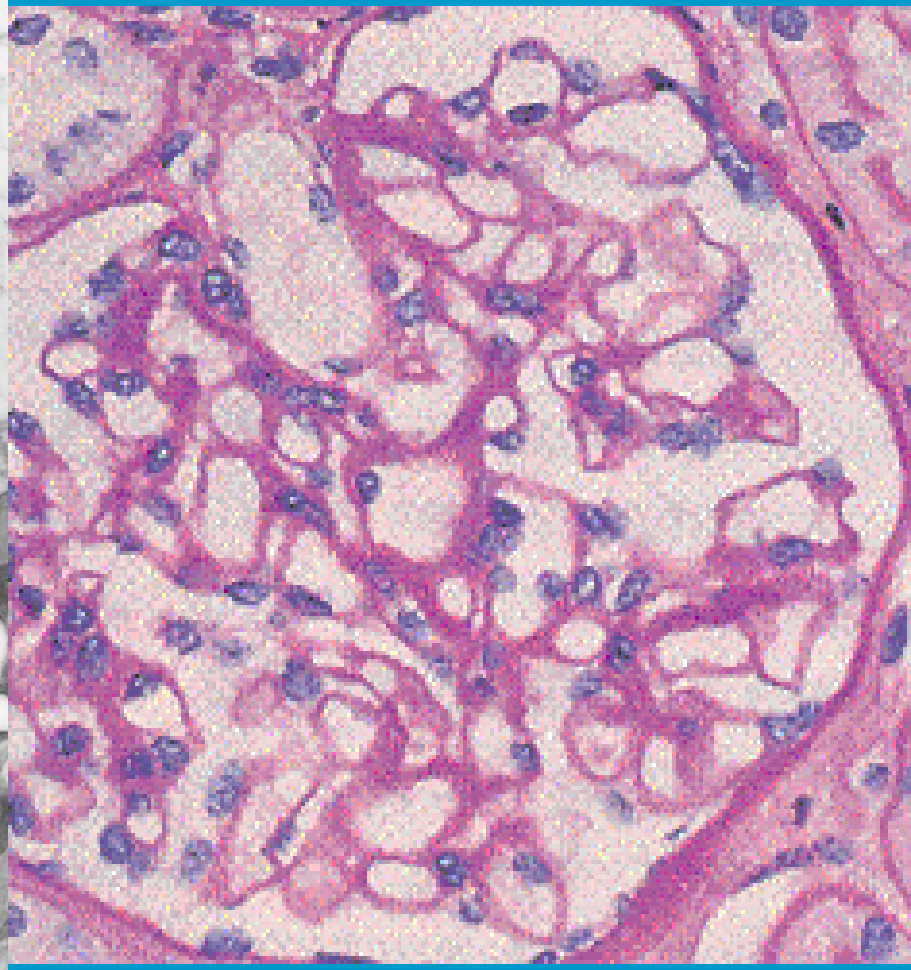
# Minimal change disease



# Minimal change disease

**Loss of epithelial foot processes in elmi, fat in tubular epithelia („lipoid nephrosis“)**





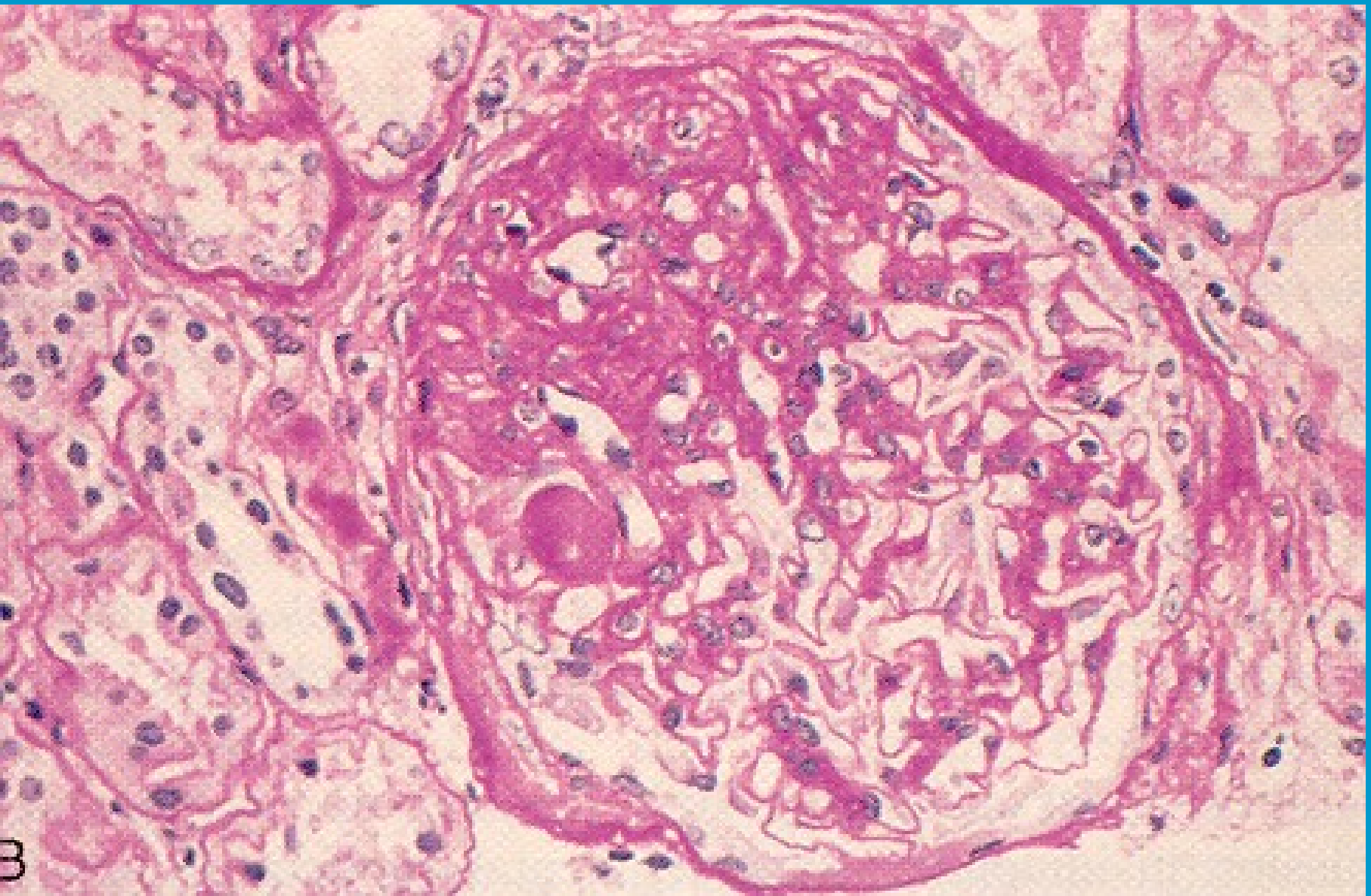
# Focal segmental glomerulosclerosis

- Nephrotic sy, ↑ incidence, any age
- Hematuria, ↓ GFR, proteinuria non-selective
- Progression usual – 50% → RF in 7 years, steroid-resistant
- Primary
  - idiopathic,
  - variable podocyte protein mutations, plasma factor ↑ permeability (soluble urokinase receptor?),apolipoprotein L1 mutations (black African descent)
- Secondary: late part of adaptive response to preexisting renal disease (renal ablation - reflux nephropathy, hypertension, glomerulopathies – IgA, SLE,…)
- Association with other diseases (HIV, obesity, toxins – heroin, drugs)

# FSGS

- epithelial damage
- hyalinosis (plasma protein leakage), foamy macrophages
- segmental sclerosis (mesangial matrix production, capillary loops collapse)
- No immune deposits on IF
- Podocyte injury on EM

# Focal segmental glomerulosclerosis



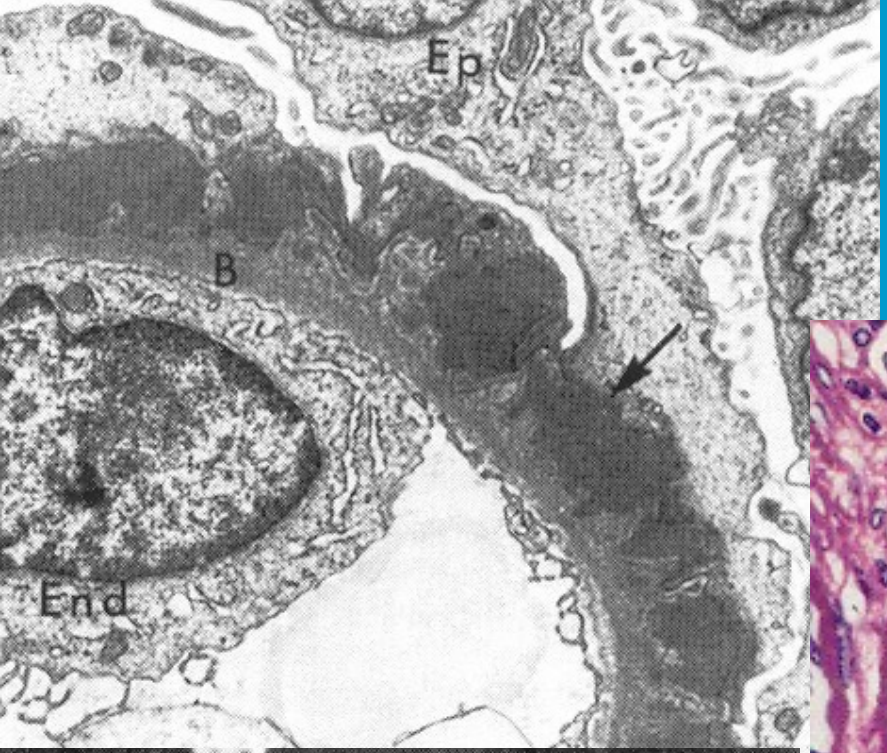
# Membranous glomerulopathy

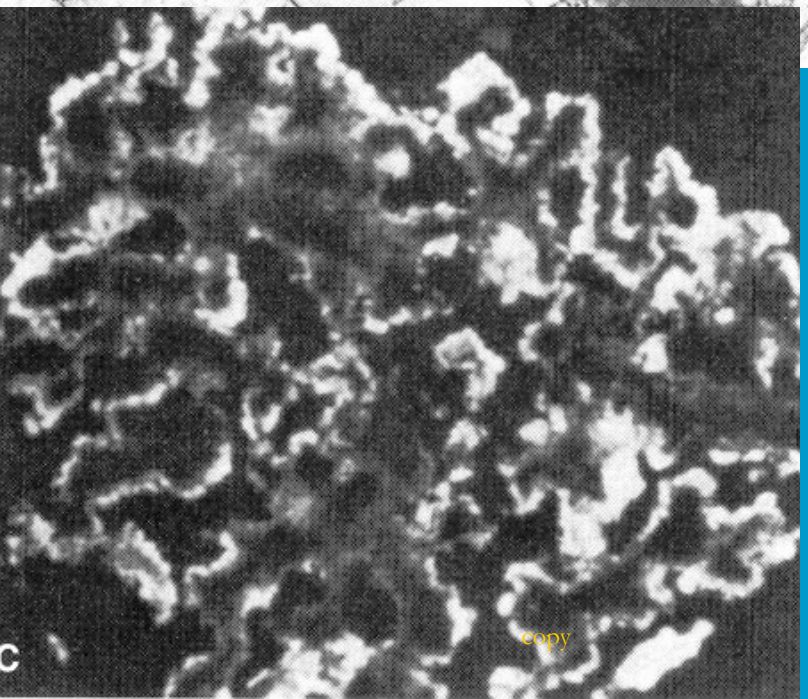
- primary: autoimmune
- mostly older adults – most common nephrotic sy in this age group
- Ab x specific receptor in podocytic membrane antigen – phospholipase A2 receptor
- proteinuria or nephrotic sy, variable course, 1/3 RF
- diffuse global glomerulopathy
- thickening of capillary wall, subepithelial IC deposits, „spikes“ - BM material in impregnation
- no increased glomerulus cellularity

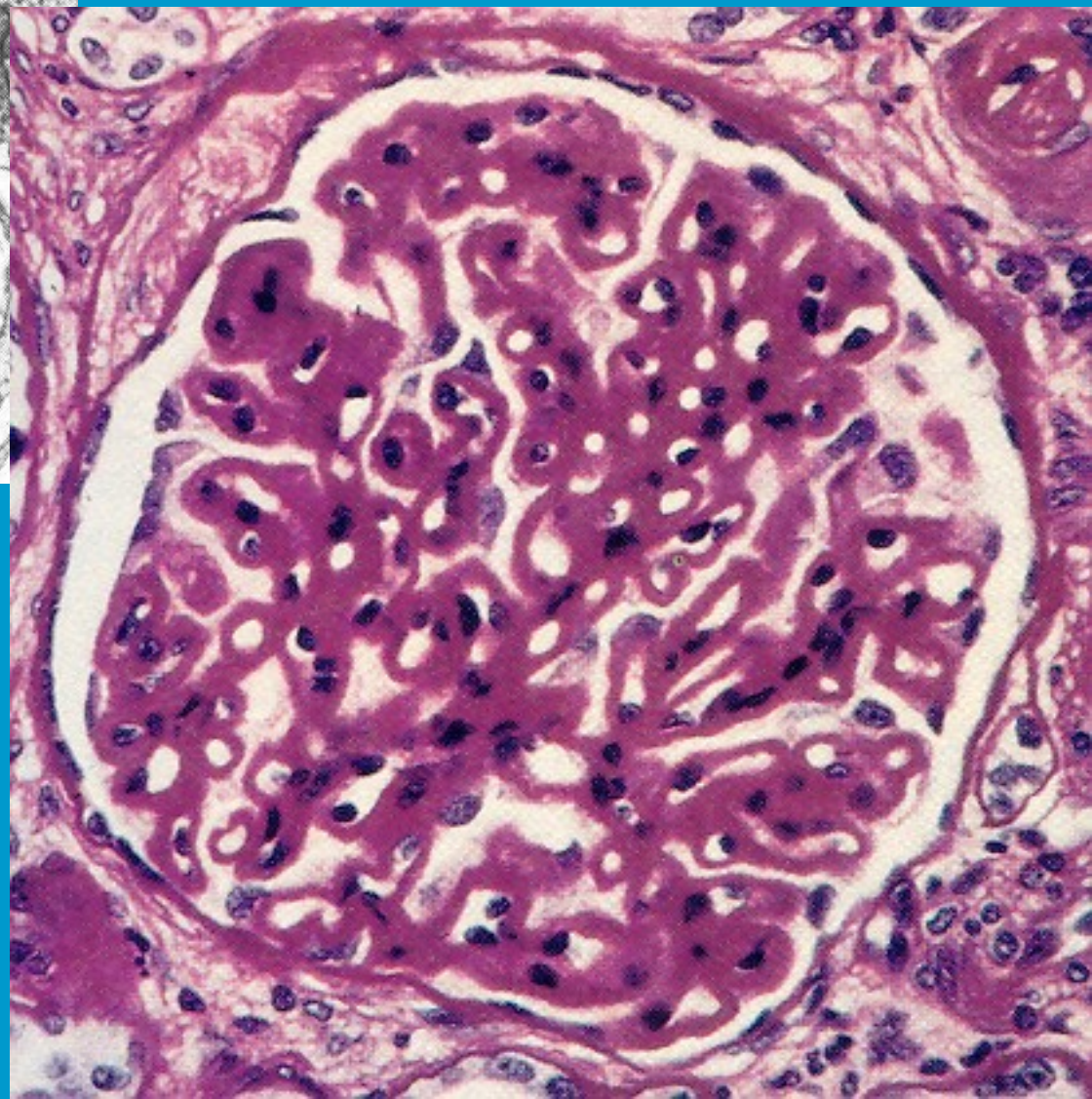
# Membranous glomerulopathy

- secondary – infections (HBV, HCV, syphilis, malaria) tumors (lung ca, colorectal ca, melanoma), drugs (NSAID), autoimmune diseases (SLE, thyroiditis)
- ! older patients may have both tumor AND autoimmune MGN

# Membranous glomerulopathy

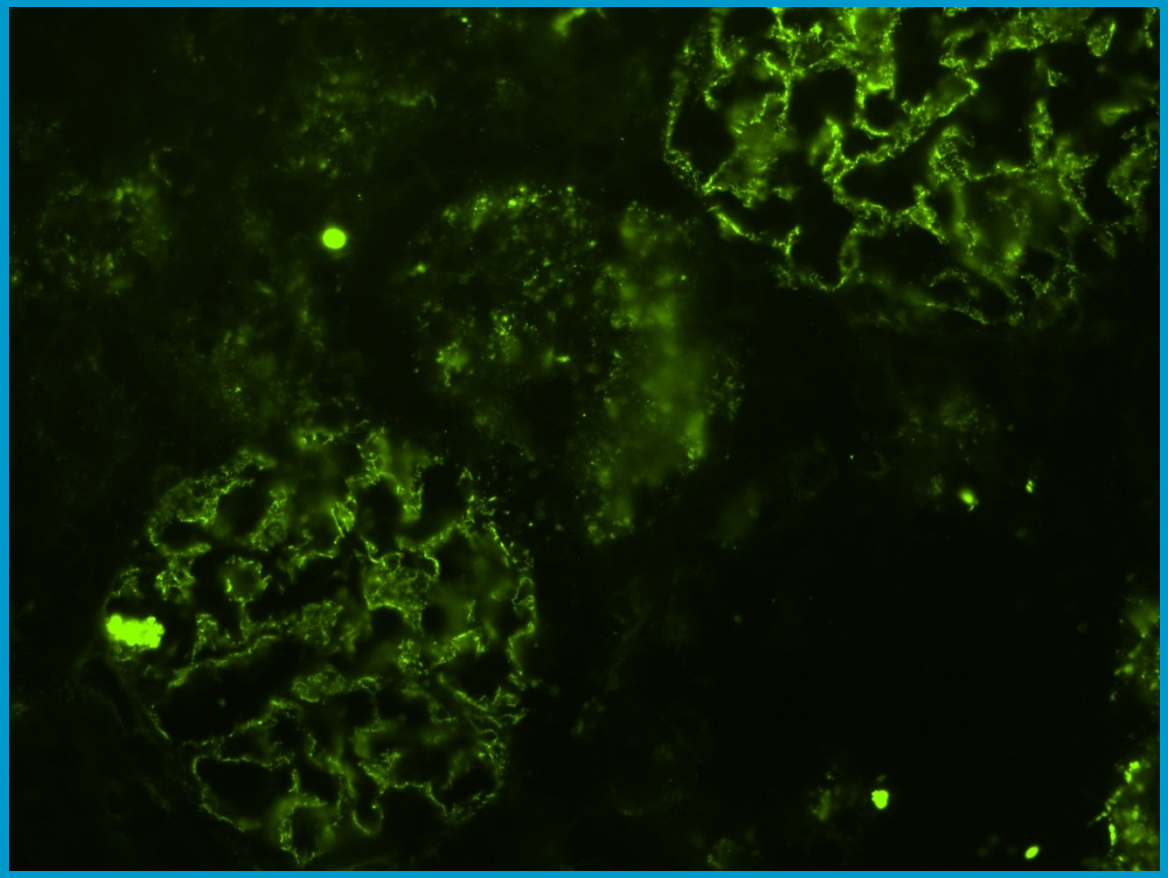


# Membranous glomerulopathy

## granular IgG deposits



# Diabetes mellitus and kidneys

- **Nonenzymatic glycosylation** of proteins – accumulation of irreversible glycosylation products in BM of vessel walls, **metabolic defect** – increased collagen synthesis, **hemodynamic changes**
- **Diabetic microangiopathy** in kidney (glomerulosclerosis) and retina (diabetic retinopathy). Diffuse thickening of capillary BM leads to ischemic changes, simultaneously increased plasmatic proteins permeability, PAS+ mesangial matrix increase; glomerular enlargement

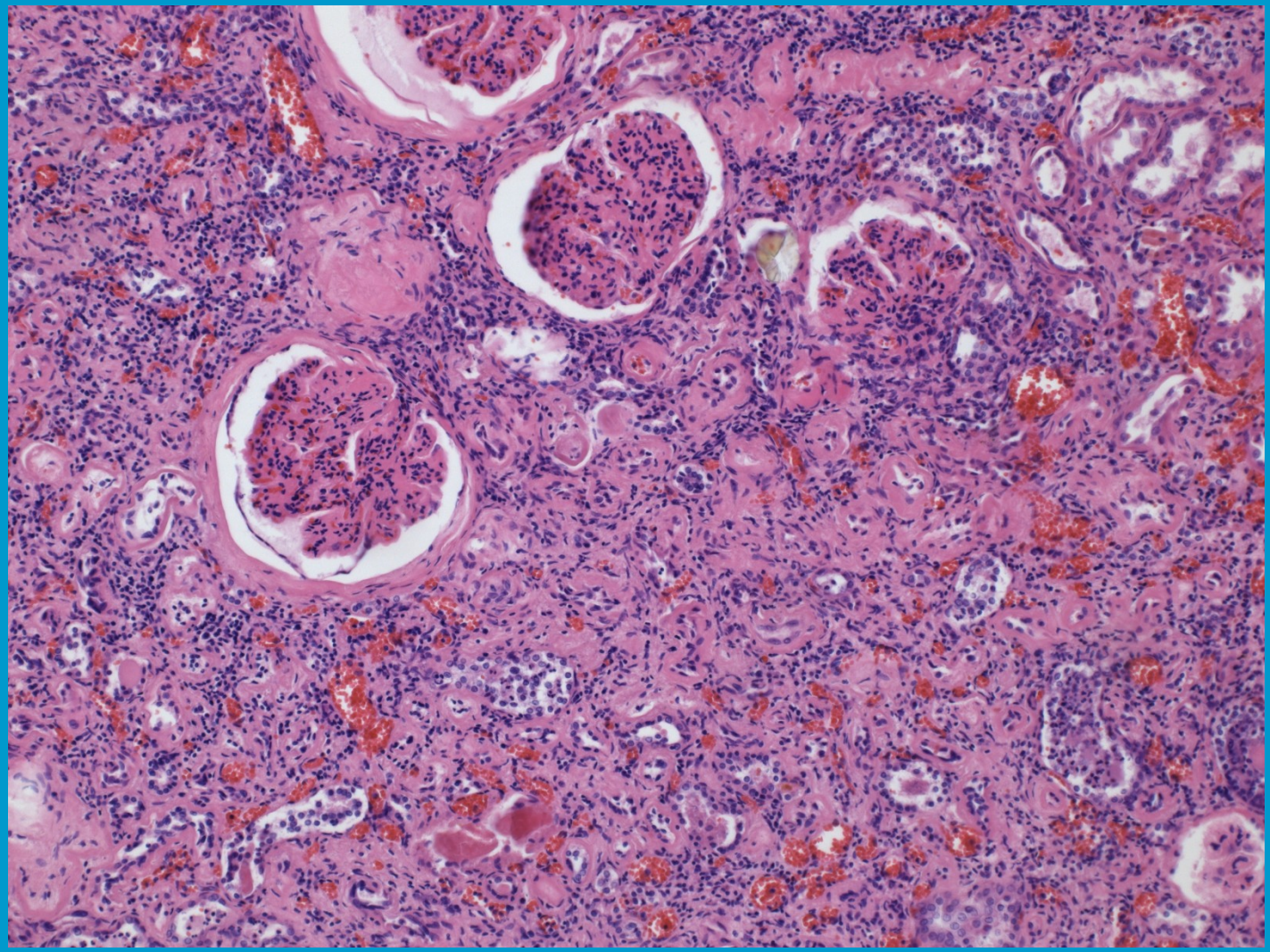
# Diabetic nephropathy

- **Diabetic microvascular disease**
- **Clinically:** non-nephrotic proteinuria, nephrotic syndrome, chronic renal failure
- **Morphology:** glomerulosclerosis (diffuse mesangial, nodular), hyalinizing arteriolar sclerosis, tubulointerstitial lesions (steatosis and glycogenation of tubular epithelium, pyelonephritis, papillary necrosis)
- the most common causes of chronic RF
- 40 % of diabetics will have nephropathy

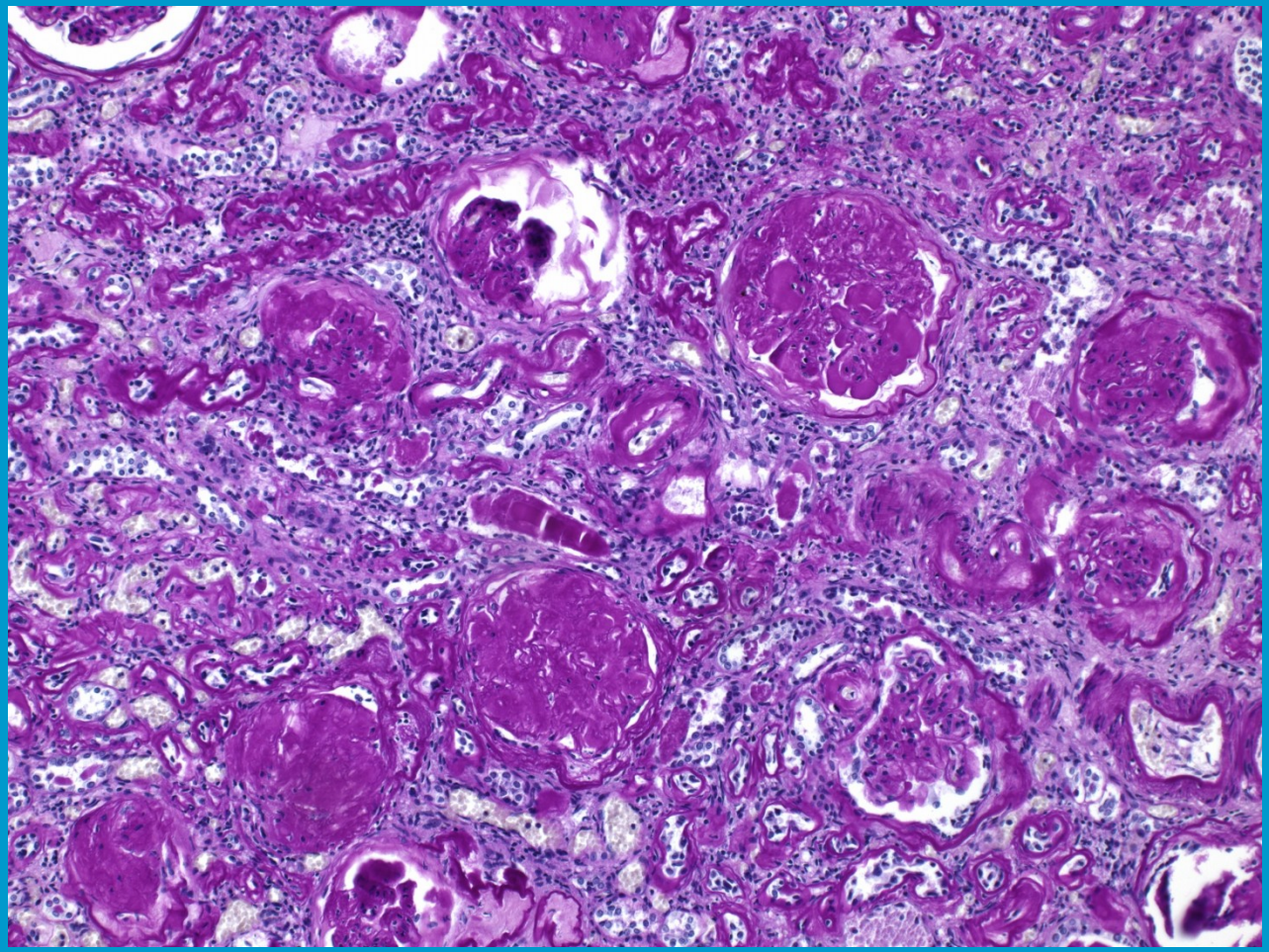
# Diabetic glomerulosclerosis

- **Diffuse glomerulosclerosis** – GBM thickening, increase in mesangial matrix + cellularity
- **Nodular glomerulosclerosis** - (Kimmelstiel-Wilson) after 10-15 yrs; PAS+ nodular acellular material deposits at the tips of capillary loops; leads to chronic renal insufficiency
- no immune deposits in IMF

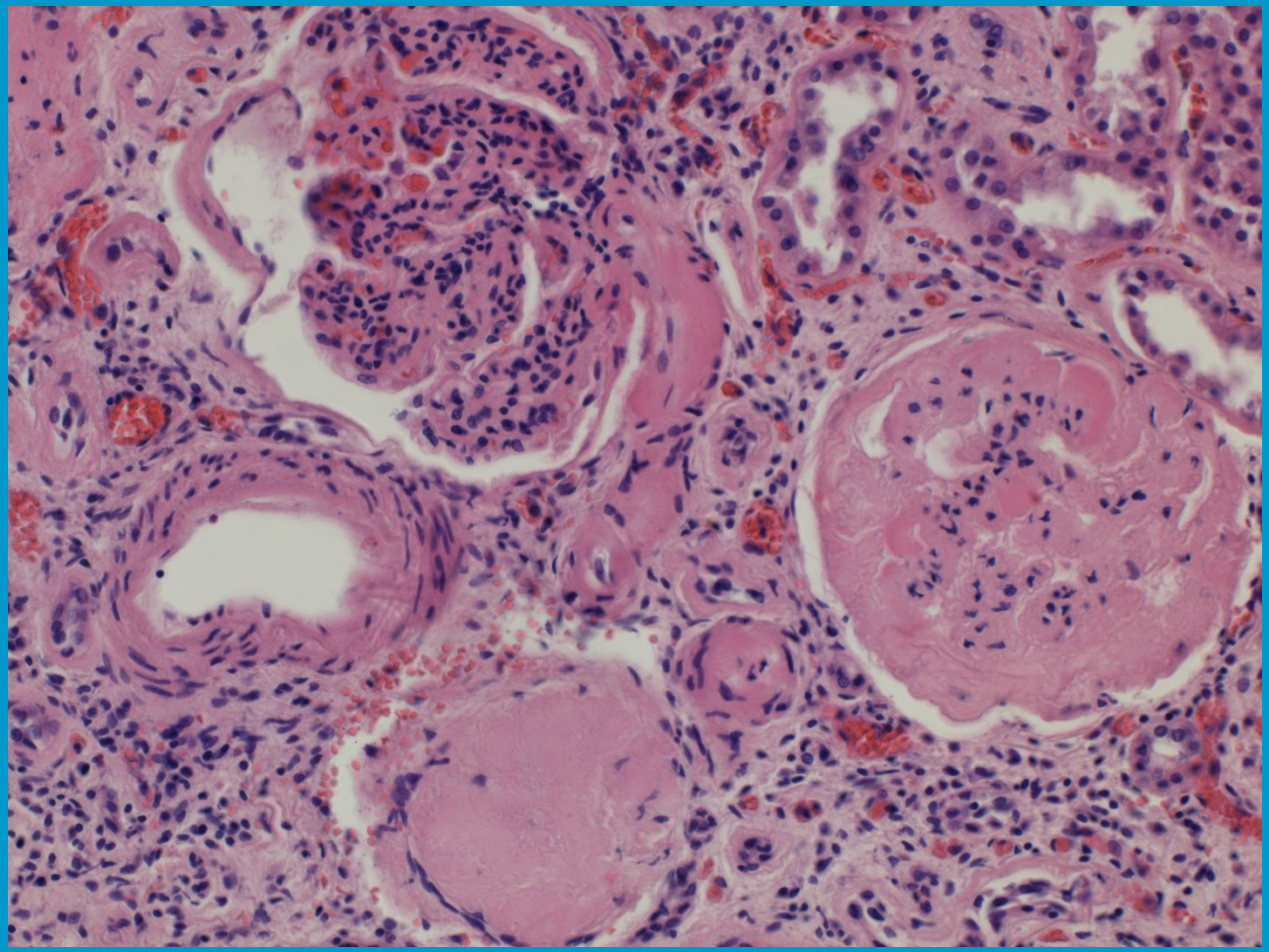
# Diabetic glomerulosclerosis

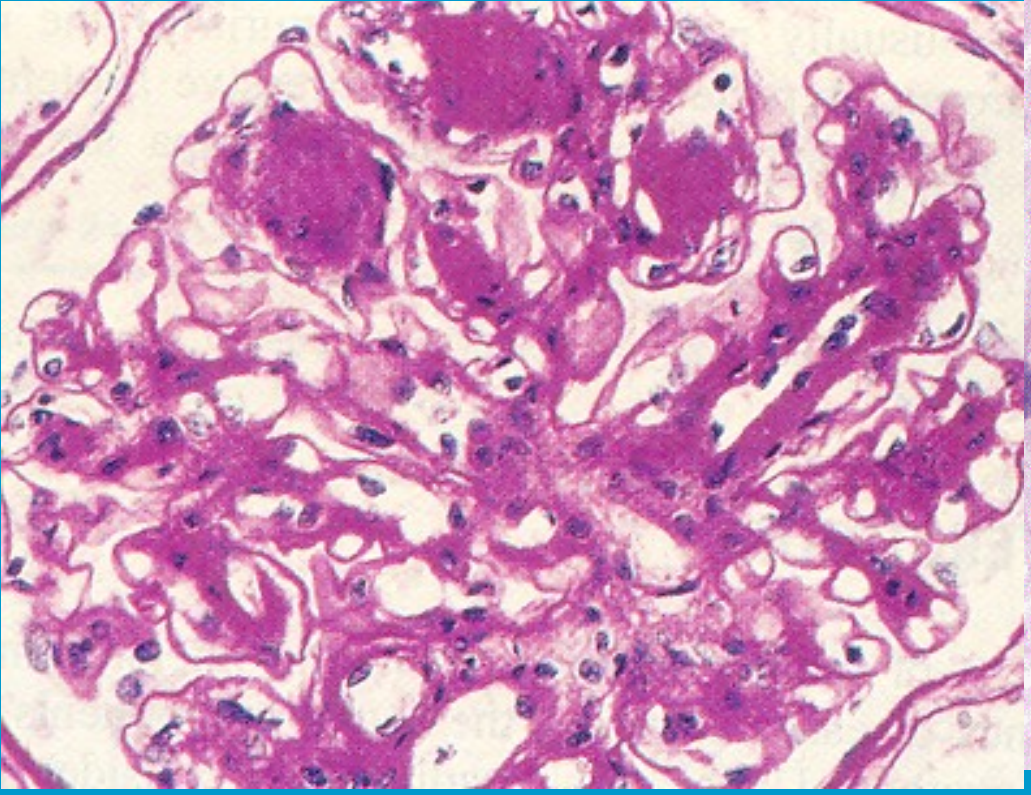


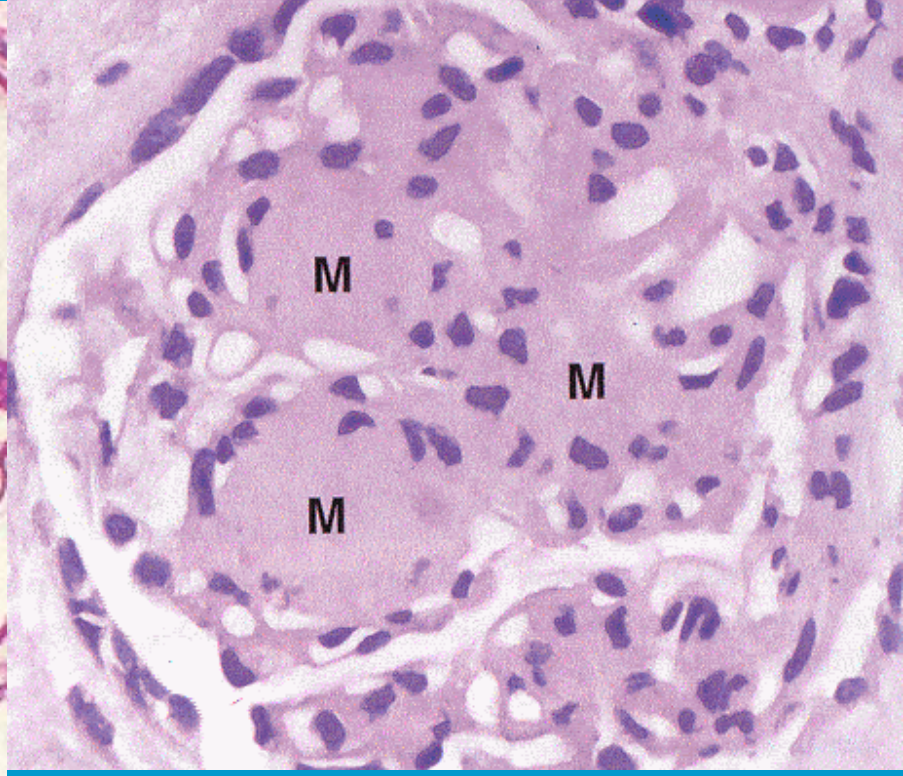
# Diabetic glomerulosclerosis



# Diabetic glomerulosclerosis








**Diabetic glomerulosclerosis**

Further renal complications in diabetics

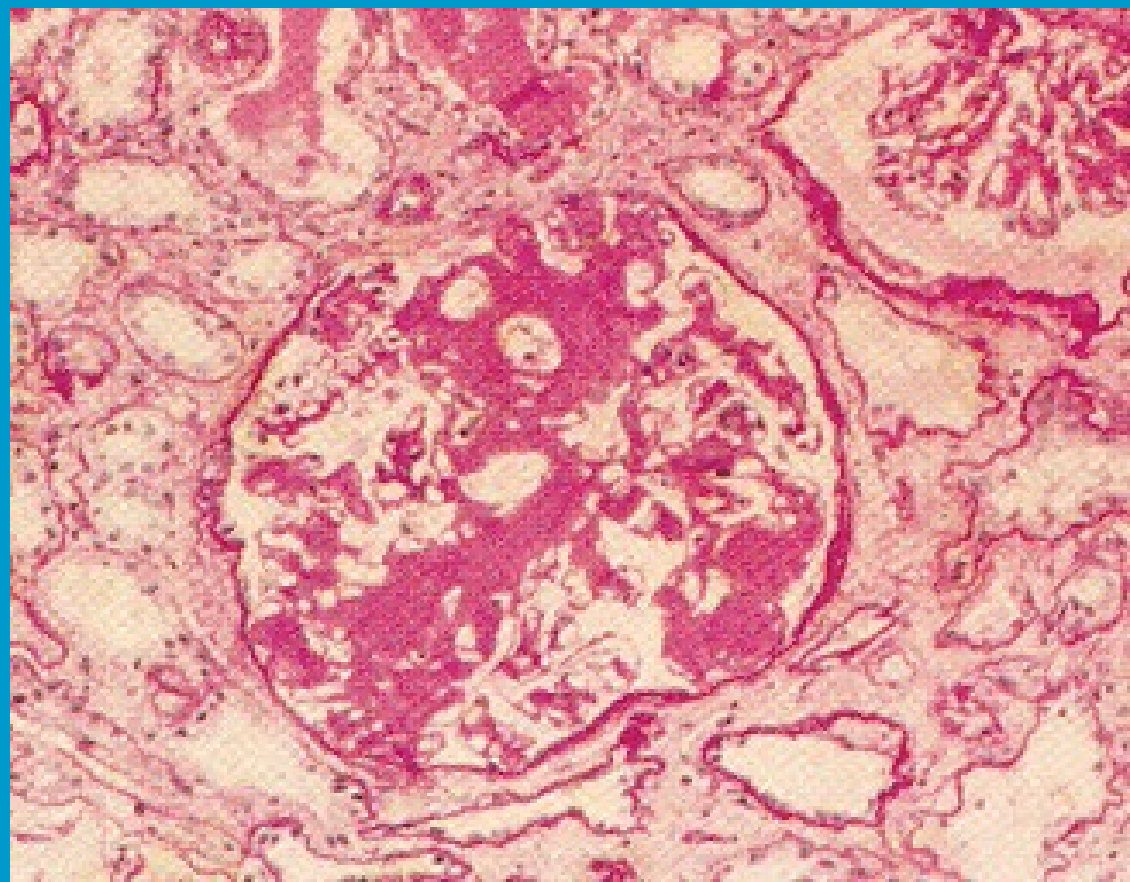
- accelerated **arteriolosclerosis and arteriosclerosis, hypertension**
- **Pyelonephritis**
- **Renal papillary necrosis** in acute PN

# Renal amyloidosis

- Amyloidosis – pathologic deposits of abnormal microfibrillary (8-10nm) proteinaceous acellular material
- Eosinophilic in HE, Kongo red +, green dichroism in polarised light
- Firm pale enlarged kidney in macroscopy

# Renal amyloidosis

- Amyloid deposits in glomerular mesangial matrix and capillary walls; glomerular obliteration
- Peritubular and blood vessel walls
- Proteinuria
- Nephrotic syndrome
- CHRI



# Glomerulopathy with hematuria

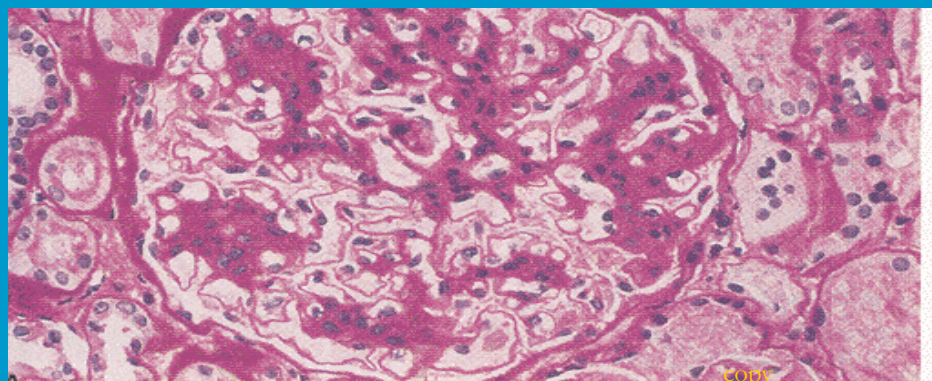
- Primary: IgA nephropathy (Berger's disease)

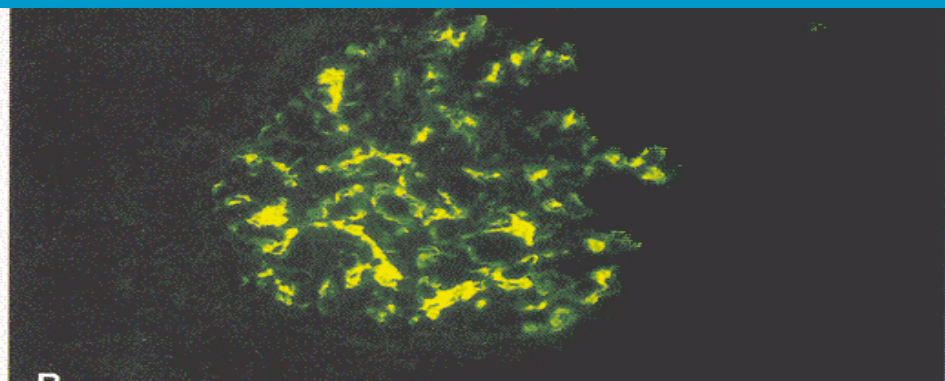
  Alport syndrome / thin basement membranes sy
- Secondary (systemic): some types of SLE

  Henoch-Schönlein purpura

# IgA nephropathy

- Recurrent hematuria, children and young adults w. genetic predisposition, after GIT, respitatory tract, urinary tract infections, may → RF; most common cause of RF in primary glomerulopathies
- variable course, recurrence after kidney transplantation
- IgA and C3 mesangial deposition, mesang. cells and matrix proliferation, segmental glomerulosclerosis
- Abnormal increase/pathologic form of IgA production, AAxIgA – IC;↓ clearance of IC in cirrhosis





# IgA nephropathy

- changes of IgA nephropathy present in Henoch-Schönlein purpura – IgA vasculitis
- preexisting respiratory infection
- purpura due to vasculitis w. IgA deposits (+ skin rash, GIT hemorrhage, arthritis)
- in children regeneration, in adults possible RF

# Alport syndrome

- Part of collagen IV glomerulopathies
- genetic disorder, 90% X-linked, AR or AD
- abnormal basement membranes (lamina densa), later FSGS, tubular atrophy, interstitial fibrosis
- manifestation mostly in kidney (hematuria – nefritis, proteinuria), RF;
- HD, transplantation
- ear – deafness
- eye – lens + cornea disorders, cataract

# Thin basement membrane

- benign familial hematuria, no progression to RF
- common inherited lesion – hereditary nephropathy
- heterozygous carriers of collagen IV mutations or less dangerous collagen IV mutations
- without other problems (ocular, …)
- differential diagnosis

# Glomerulopathy w. acute nephritic sy

proliferative GN w. increased mesangial/ endocapillary cellularity, commonly crescentic

- acute (diffuse endocapillary) proliferative GN
- membranoproliferative GN (C3, prim. IC),
- rapidly progressive GN
- secondary mostly in vasculitis – SLE,
  microscopic polyangiitis
  granulomatosis with polyangiitis (Wegener)

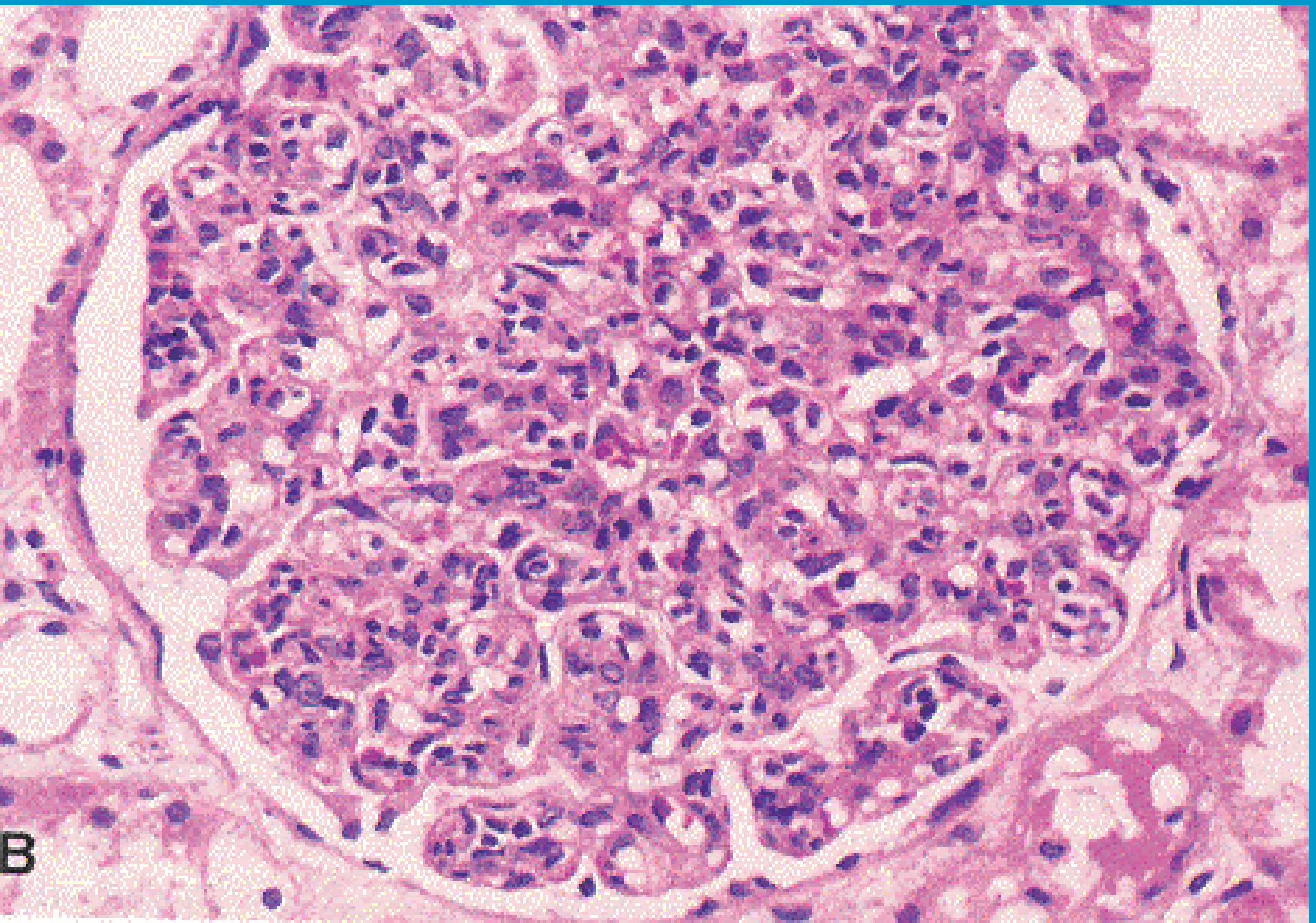
# Diffuse proliferative GN

- postinfectious (str., staph., viruses, protozoan - malaria, toxoplasmosis; schistosomiasis)
- in systemic disorders (inf. endocarditis, necrotising arteritis
- any age,
  - formerly children more commonly, after strep.
  - now adults after staph. (+ DM, alcohol, age)
- acute nephritis (+ fever, nausea)
- may be partially crescentic (→ progressive)
- prognosis – regeneration usual in children, in adults possible ↓ renal function

# Diffuse proliferative GN

- variable signs: hematuria, proteinuria, hypertension, edemas, renal insufficiency
- possible without signs
- capillary stenosis, increased endocapillary and mesangial cellularity
- IMF: granular deposits in capillary loops and mesangium – IgG, C3
- EM: subepithelial, mesangial deposits - humps

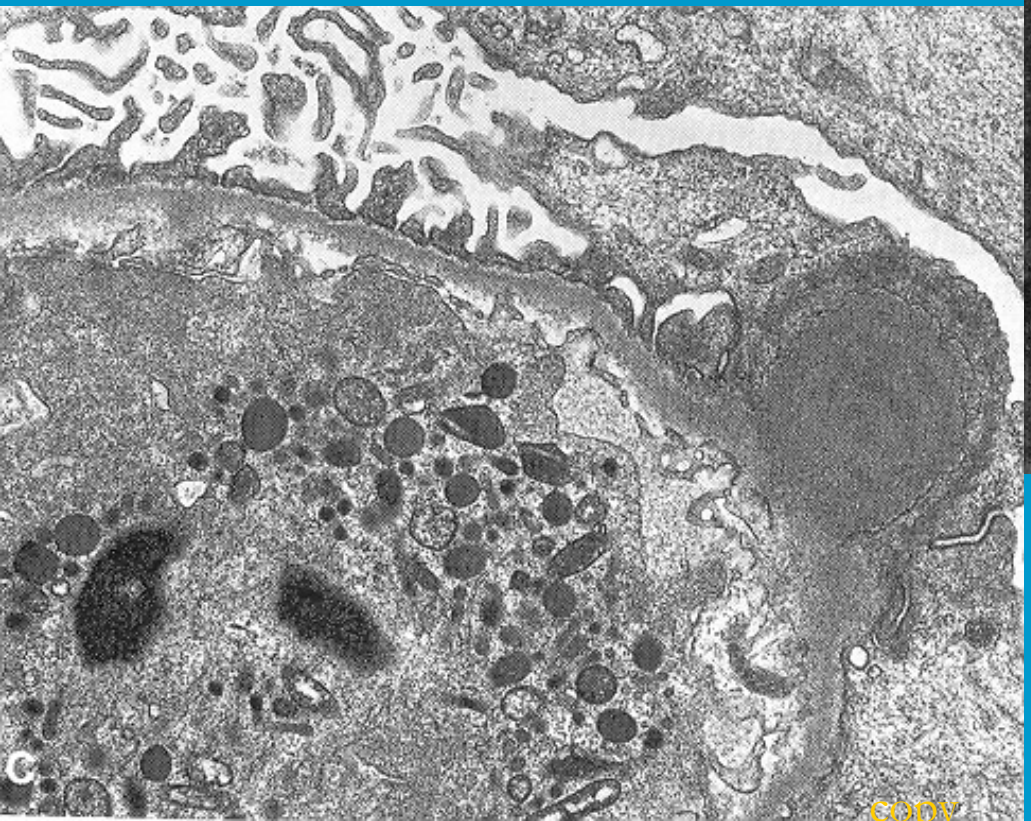
# Diffuse proliferative GN



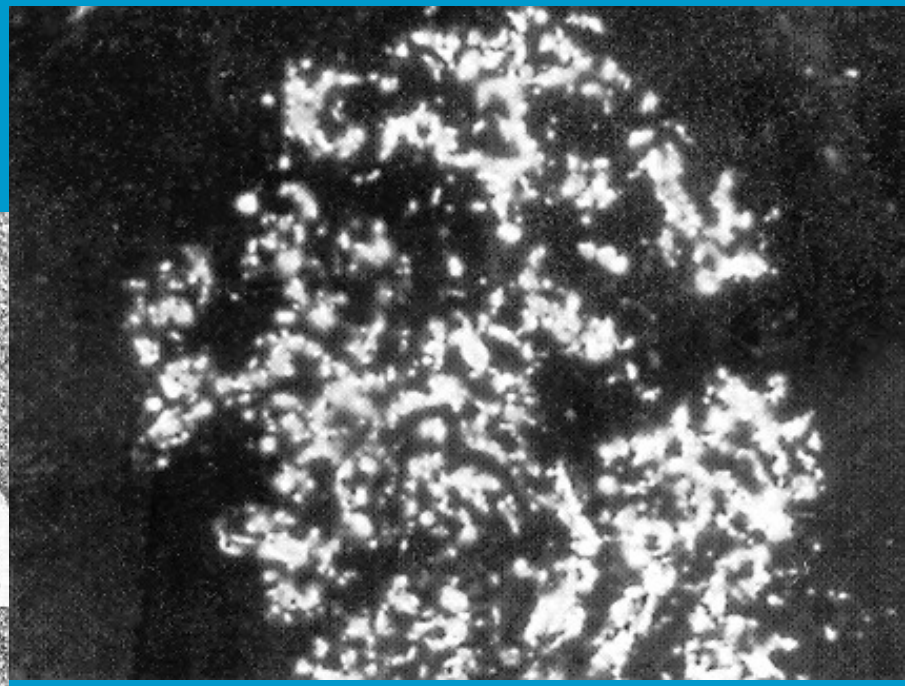
# Diffuse proliferative GN

**subepithelial immune complex deposition, postinfective**

Elmi
„humps“



Immunofluorescence



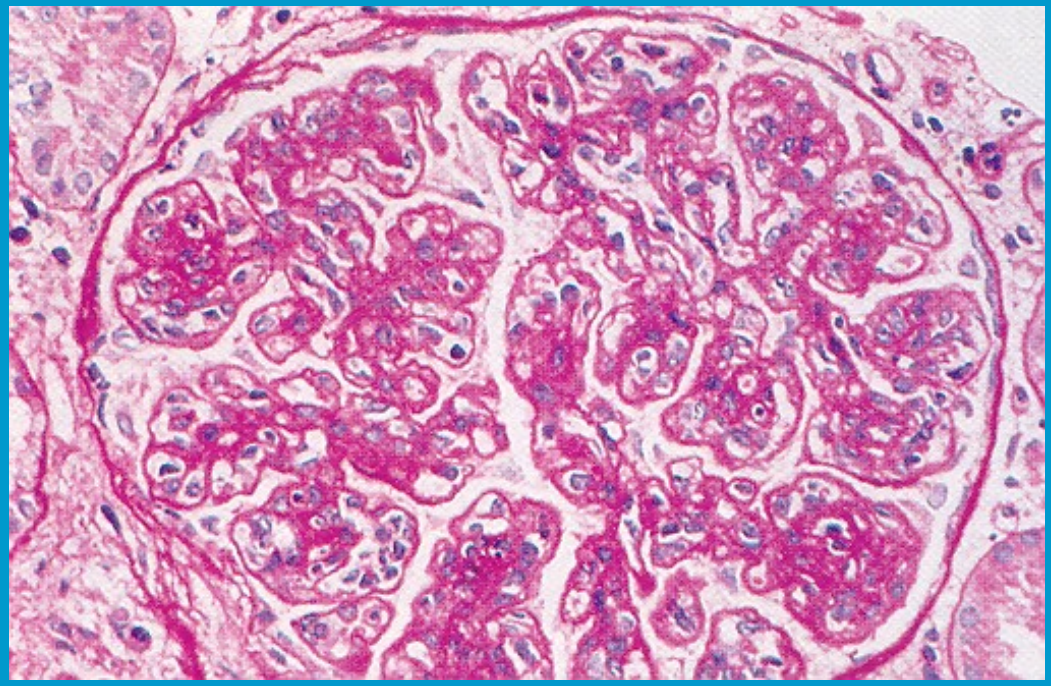
granular deposits in IgG and C3

# Membranoproliferative GN

- formerly type I-III MPGN
- Now: a group of disorders w. complement abnormalities
  - C3 part of complement present in biopsy, dysregulation, inflammation
- Immune complexes GN
  - inflammatory diseases w. proliferative GN, IMF IgG+, C3+
  - IC: cryoglobulinemia (80% due to HCV); SLE, HIV; malignancy (CLL, ML), alpha1- AT deficiency),
- C3 nephropathy (C3 GN and dense deposit disease)
- young, poor progn., CHRI, recurrent in graft

# Membranoproliferative GN

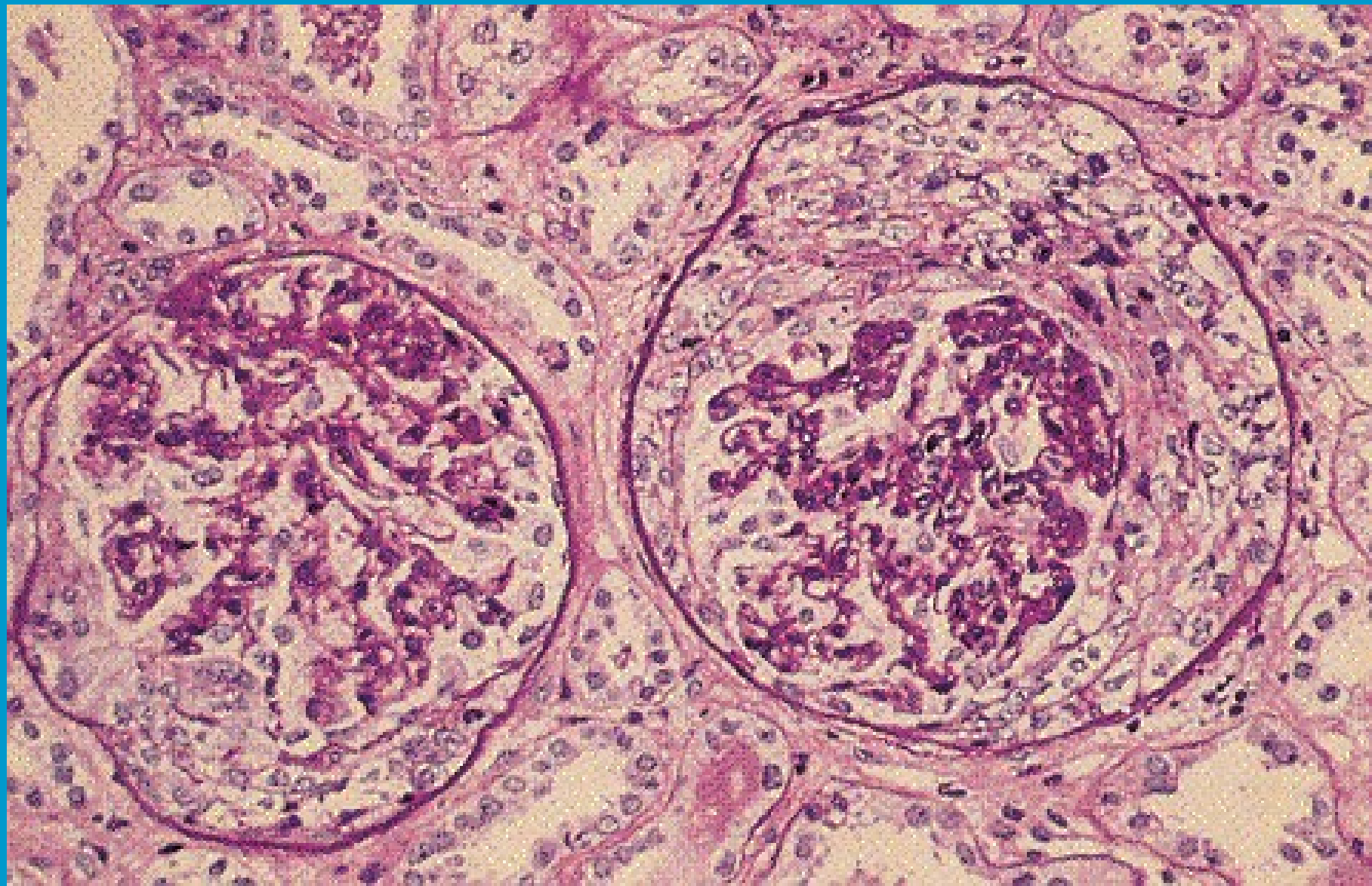
- diffuse mesangial + endothelial cells activation and proliferation (mesangiocapillary GN), mesangial matrix expansion, BM thickening – „duplication – tram-track“



# Rapidly progressive (crescentic) GN

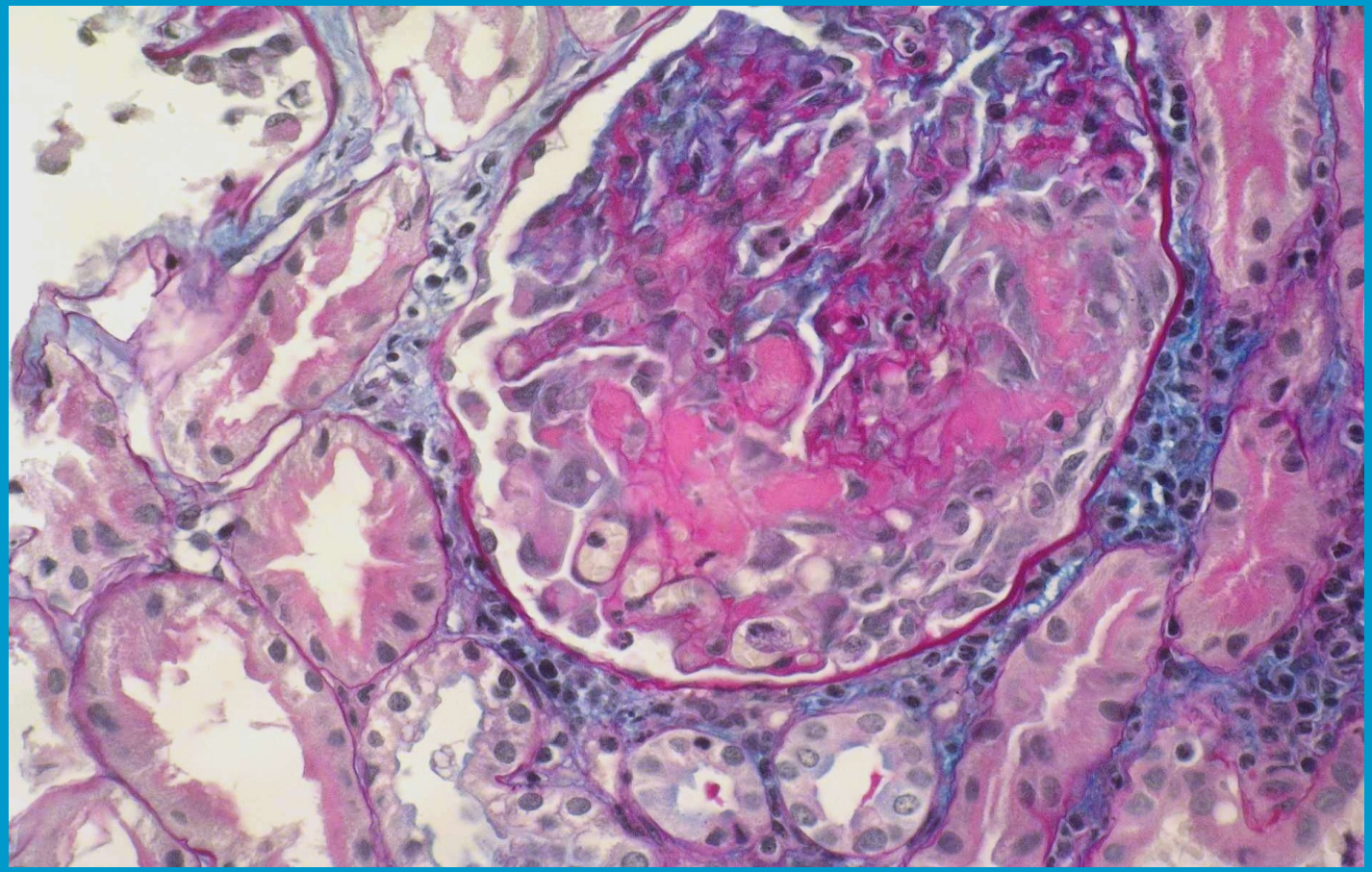
- clinically rapidly progressive GN,
- various etiology (immune-complex mediated incl. IgA, pauci-immune + ANCA, anti-GMB)
- small vessel vasculitis, SLE,…
- necrotising GN – capillary rupture, exudation – extracapillary proliferation - crescentic
- Immunosuppression in active lesion + plasma exchange in known circulating AB (anti-GBM)
- No direct therapy in fibrosing lesion

# Rapidly progressive (crescentic) GN



# Rapidly progressive (crescentic) GN

fibrinoid necrosis, fibrin in a cellular crescent



# Anti-GBM disease

- uncommon
- rapidly progressive renal failure +/- hemoptysis (Goodpasture sy)
- linear deposits of IgG

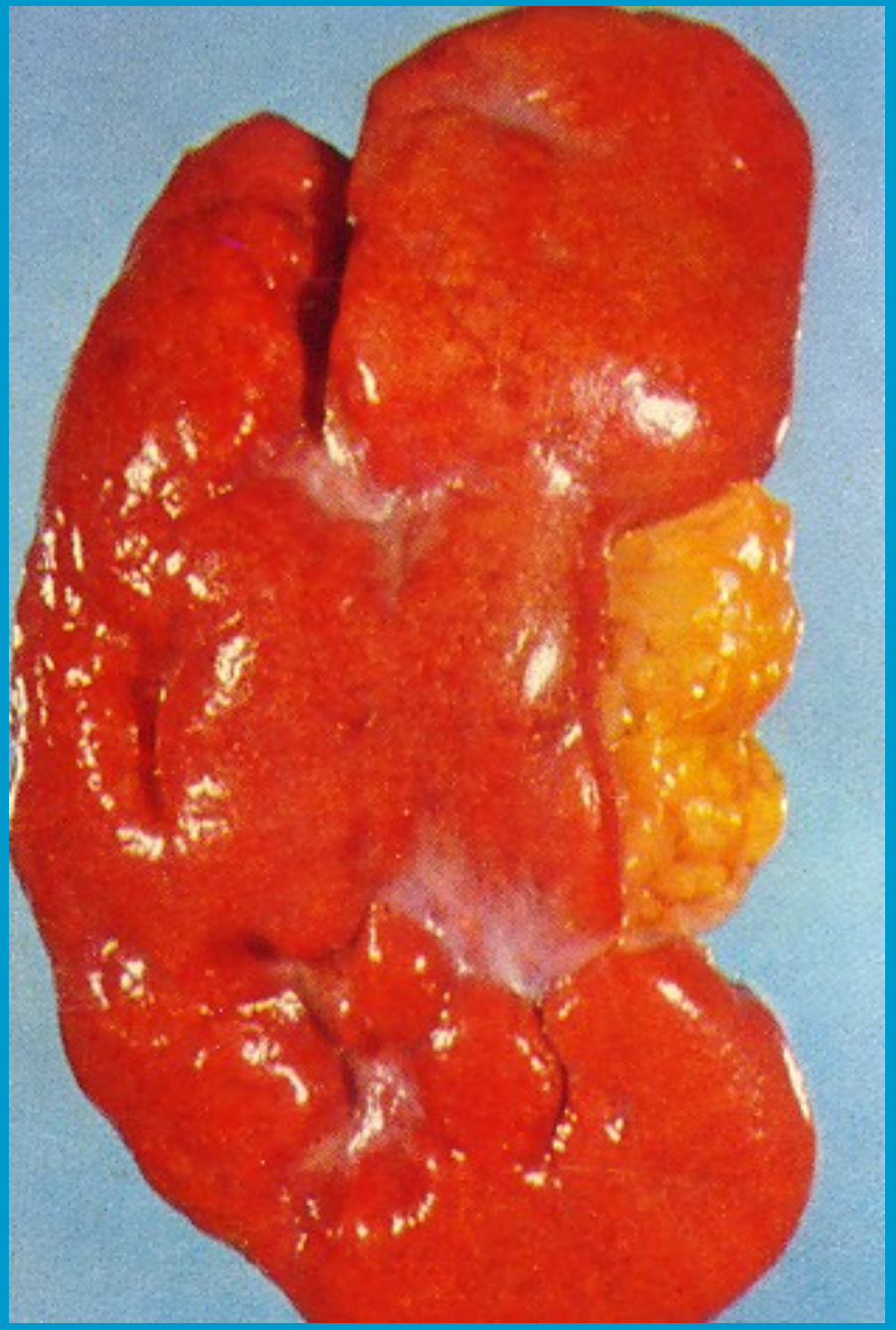
# Glomerulopathy due to vascular disorders

- in hypertension
- renal infarction
- renal artery stenosis
- thrombotic microangiopathy (HUS, thrombotic thrompocytopenic purpura)
- systemic vasculitis (ANCA+, microscopic polyangiitis, anti-GBM GN)

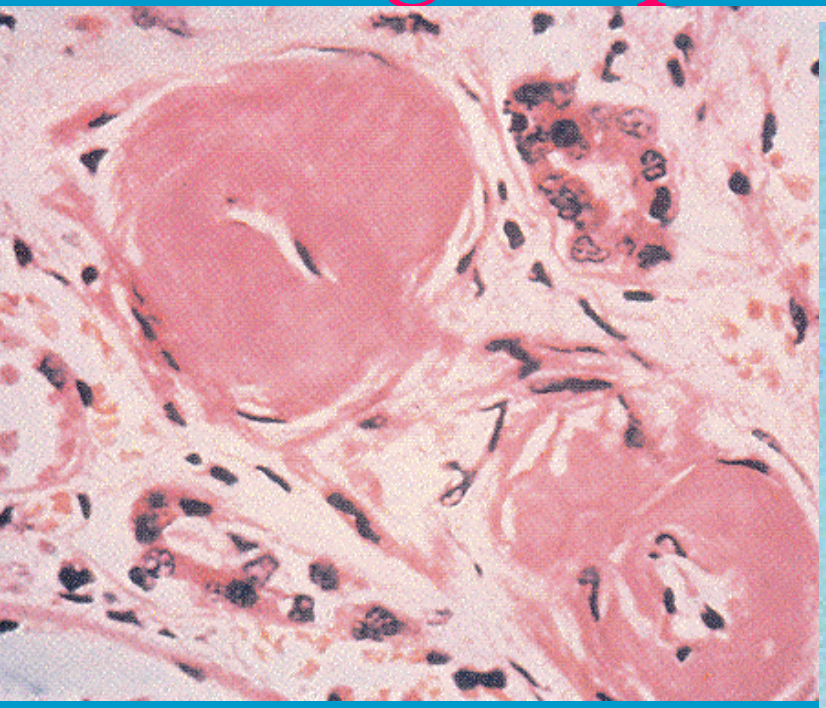
# Nephropathy in hypertension

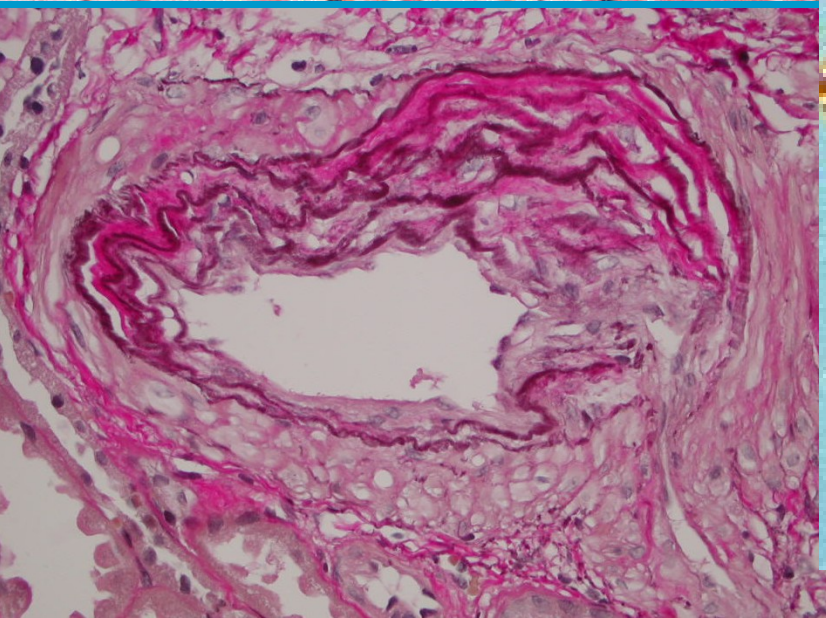
- Benign nephrosclerosis= compensated hypertension
  - macro: decreased size, granulated surface, atrophic cortex 2-3 mm
  - micro: hyaline insudation on arteriolar wall, arteries w. hypertrophic media, intimal sclerosis, glomerular ischemic changes + loss, tubular atrophy, interstitial fibrosis
  - GBM wrinkling

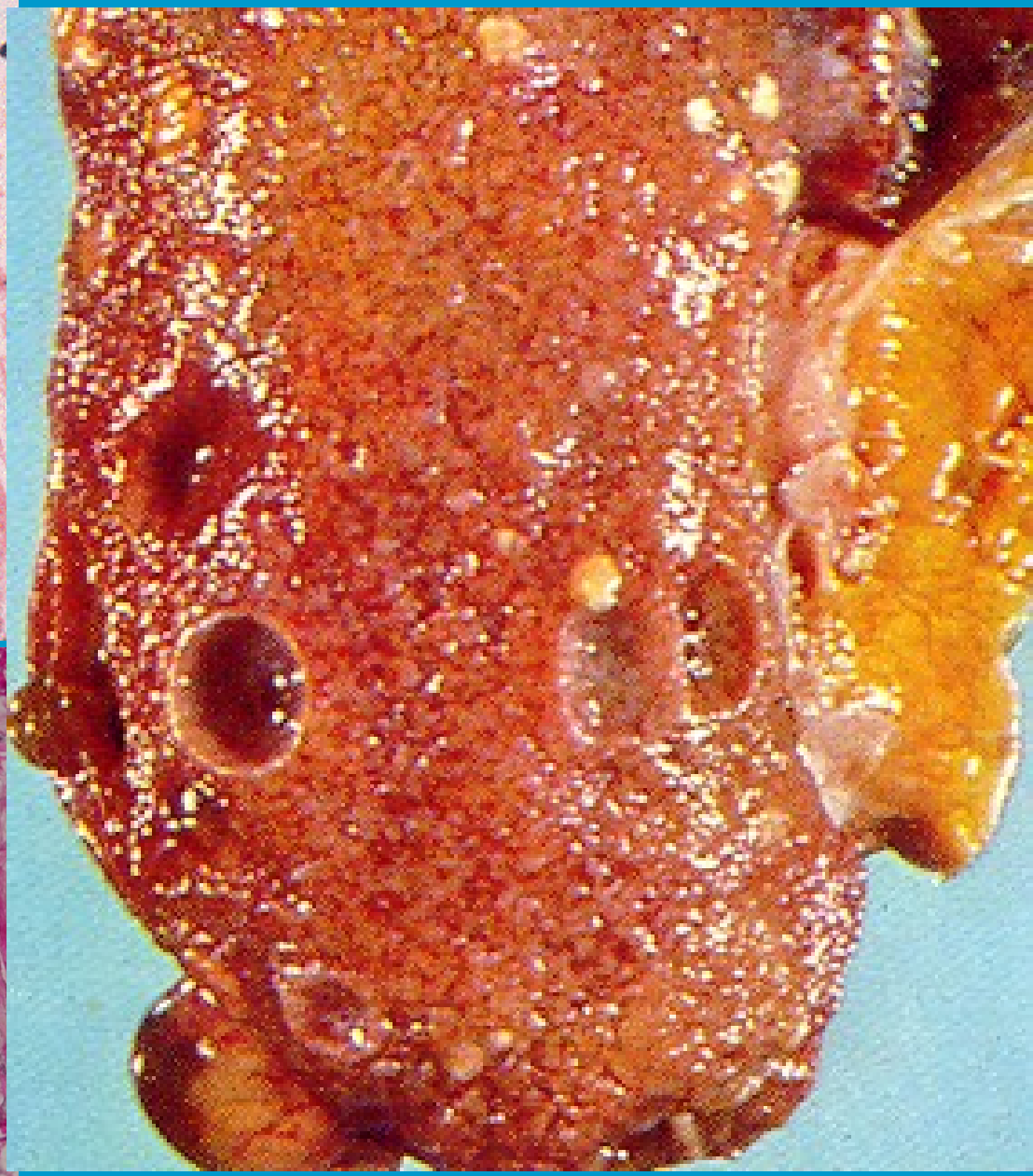
# Benign nephrosclerosis



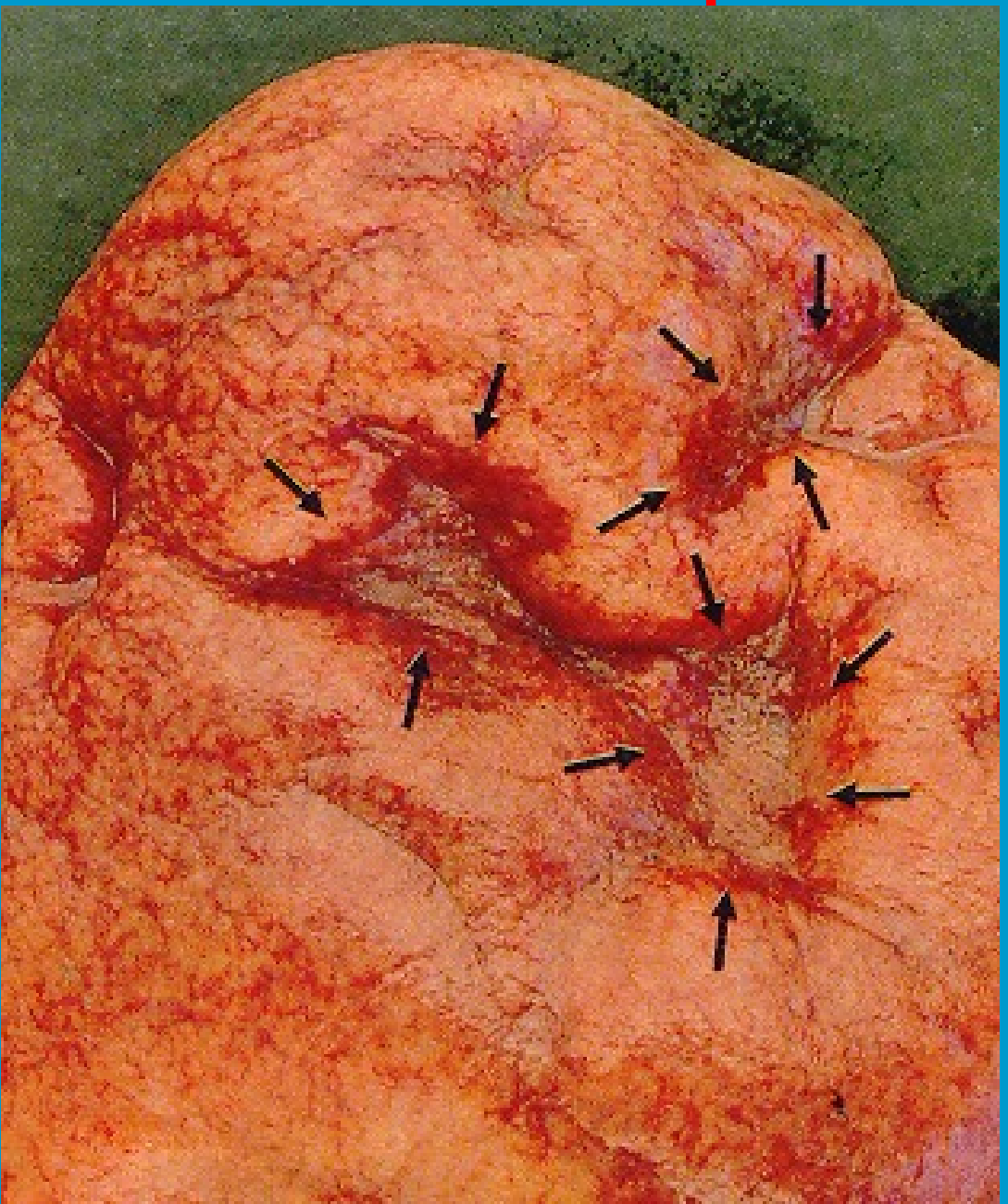
# Benign nephrosclerosis arteriolosclerotic





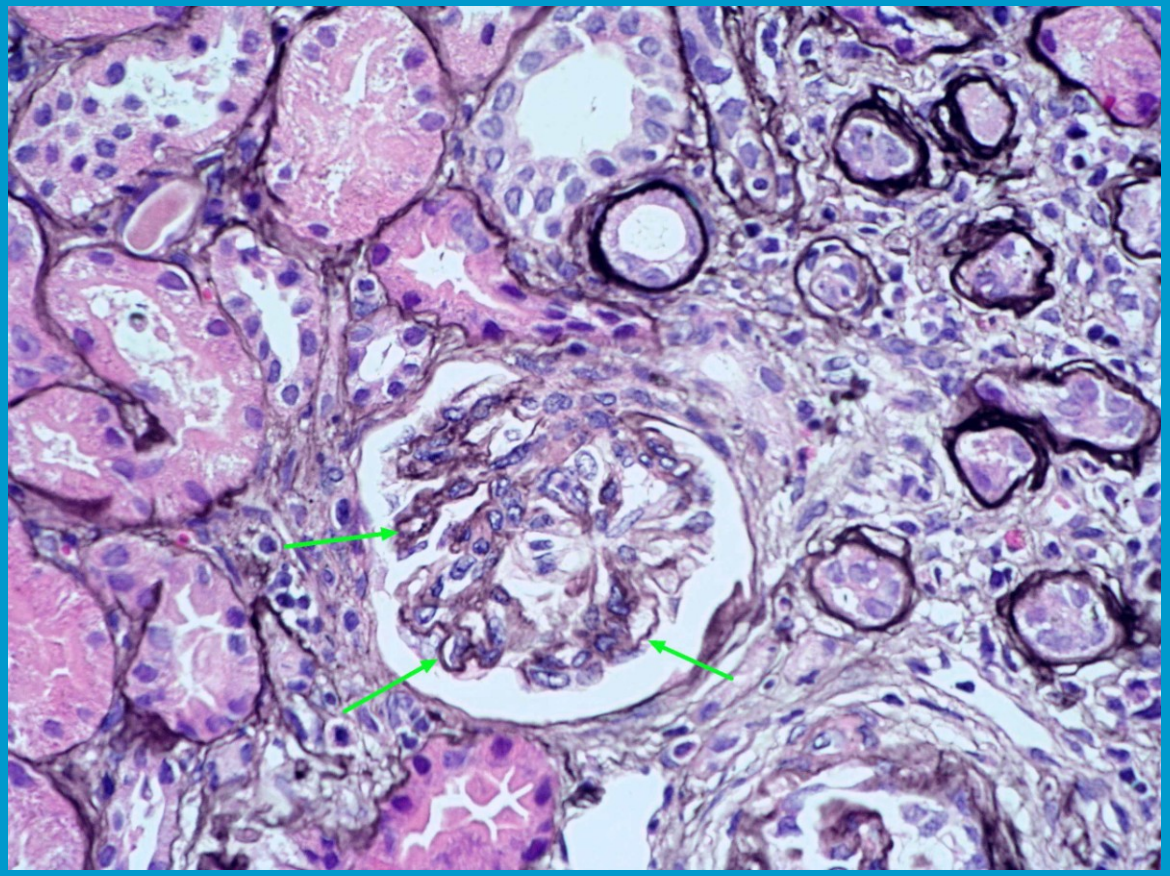


# Nephrosclerosis



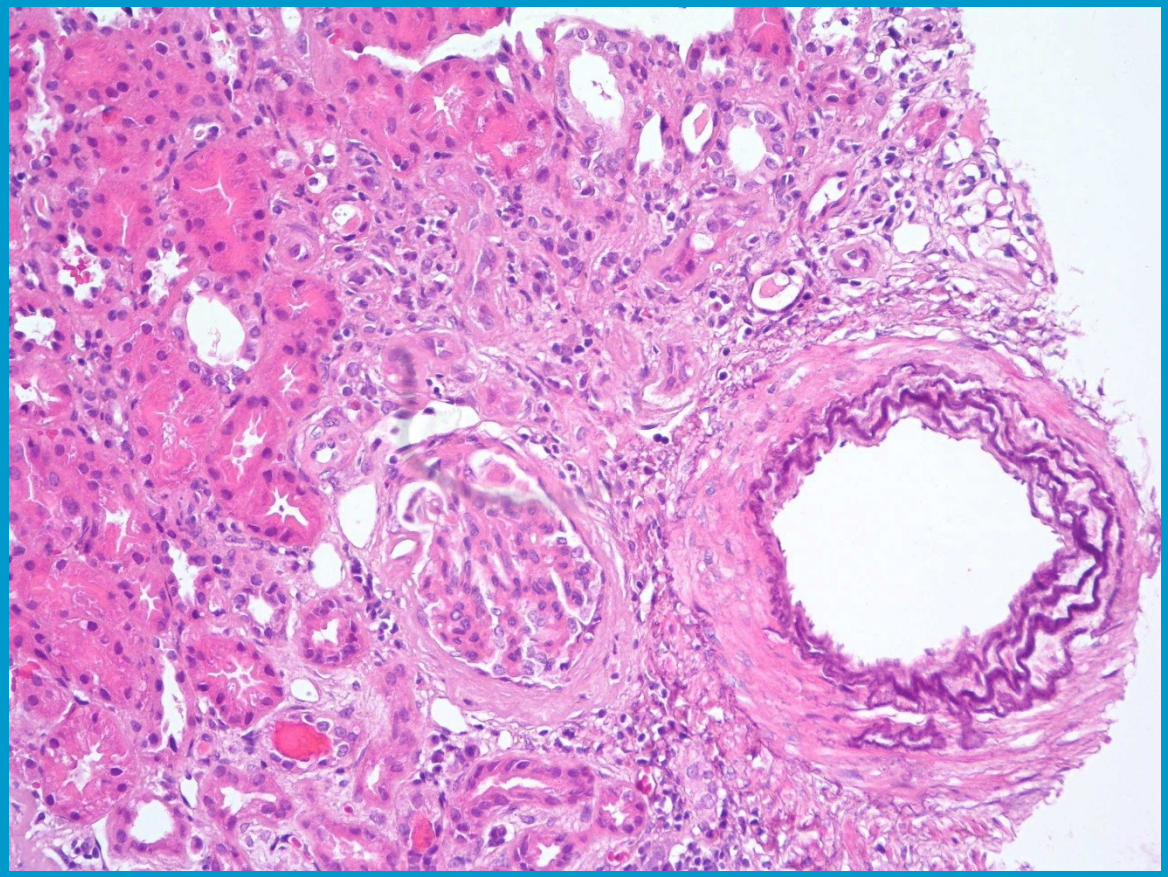
**granulations**
and post-infarct
scars

# Nephrosclerosis



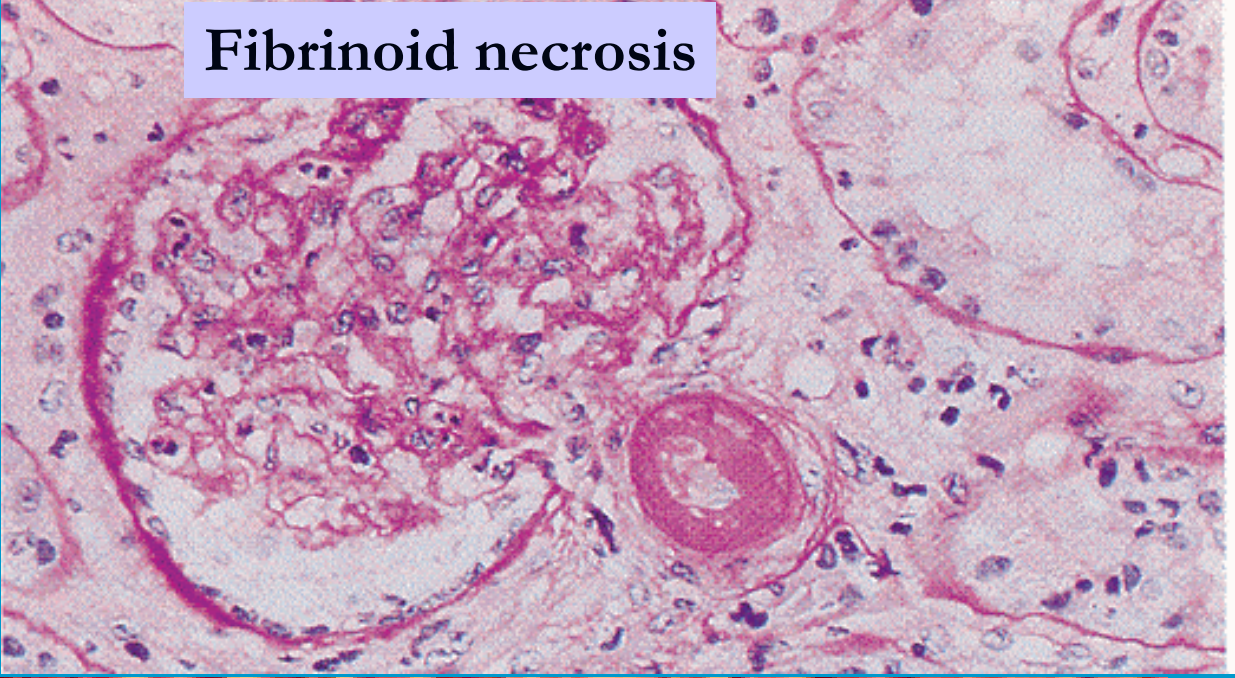
GBM wrinkling, G ischemic changes

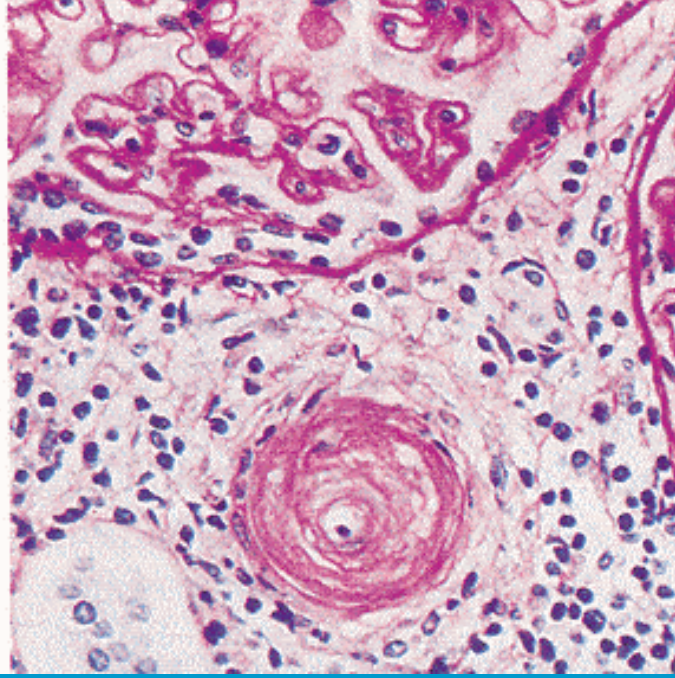
# Nephrosclerosis

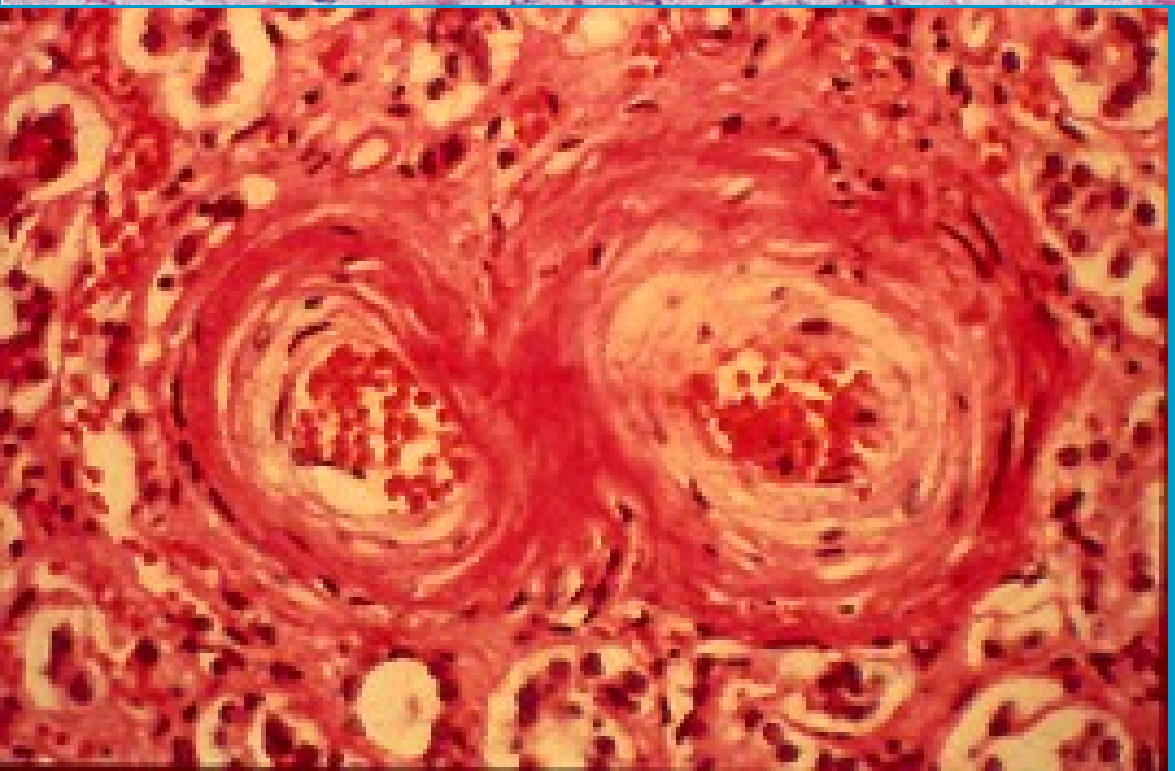


arterial wall
fibrointimal
thickening

Fibrinoid necrosis







## Onion-skin

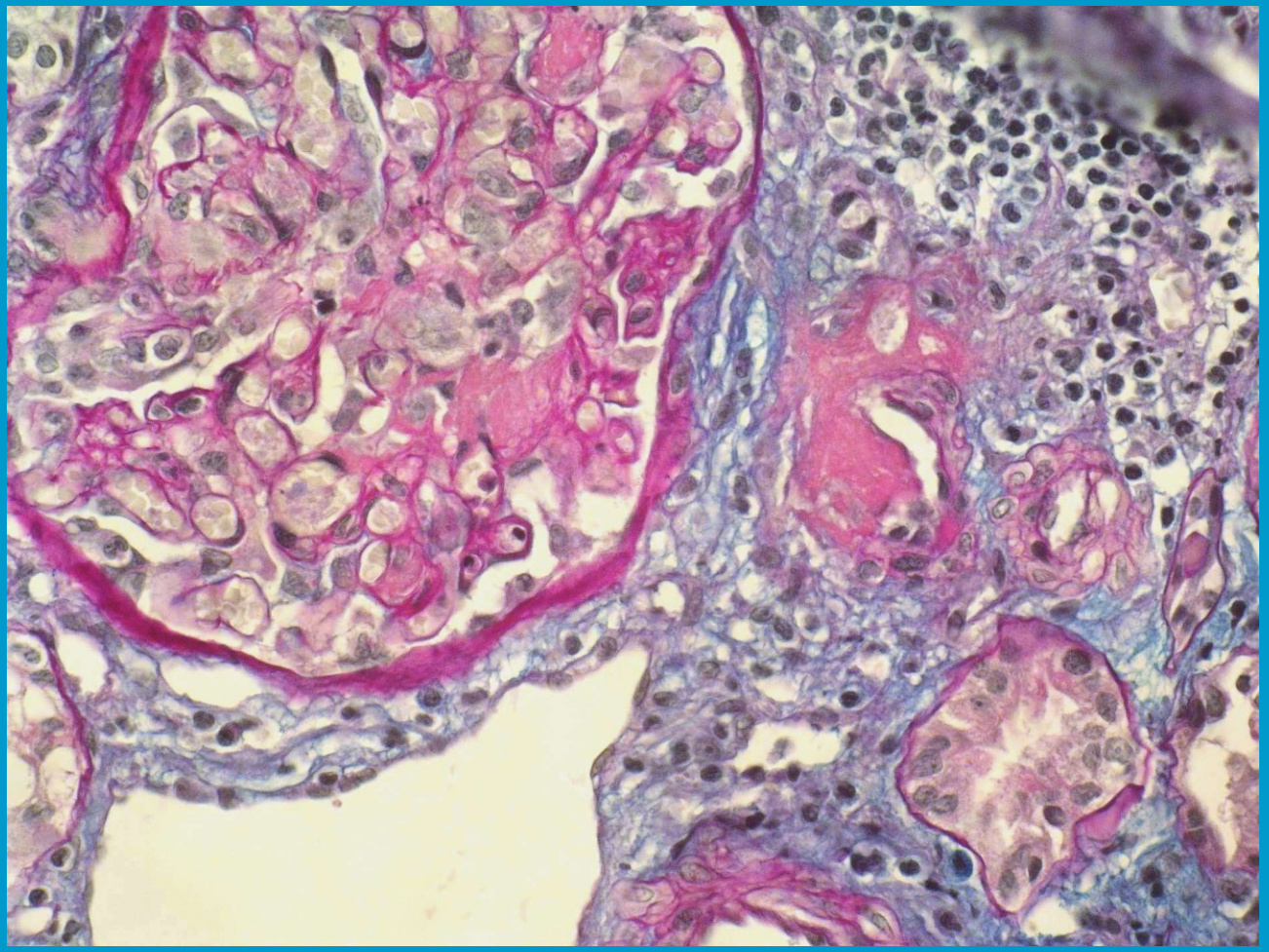
formations – hyperplastic arteriolosclerosis +/- arteriolonecrosis; hyaline arteriolosclerosis hypertension

# Nephropathy in hypertension

- Malignant nephrosclerosis = accelerated hypertension (190/130 mm Hg)
  - approx. 5 % HT
  - emergency, radical antihypertensive th. necessary
  - high risk of RF, heart failure, brain haemorrhage
  - endothelial damage
    - macro edema, pinpoint bleeding, infarctions
    - micro edema, fibrinoid necrosis, possible thrombi, haemorrhagic necrosis or oschemic collapse of glomeruli

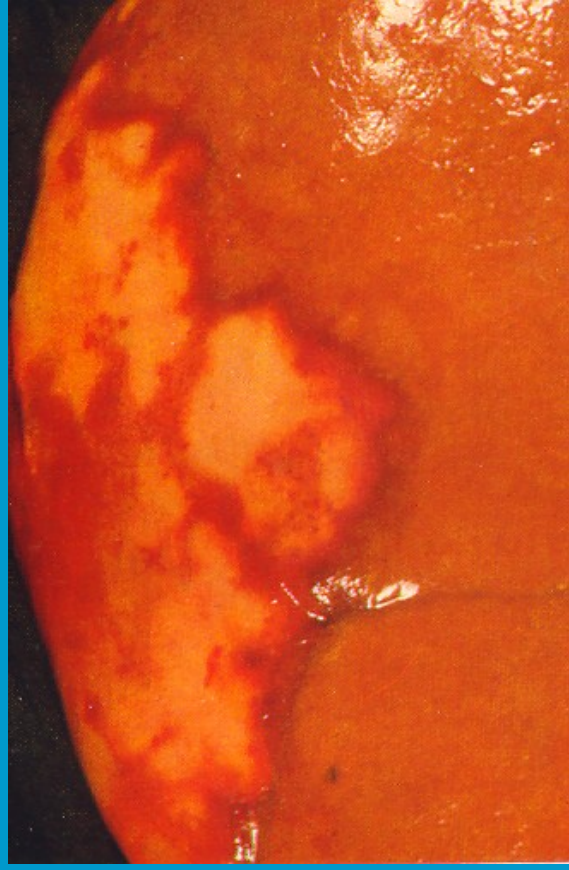
# Nephropathy in hypertension

arteriolar fibrinoid necrosis



# Renal infarction

- Causes of renal artery branches obstruction
  - thrombembolia;
  - thrombosis
  - vasculitis
  - aneurysm of abdominal aorta



# Renal artery stenosis

- cause of renovascular hypertension
  - ↓ of blood pressure in afferent arteriole
  - activation of renin-angiotensin system →
  - ↑ BP, atrophy in longer duration
  - hypertension in contralateral kidney

# Benign nephrosclerosis – hypertensive nephropathy

- **a. renalis** stenosis, renal atrophy and hypertension (Goldblatt)

# Thrombotic microangiopathy

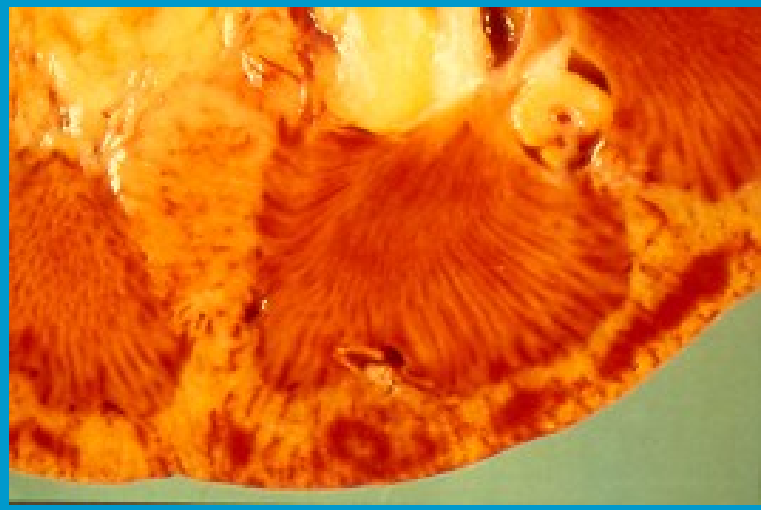
- Endothelial damage → microthrombi → damage of erythocytes + platelets → hemolytic anaemia
  - fibrinoid necrosis without vasculitis
- Hemolytic-uremic sy (typical – epidemic – Shiga toxin; atypical – antiphospholipid antibodies, malignant hypertension, pregnancy, drugs, irradiation, = in complement dysregulation
- Thrombotic thrombocytopenic purpura
  - genetic defficiency in von Willebrand-cleaving factor
  - acquired (AI, therapy) sudden, CNS, heart damage
- Pregnancy complications: pre- eclampsia

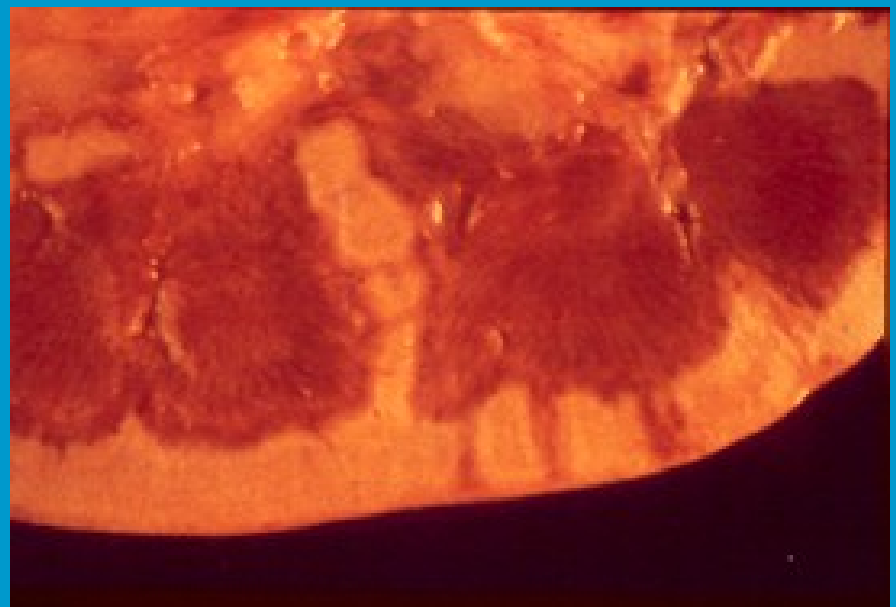
# Hemolytic-uremic syndrome

1)Ischemic cortical changes with tubular dilatation

2)Disperse focal hemoragies,
necroses

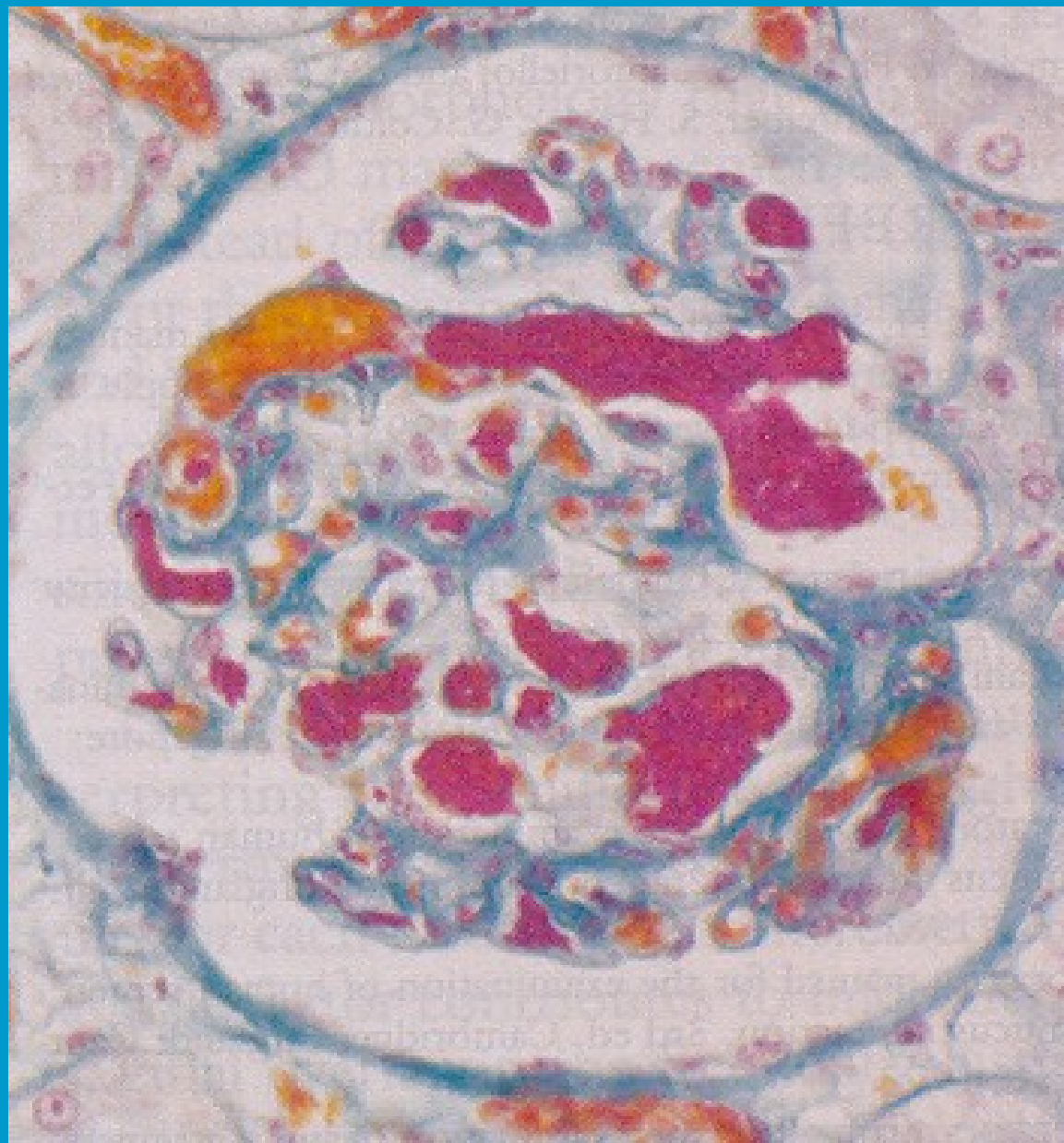
Acute nephropathy
+ haemolysis
thrombocytopenia





# Hemolytic-uremic syndrome

- Microtrombi in glomerular capillaries (endothelial injury + platelet activation)
- Thickening of capillary walls
- Necrosis and intimal hyperplasia of small arteries



# Systemic vasculitis

- 3 main types
  - vasculitis directly caused by autoantibodies
    - anti-GBM glomerulonephritis – Goodpasture sy
  - immune complex vasculitis
    - Henoch-Schönlein purpura
  - ANCA vasculitis
    - granulomatosisi w. polyangiitis (Wegener v.) c-ANCA
    - microscopic polyangiitis p-ANCA
    - Churg-Strauss eosinophilic granulomatosis w. polyangiitis

# Systemic vasculitis c-ANCA

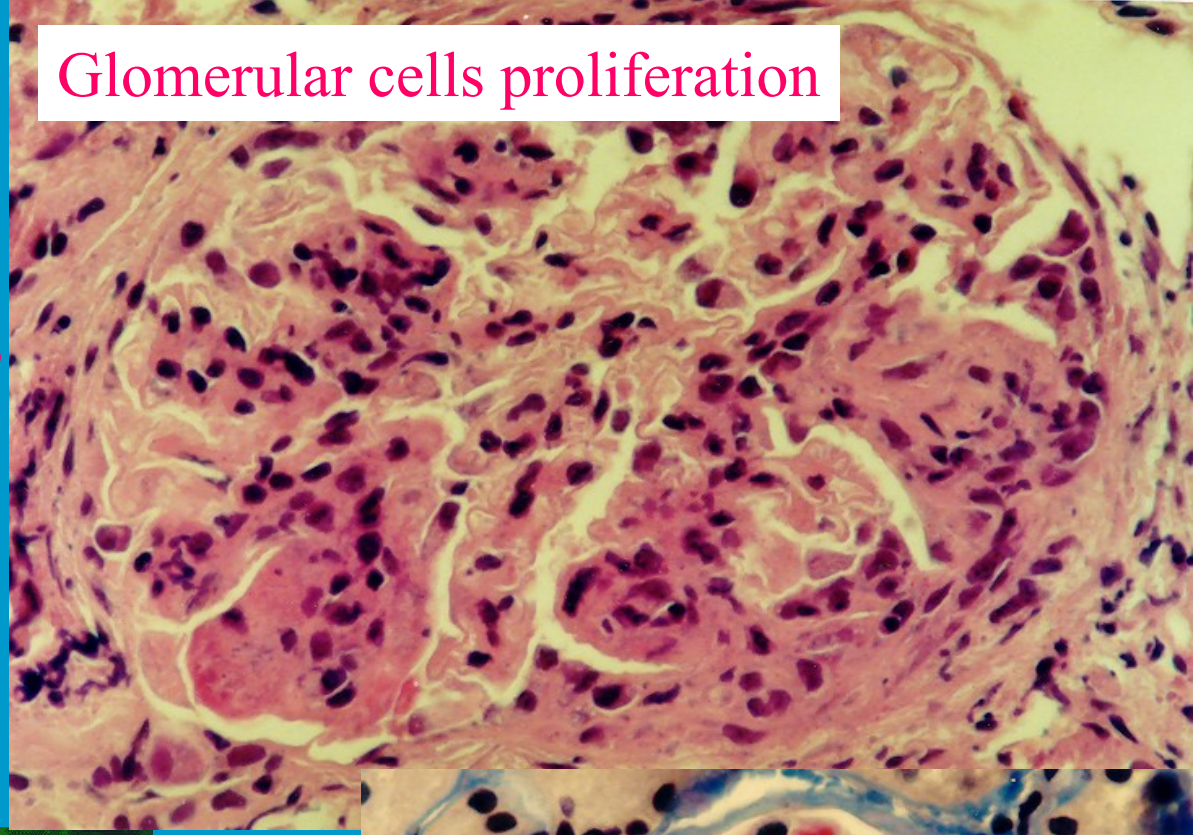
- Small vessel vasculitis
- Incidence ↑ with age
- High mortality
- Renal or multiorgan
- Rapidly progressive GN, hematuria, proteinuria, red cell casts

# Glomerulopathy in SLE

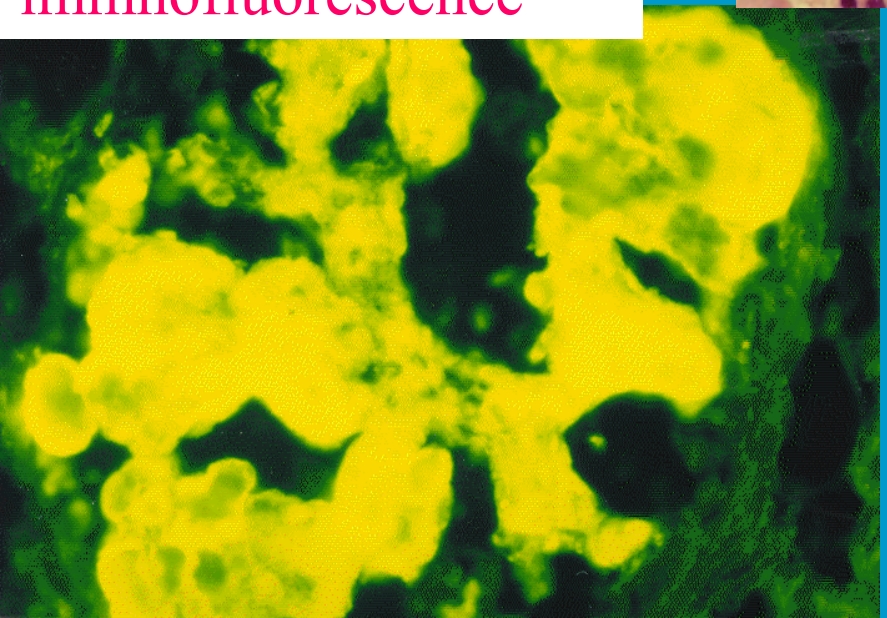
- Multiorgan AI disease
- Variable autoantibodies
- Kidney damage in 80 %
- Variable presentation and/or type of kidney damage
  - asymptomatic hematuria + proteinuria
  - nephrotic sy
  - RPGN
- 6 classes of lupus nephritis

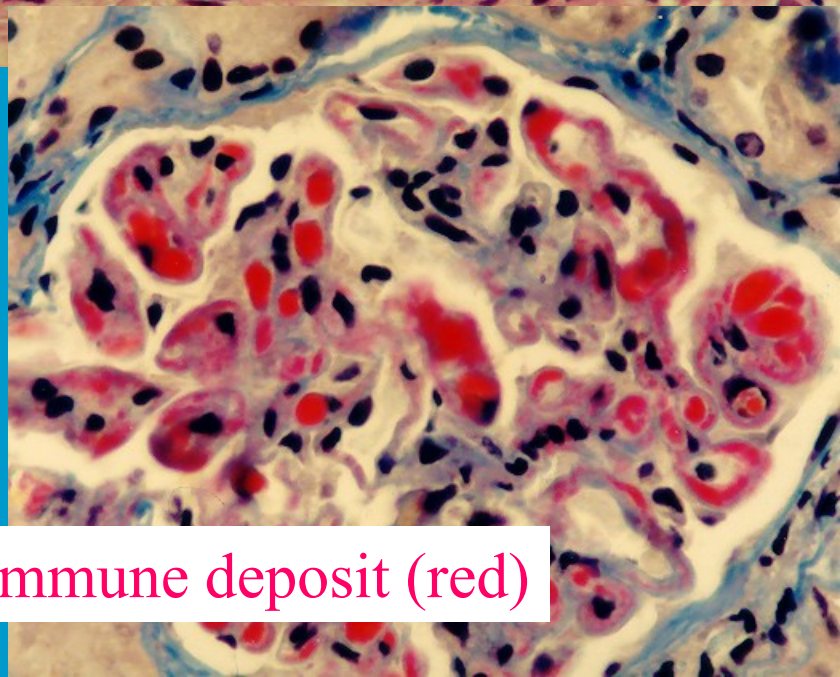
# Lupus nephritis

Glomerular cells proliferation



Deposits in direct immnofluorescence





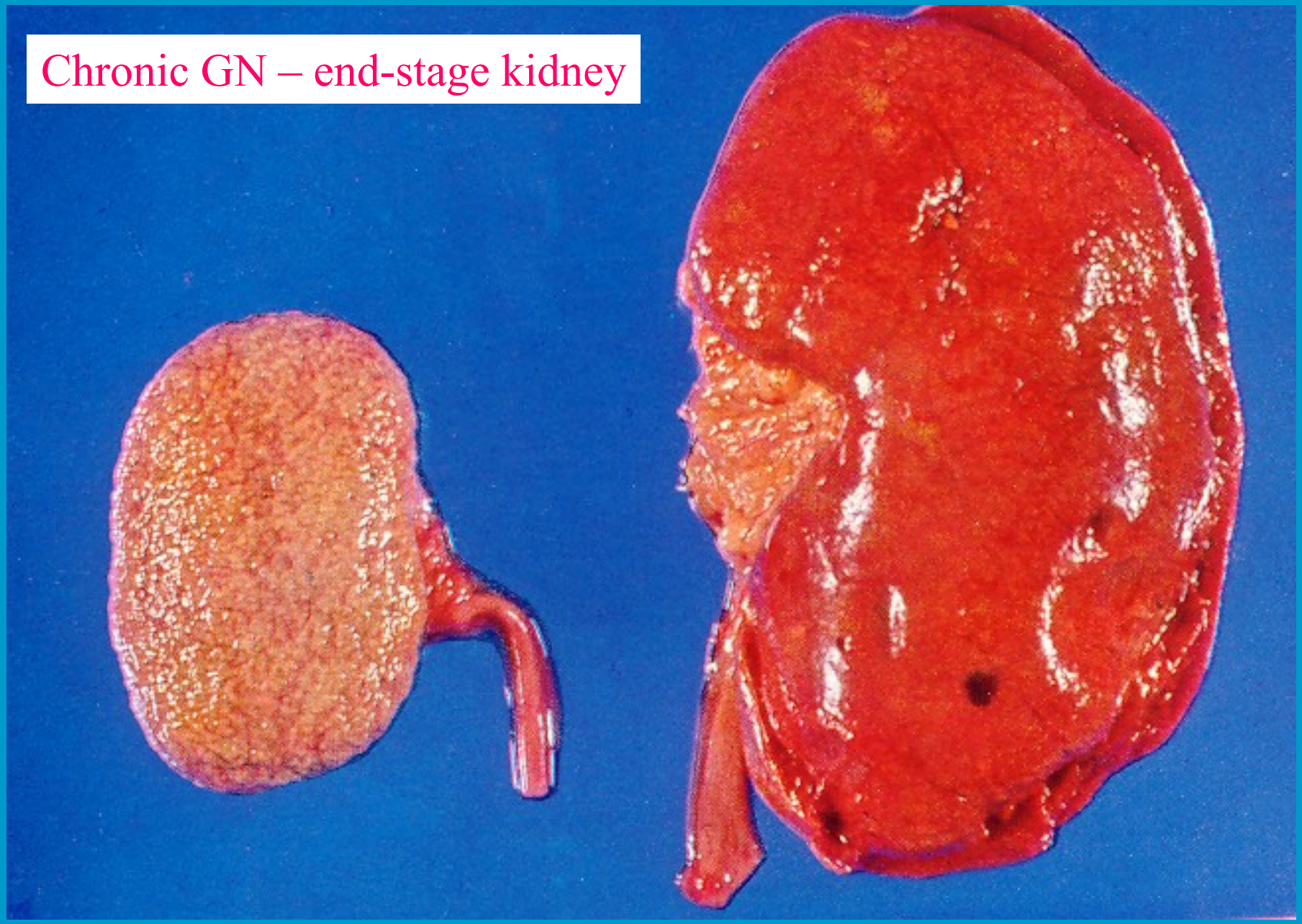
Immune deposit (red)

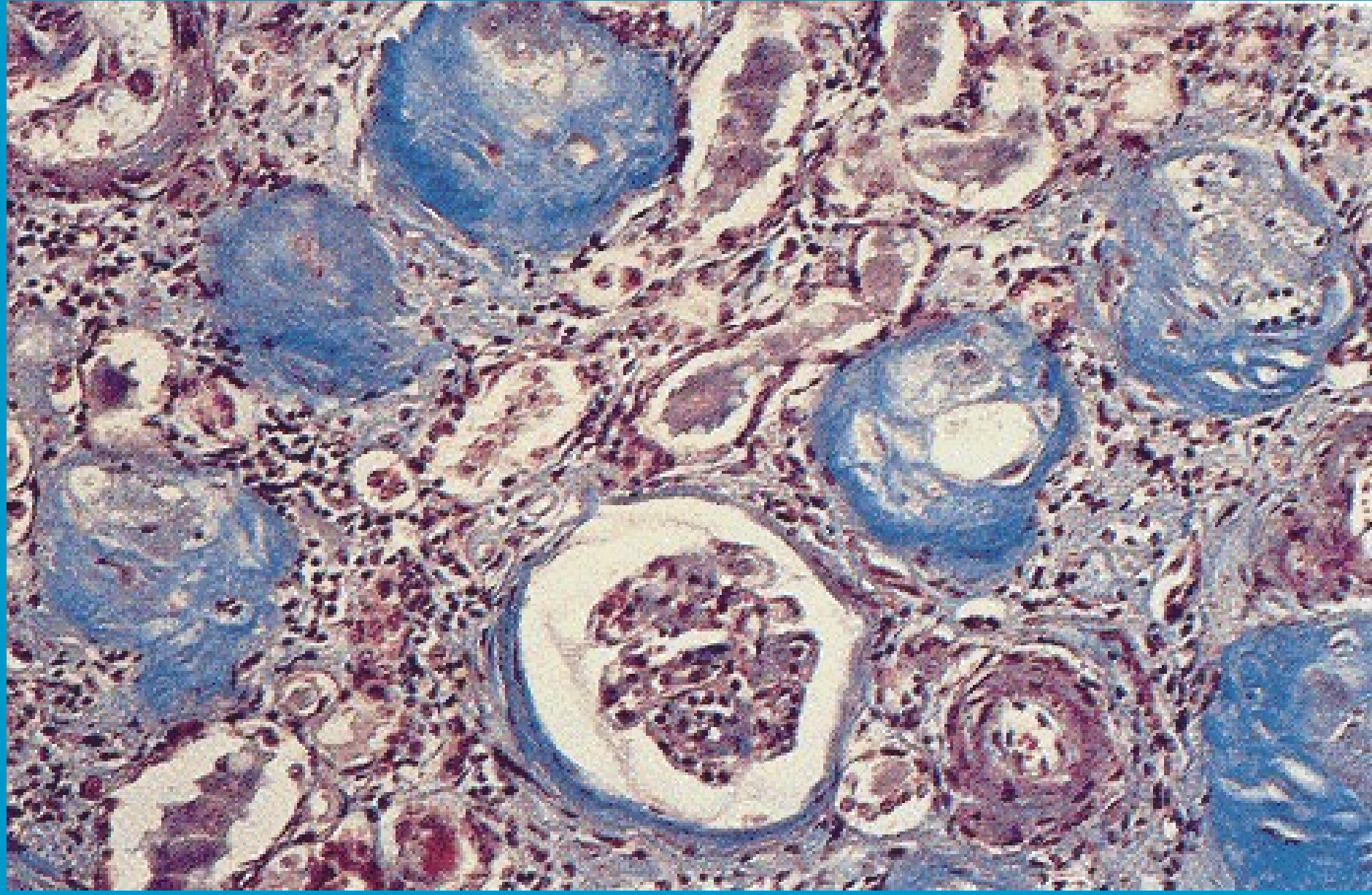
# Chronic glomerulonephritis

- end stage of variable glomerular disease
- commonly no more identifiable
- different rate of progression in different diseases
- FSGS 50-80%
- RPGN, membranous, membranoproliferative ~ 50%
- poststreptococcal 1-2%

# Chronic glomerulonephritis

- granular surface (!x chronic interstitial nephritis, nephrosclerosis, diabetic nephropathy,…)
- thin cortex
- obliterated glomeruli, arterio- and arteriolosclerosis (hypertension), tubular atrophy


Chronic GN – end-stage kidney



# Tubulo-interstitial disorders

- Concurrent damage to the tubular epithelium and interstitium
- Usually no glomerular damage, or only secondary (e.g. glomerulosclerosis)

# Tubulo-interstitial disorders - groups

TUBULOINTERSTITIAL NEPHRITIS (TIN)

- Acute pyelonephritis
- Chronic pyelonephritis, reflux nephropathy
- Abacterial interstitial nephritis (drugs, etc.)

ISCHEMIC AND TOXIC INJURY

- Acute tubular necrosis

OTHERS (e.g. obstructive uropathy, tbc, myeloma, urate nephropathy, immunologic reaction AI, posttransplant)

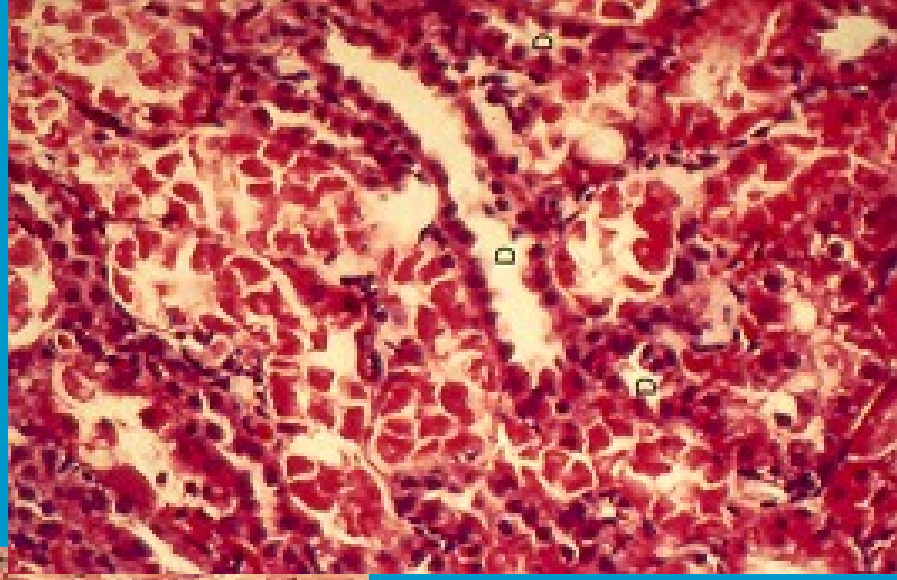
# Acute tubular necrosis (ATN)

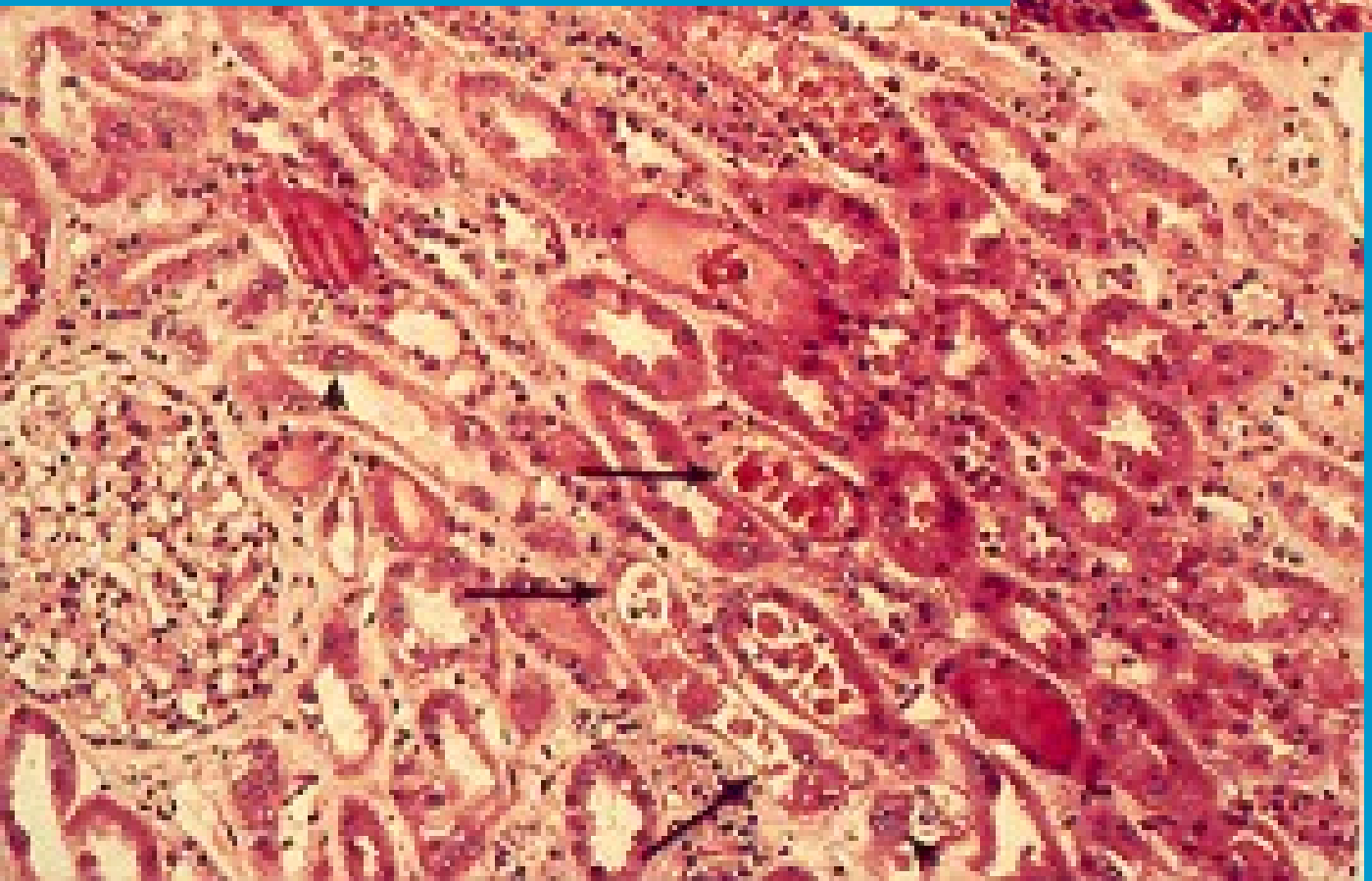
- Destruction/injury of tubular epithelium, leading to acute diminution or loss of renal function
- **Ischemic ATN** – due to decreased or interrupted blood flow, e.g. in shock, trauma, acute pancreatitis, polyarteritis nodosa, haemoglobinuria (haemolysis), myoglobinuria (crush), etc.
- **Nephrotoxic ATN** – direct toxic injury to the tubules by drugs, heavy metals (mercury), organic solvents (carbon tetrachloride), ethylene glycol

# Acute tubular necrosis (ATN)

- Morphology: **ischemic ATN** with loss of proximal epithelial brush border, cell flattening, focal tubular epithelial necrosis along the whole nephron, BM rupture, occlusion by casts; interstitial oedema, inflammatory infiltrate
- Later epithelial regeneration starting from uninjured parts
- **Toxic ATN:** extensive tubular necrosis/cytotoxic changes along the proximal tubules

# Acute tubular necrosis (ATN)





# Tubulointerstitial nephritis induced by drugs and toxins (hypersensitivity nephritis)

- Sulfonamids, synthetic penicilins, some diuretics, NSAIDs
- 7-15 days after exposure fever, eosinophilia, rash, hematuria, proteinuria, leukocyturia, cca 50% acute renal failure with oliguria
- Late-phase reaction of an IgE-mediated hypersensitivity (type I)
- Oedema and mononuclear **interstitial infiltration,** commonly with **eosinophils**, giant cell **granulomas** may be present. Tubulitis and tubular regressive changes.

# Analgesic nephropathy

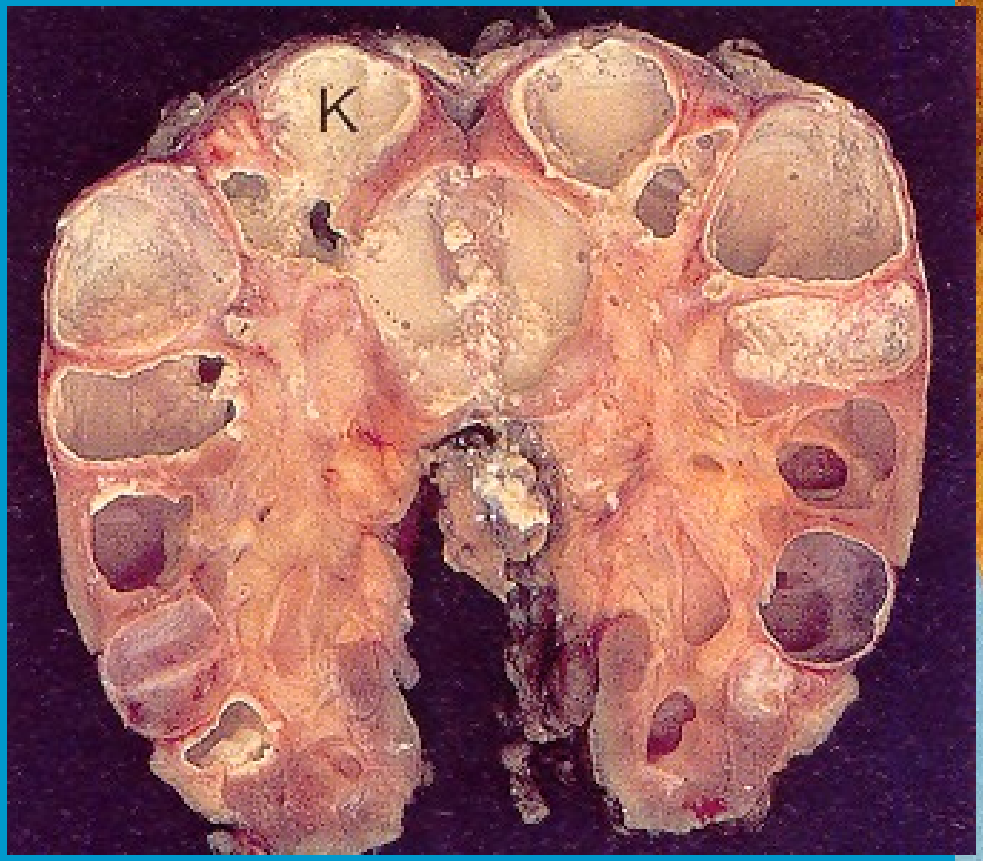
- Chronic renal disease due to excessive use of analgesic mixtures
- Form of chronic tubulointerstitial nephritis with renal papillary necrosis
- Combination effects of aspirin (papillary ischaemia), phenacetin (toxic metabolites)

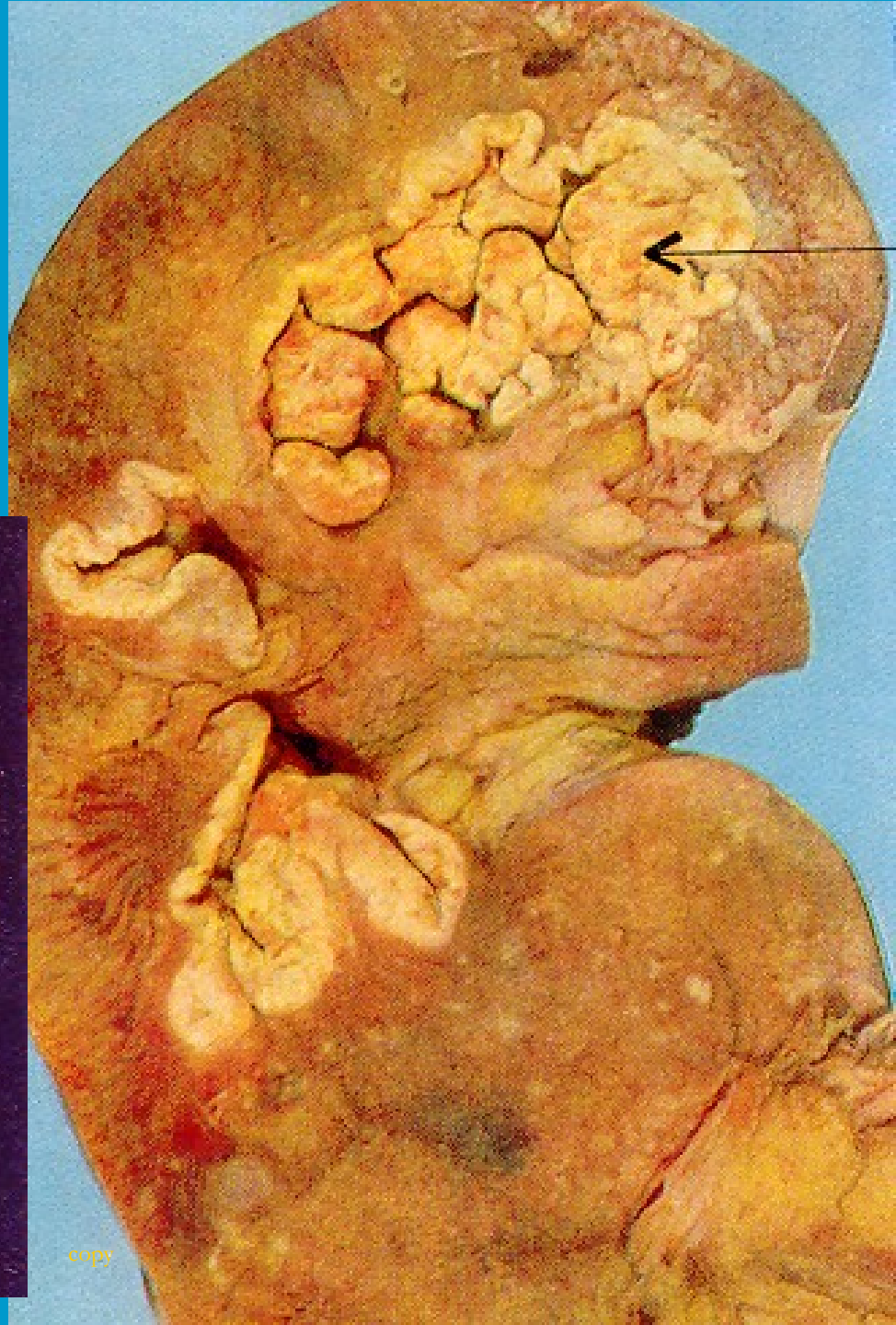
# Renal TBC

- Part of miliary spread
- Solitary postprimary tbc lesion
- Gross: caseous-cavernous mass with fibrous capsule (closed tbc) or rupture and drain into pelvis (open tbc), possible infection of urinary tract.

# Renal TBC

Caseation

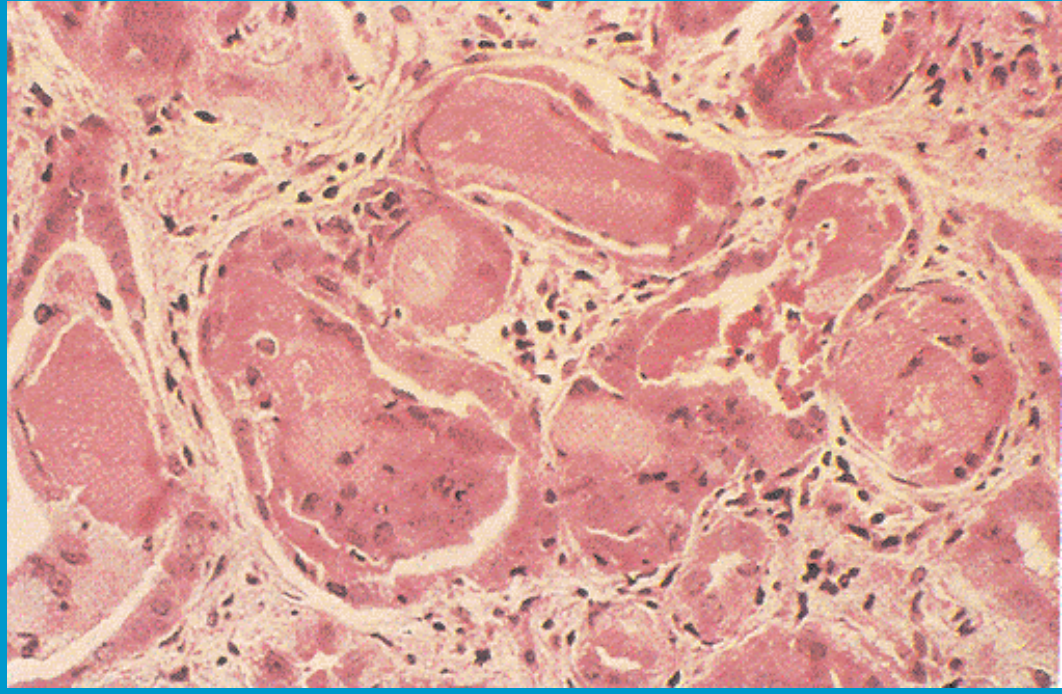


# Urate nephropathy

- Hyperuricemic disorders (urate crystals formation) may lead to 3 forms of injury:
- **Acute urate nephropathy** in patients with haematologic malignancies, commonly during chemotherapy (extensive cell breakdown – release of nucleic acids – urate crystals in tubules – acute renal failure
- **Chronic urate nephropathy** – in gout. Urate crystals surrounded by foreign body giant cells, tubulo-interstitial nephritis
- **Urate stones**

# Multiple myeloma



- Amyloidosis
- Myeloma nephrosis: tubular casts formed by precipitated Bence-Jones protein,
  nephrohydrosis
  giant cell reaction

# Renal tumors

# WHO histological classification of renal tumors

- Renal cell tumours
- Metanephric tumours
- Nephroblastic tumours
- Mesenchymal tumours
- Mixed mesenchymal and epithelial tumours
- Neuroendocrine tumours
- Haematopoietic and lymphoid tumours
- Germ cell tumours
- Metastatic tumours

# WHO classification of renal cell tumors

- Clear cell renal cell carcinoma
- Multilocular cystic renal neoplasm of low malignant potential
- Papillary renal cell carcinoma
- Hereditary leiomyomatosis and renal cell carcinoma (HLRCC)-associated renal cell carcinoma
- Chromophobe renal cell carcinoma
- Collecting duct carcinoma
- Renal medullary carcinoma
- MiT Family translocation carcinomas
- Succinate dehydrogenase (SDH)-deficient renal carcinoma
- Mucinous tubular and spindle cell carcinoma
- Tubulocystic renal cell carcinoma
- Acquired cystic disease associated renal cell carcinoma
- Clear cell papillary renal cell carcinoma
- Renal cell carcinoma, unclassified
- Papillary adenoma
- Oncocytoma

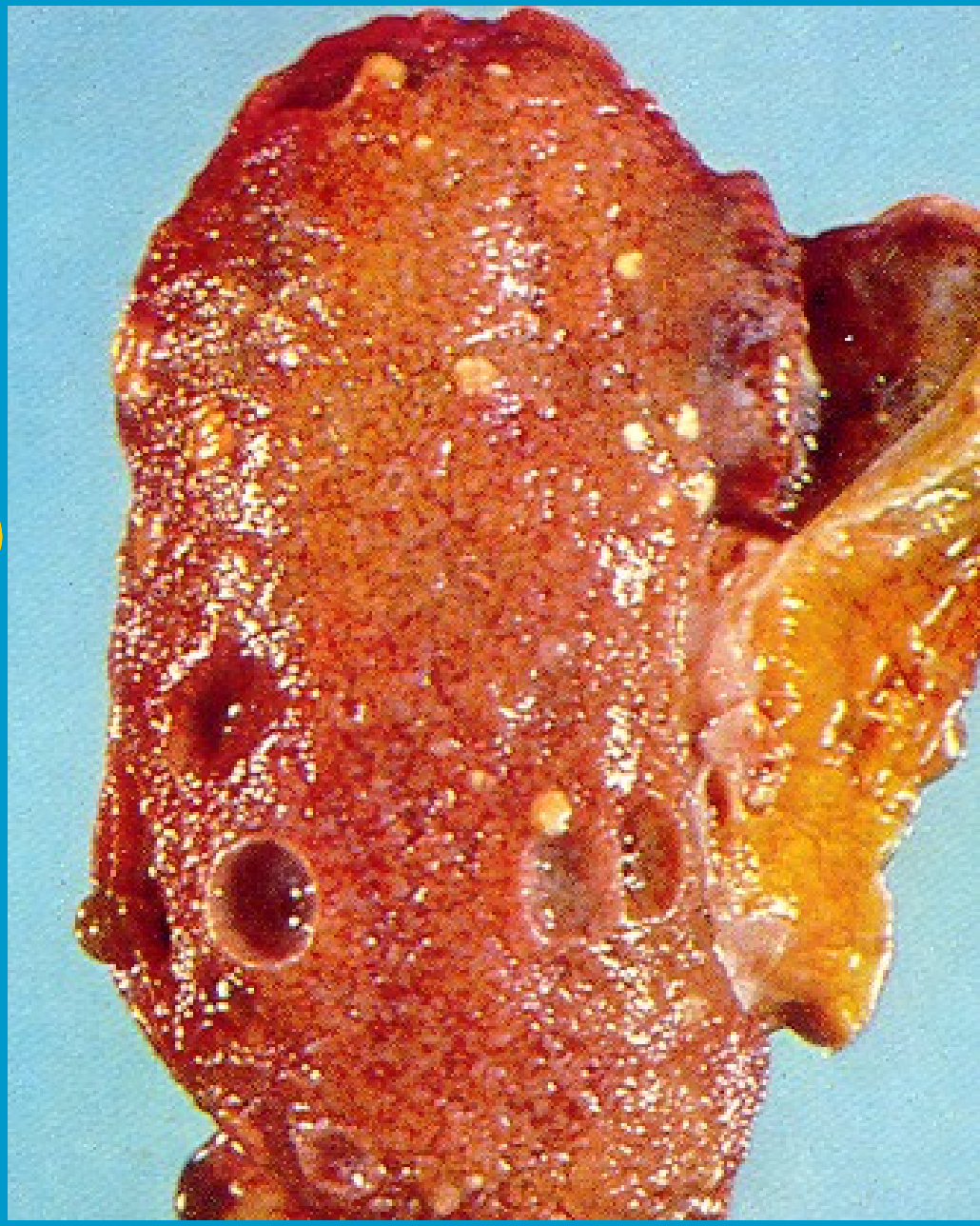
# WHO classification of renal cell tumors 2021

- ***Clear cell renal tumours***
- 8310/3 Clear cell renal cell carcinoma
- 8316/1 Multilocular cystic renal neoplasm of low malignant potential
- ***Papillary renal tumours***
- 8260/0 Papillary adenoma
- 8260/3 Papillary renal cell carcinoma†
- ***Oncocytic and chromophobe renal tumours***
- 8290/0 Oncocytoma
- 8317/3 Chromophobe cell renal carcinoma
- Other oncocytic tumours of the kidney
- ***Collecting duct tumours***
- 8319/3 Collecting duct carcinoma
- ***Other renal tumours***
- 8323/1 Clear cell papillary renal cell tumour†
- 8480/3 Mucinous tubular and spindle cell carcinoma
- 8316/3 Tubulocystic renal cell carcinoma
- 8316/3 Acquired cystic disease–associated renal cell carcinoma
- 8311/3 Eosinophilic solid and cystic renal cell carcinoma
- 8312/3 Renal cell carcinoma, NOS
- ***Molecularly defined renal carcinomas***
- 8311/3 *TFE3*-rearranged renal cell carcinomas
- 8311/3 *TFEB*-altered renal cell carcinomas
- 8311/3 *ELOC* (formerly *TCEB1*)-mutated renal cell carcinoma
- 8311/3 Fumarate hydratase–deficient renal cell carcinoma
- 8311/3 Hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome–associated renal cell carcinoma
- 8311/3 Succinate dehydrogenase–deficient renal cell carcinoma
- 8311/3 *ALK*-rearranged renal cell carcinomas
- 8510/3 Medullary carcinoma, NOS
- 8510/3 SMARCB1-deficient medullary-like renal cell carcinoma
- 8510/3 SMARCB1-deficient undifferentiated renal cell carcinoma, NOS
- 8510/3 SMARCB1-deficient dedifferentiated renal cell carcinomas of other specific subtypes

# Benign renal tumors

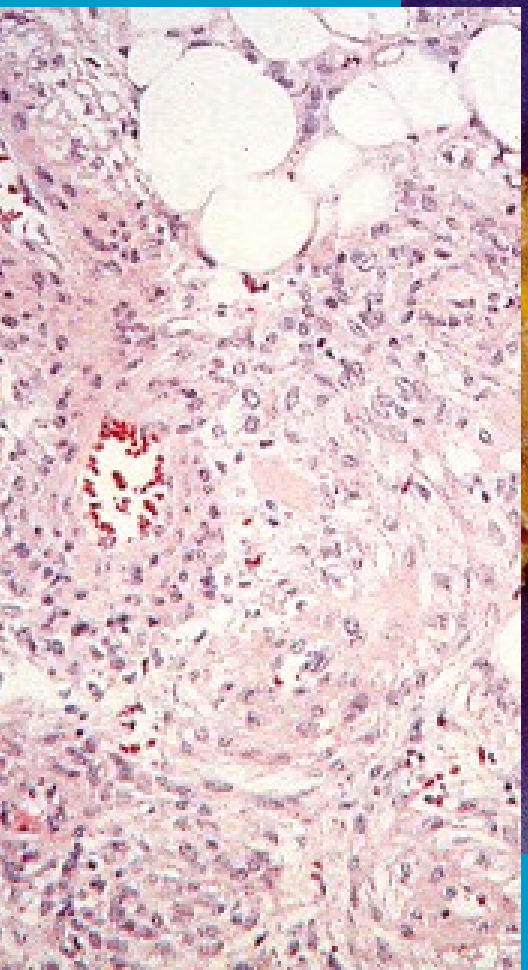
## Cortical papillary adenoma

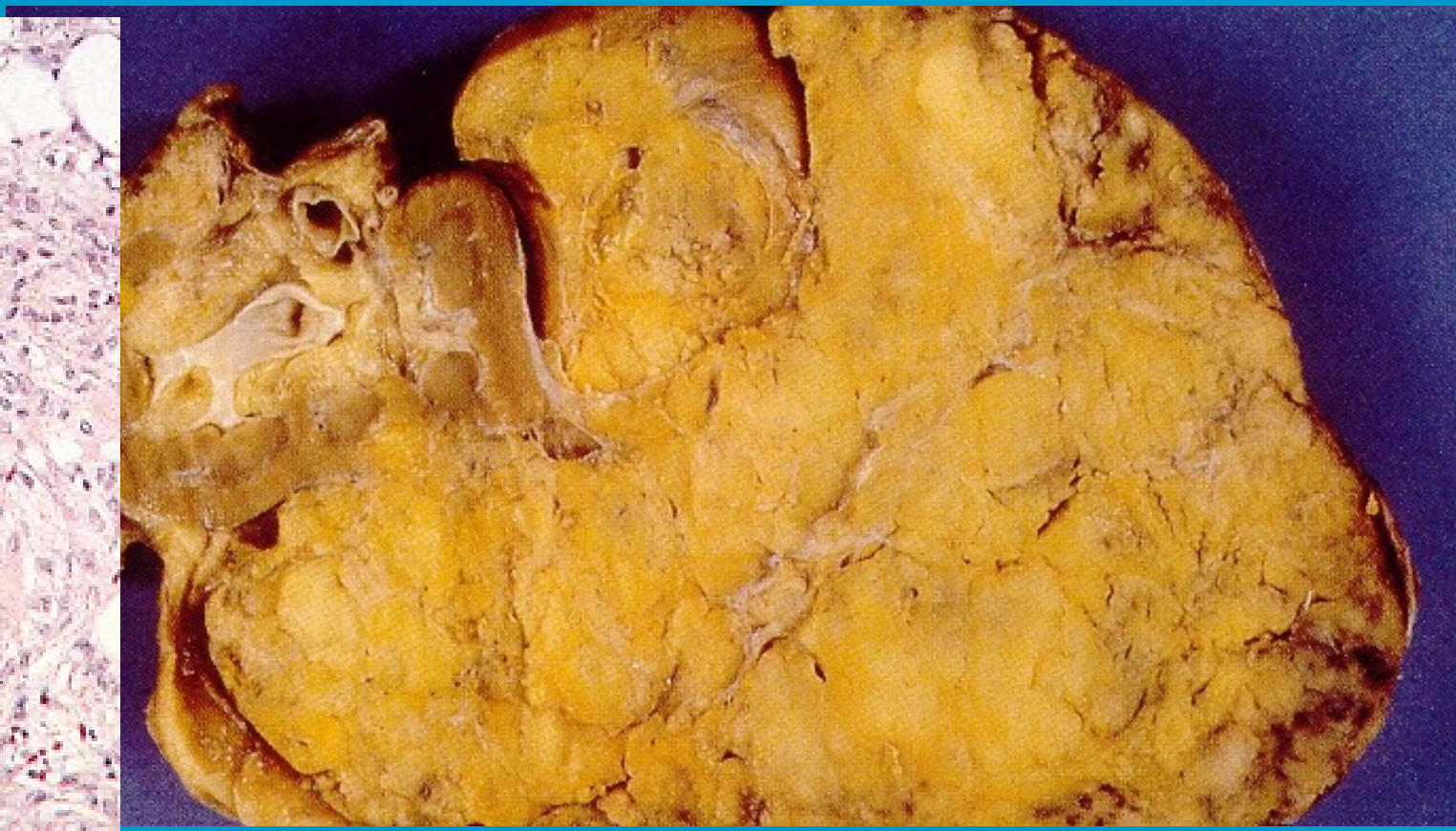
- Small tumors (1-15 mm)
- May be multiple
- Papillary structure



# Benign renal tumors

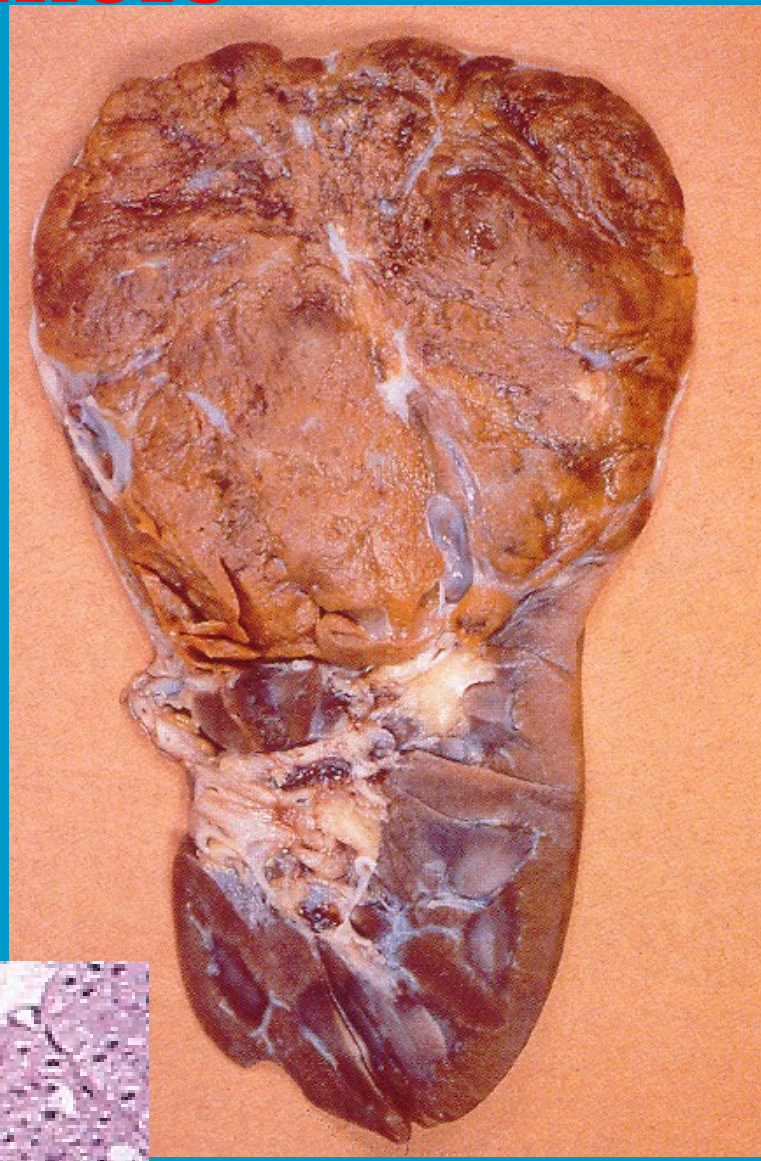
- **Angiomyolipoma** (PEComa), mesenchymal

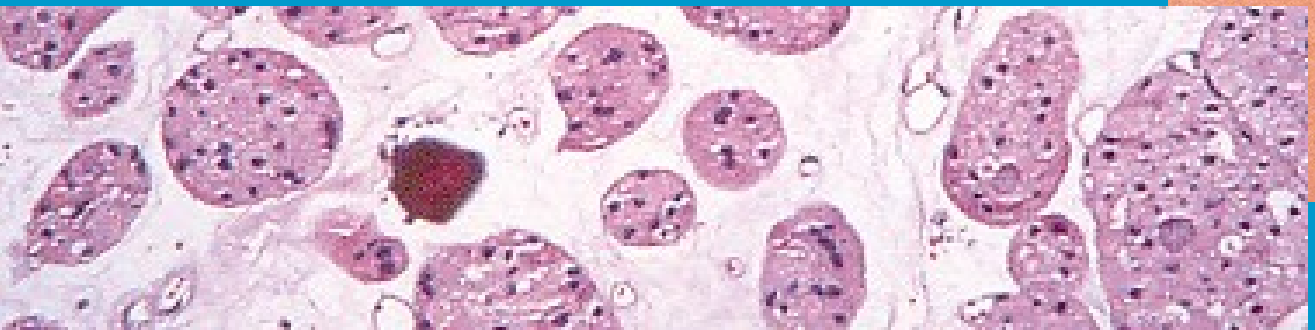




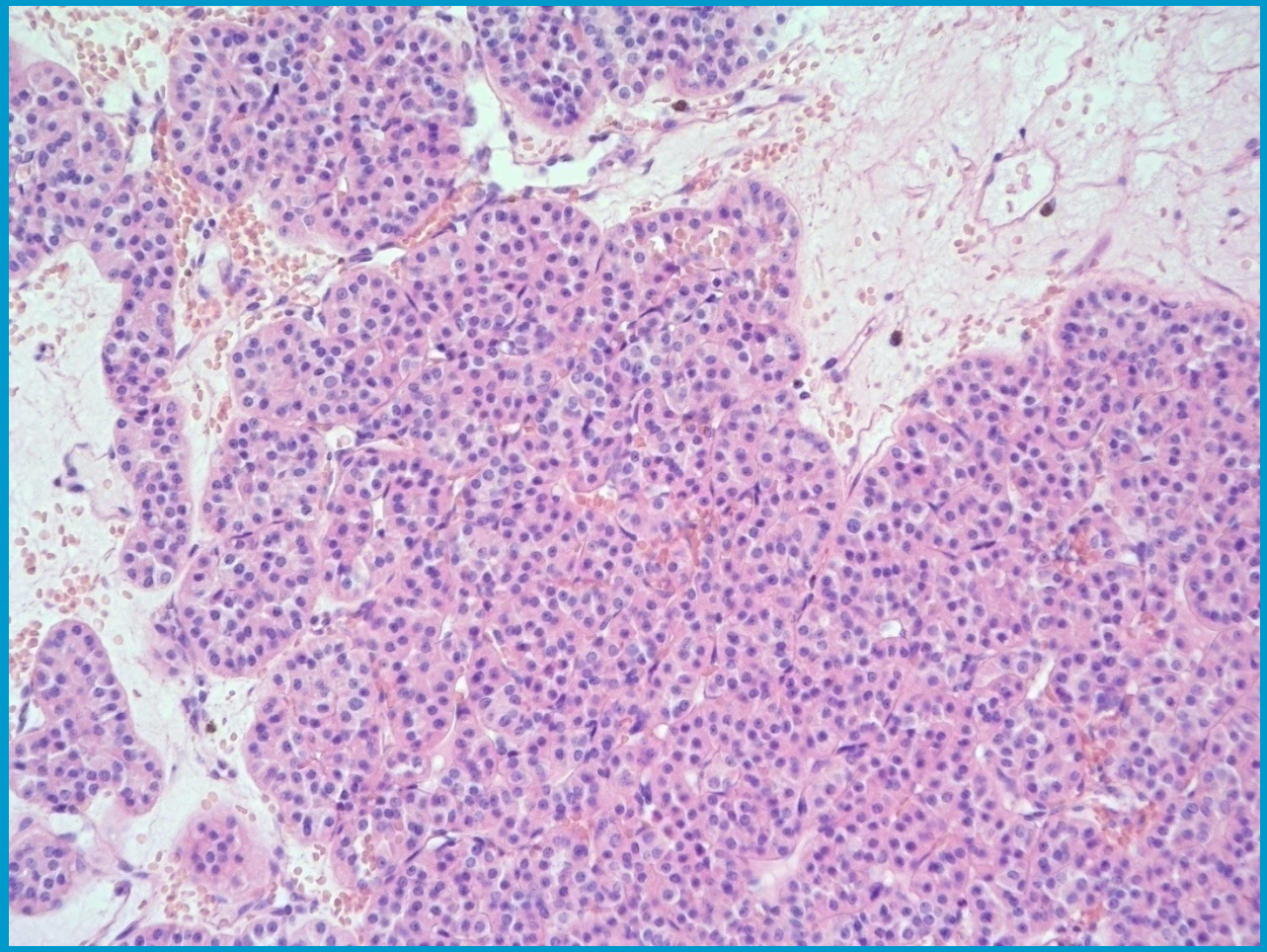
# Benign renal tumors

- Oncocytoma epithelial, asymptomatic



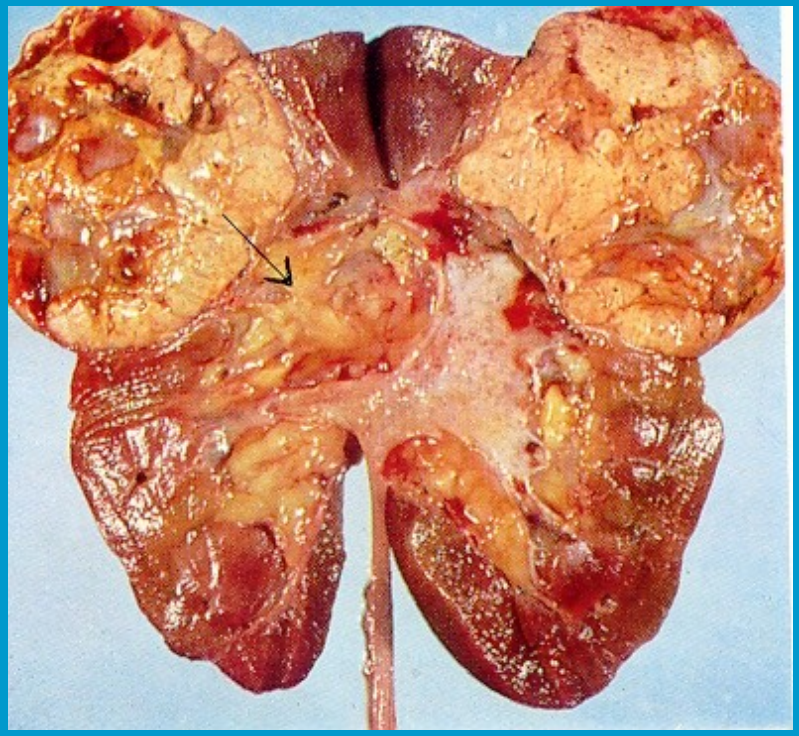


# Renal oncocytoma



# Renal cell carcinoma

- Adenocarcinoma from tubular epithelium (clear cell - Grawitz )
- 85% of renal malignancies

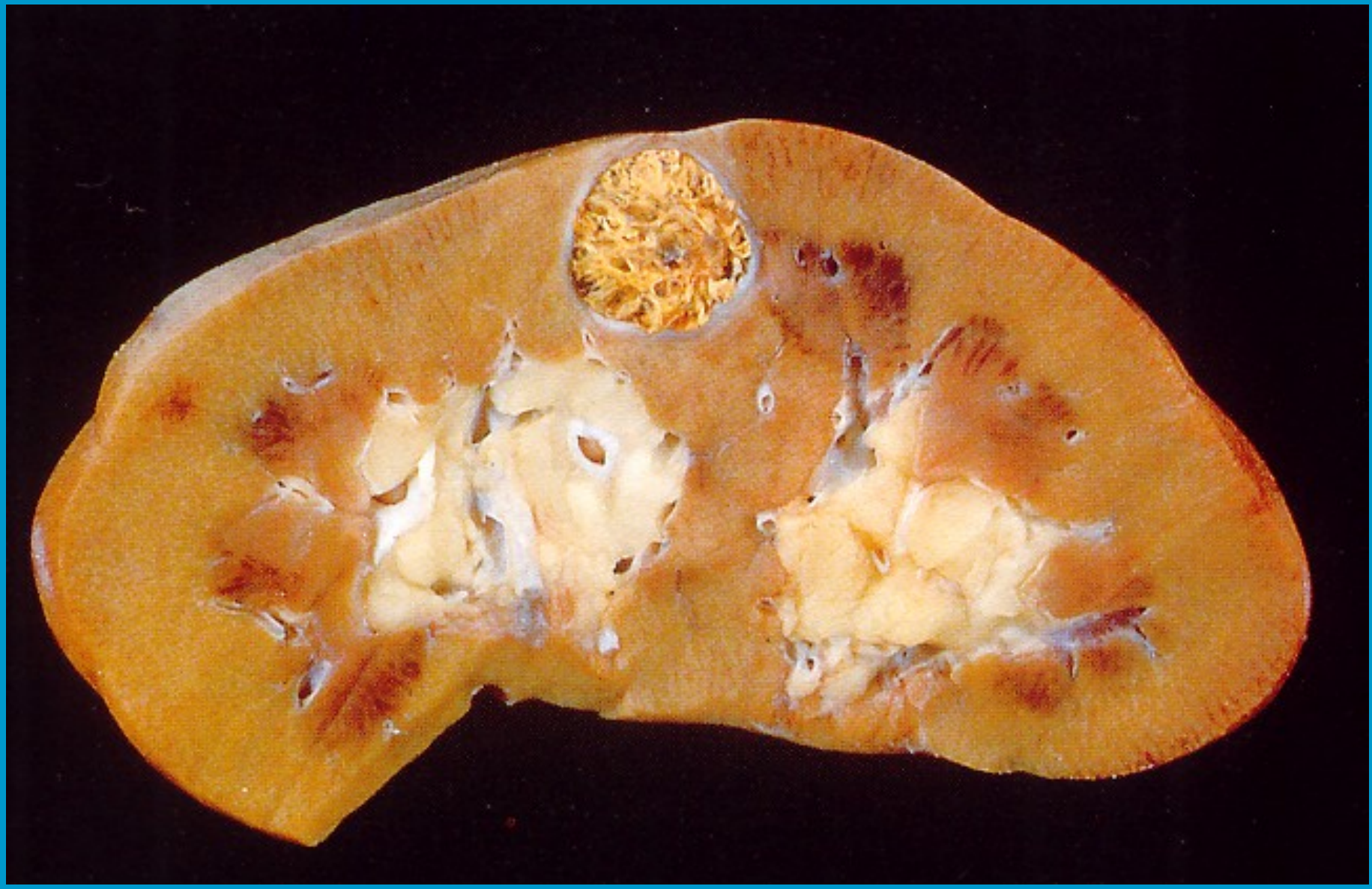


# RCC

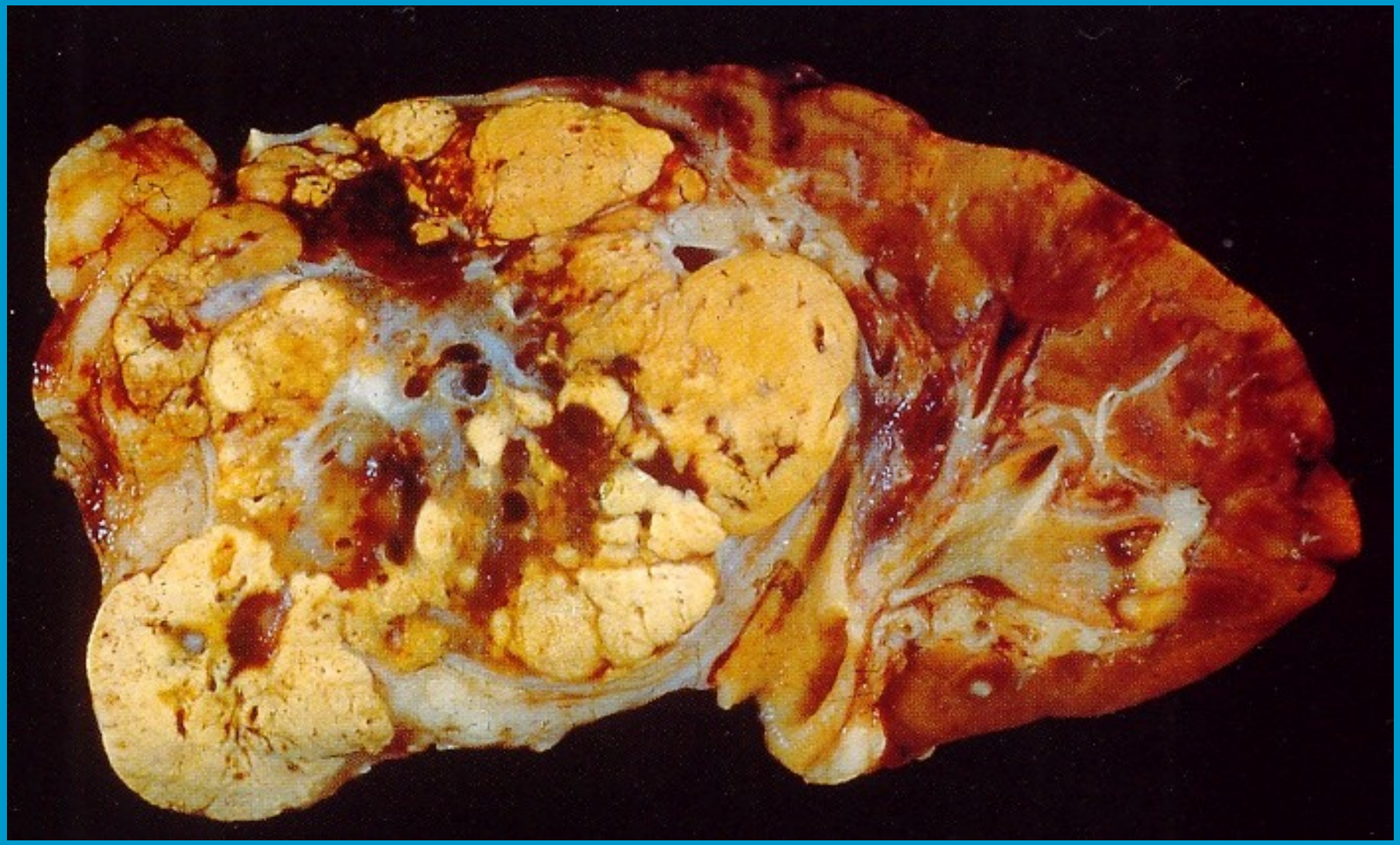
- Clear cell (conventional) RCC (80%)
- Chromophobe RCC
- Papillary RCC

- Risk f.: smoking, obesity, HT, genetic factors, industrial pollution, chemicals (asbestos, arsenic, organic diluents, ...)
- Incidental finding, hematuria, metastasis

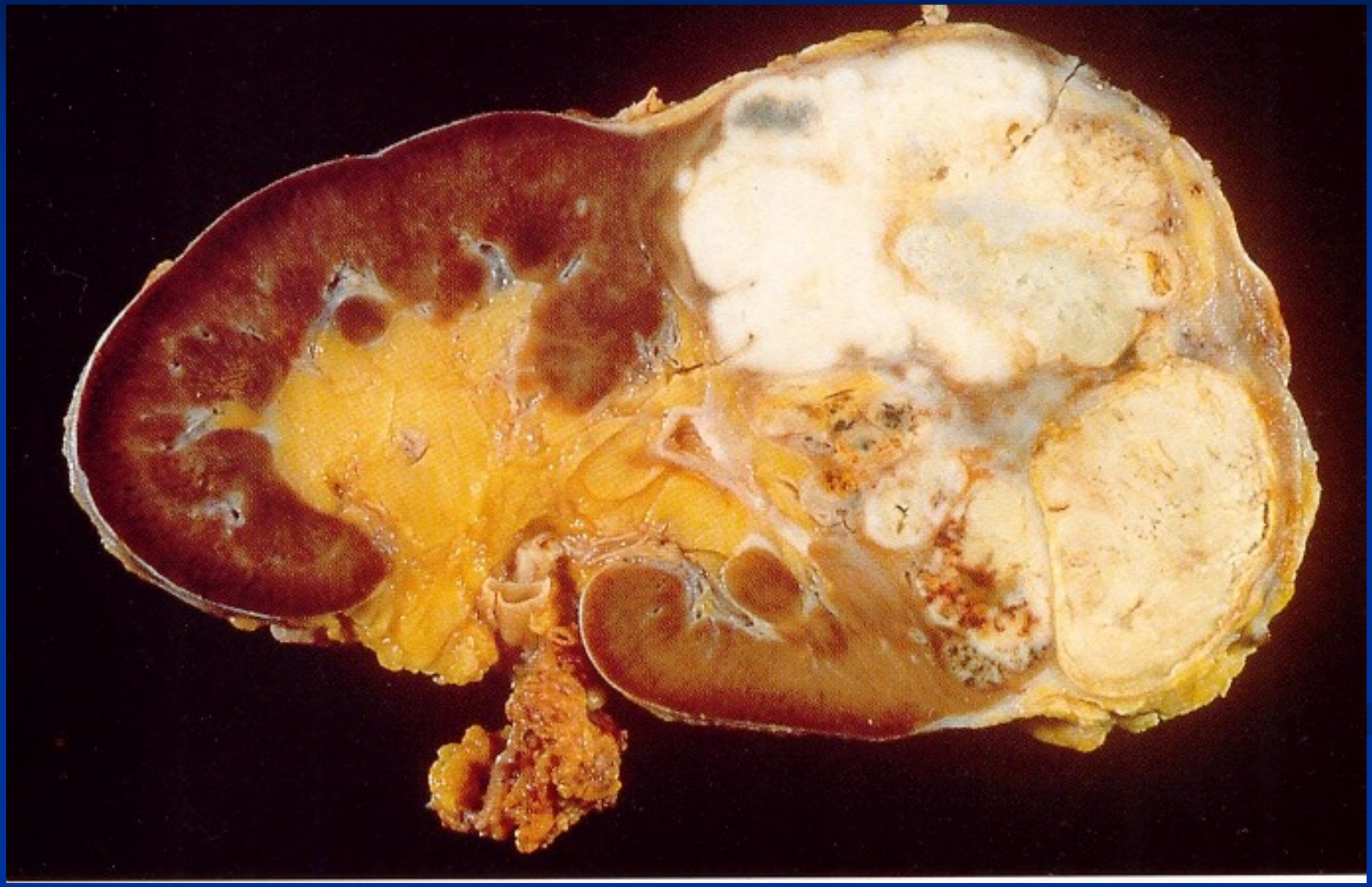
# Renal cell carcinoma



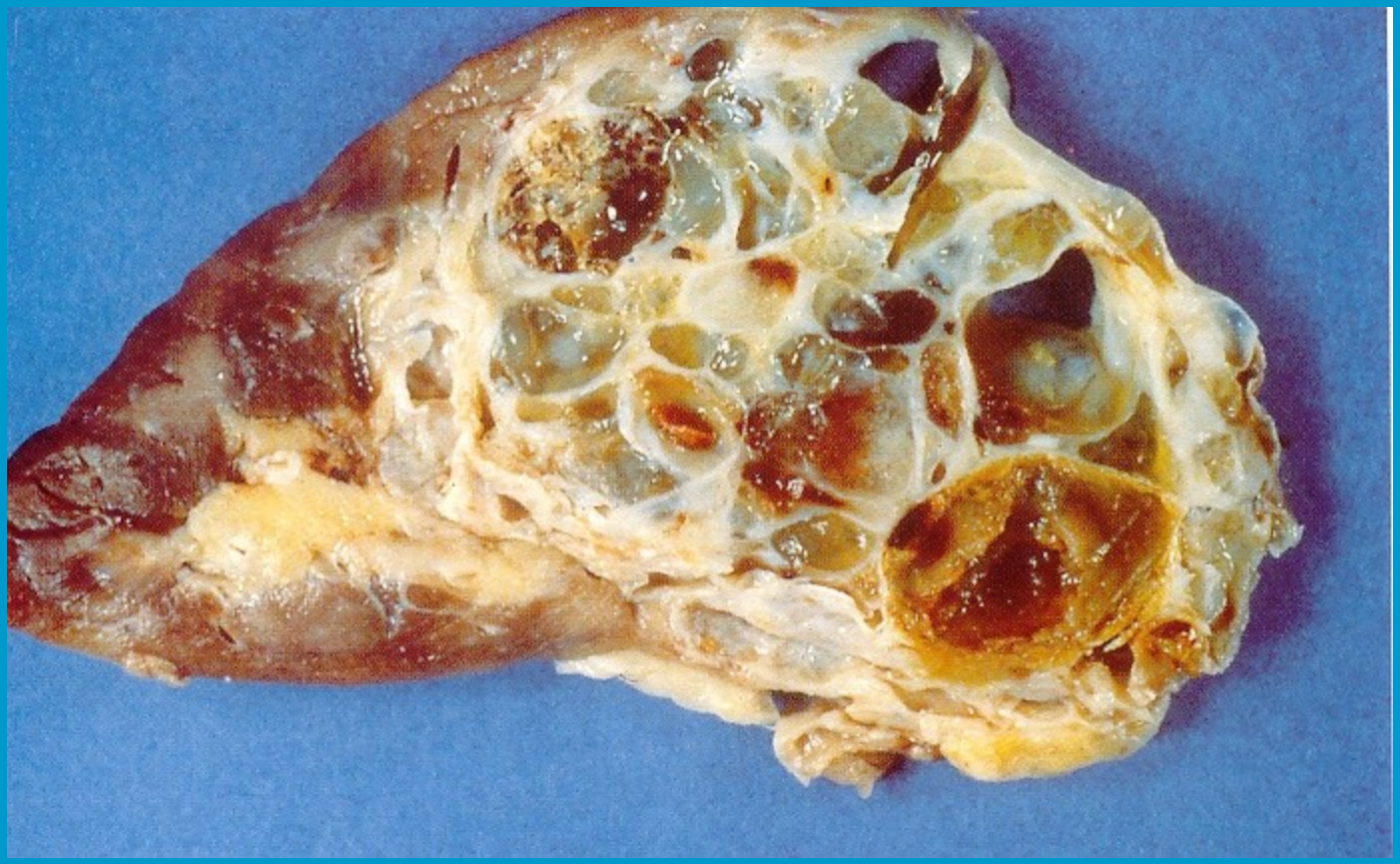
# Renal cell carcinoma



# Renal cell carcinoma



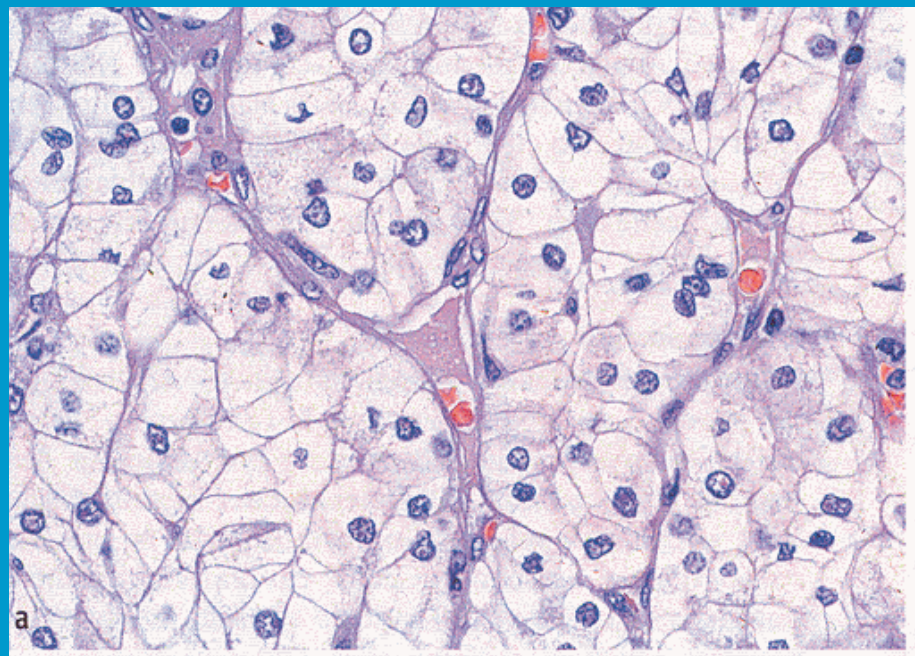
# Renal cell carcinoma

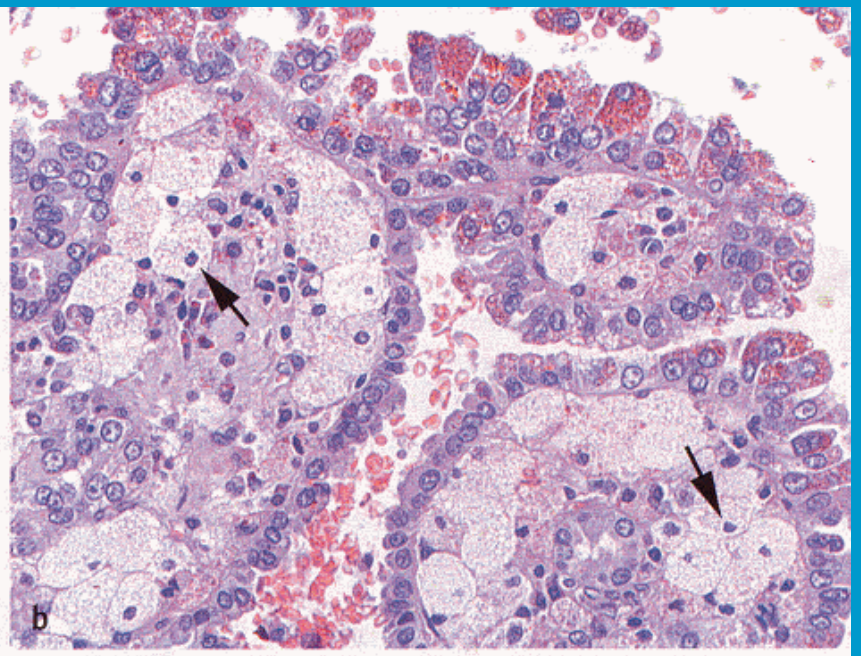


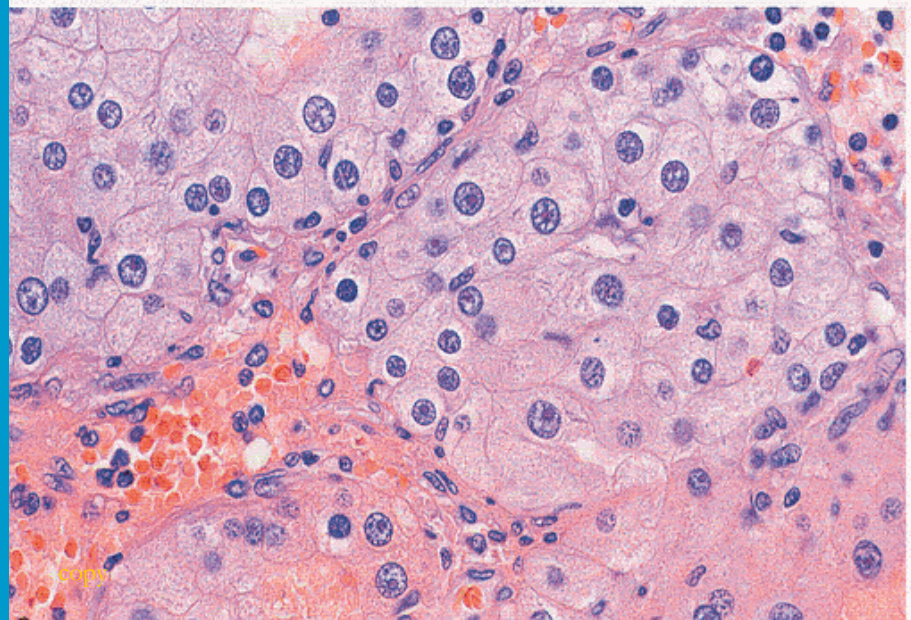
# RCC

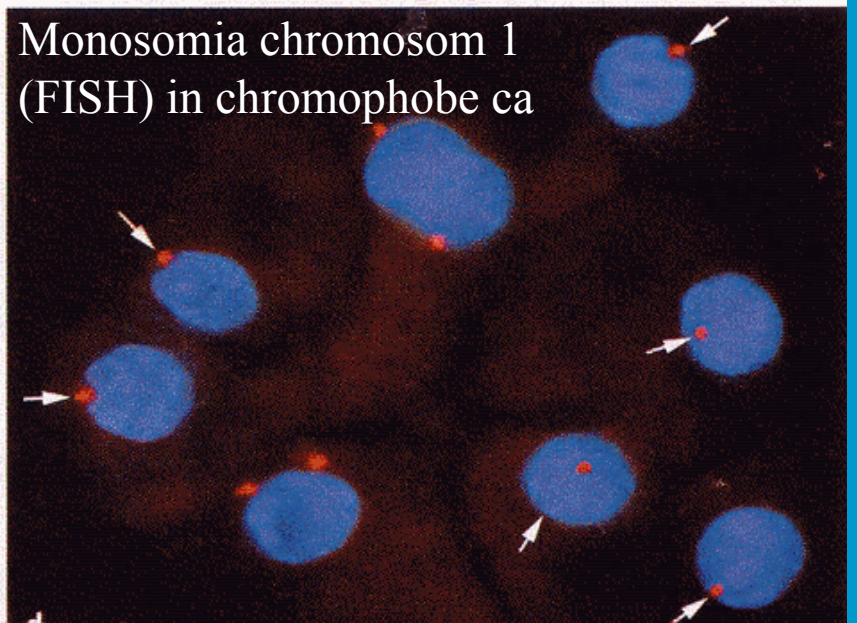
- Clear cell (conventional) RCC (80%)
  - glycogene + lipids in cytoplasm, common regressive changes, venous invasion, may have late metastasis
    - nuclear grading
- Chromophobe RCC 5 %
  - very good prognosis, eosinophilic granular cytoplasm
- Papillary RCC: 15 %,
  - commonly multifocal / bilateral, stromal foam macrophages

# Renal cell carcinoma

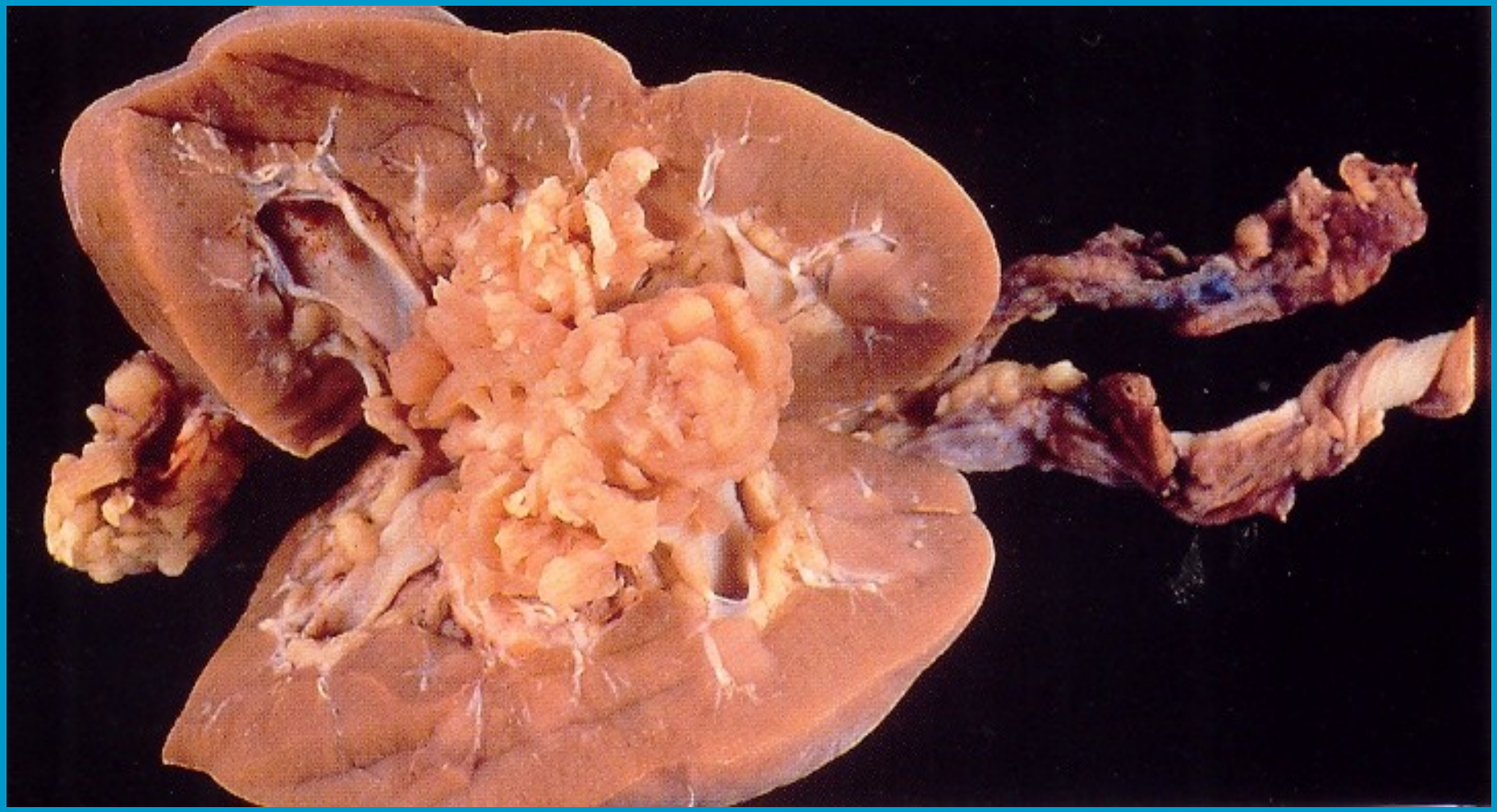


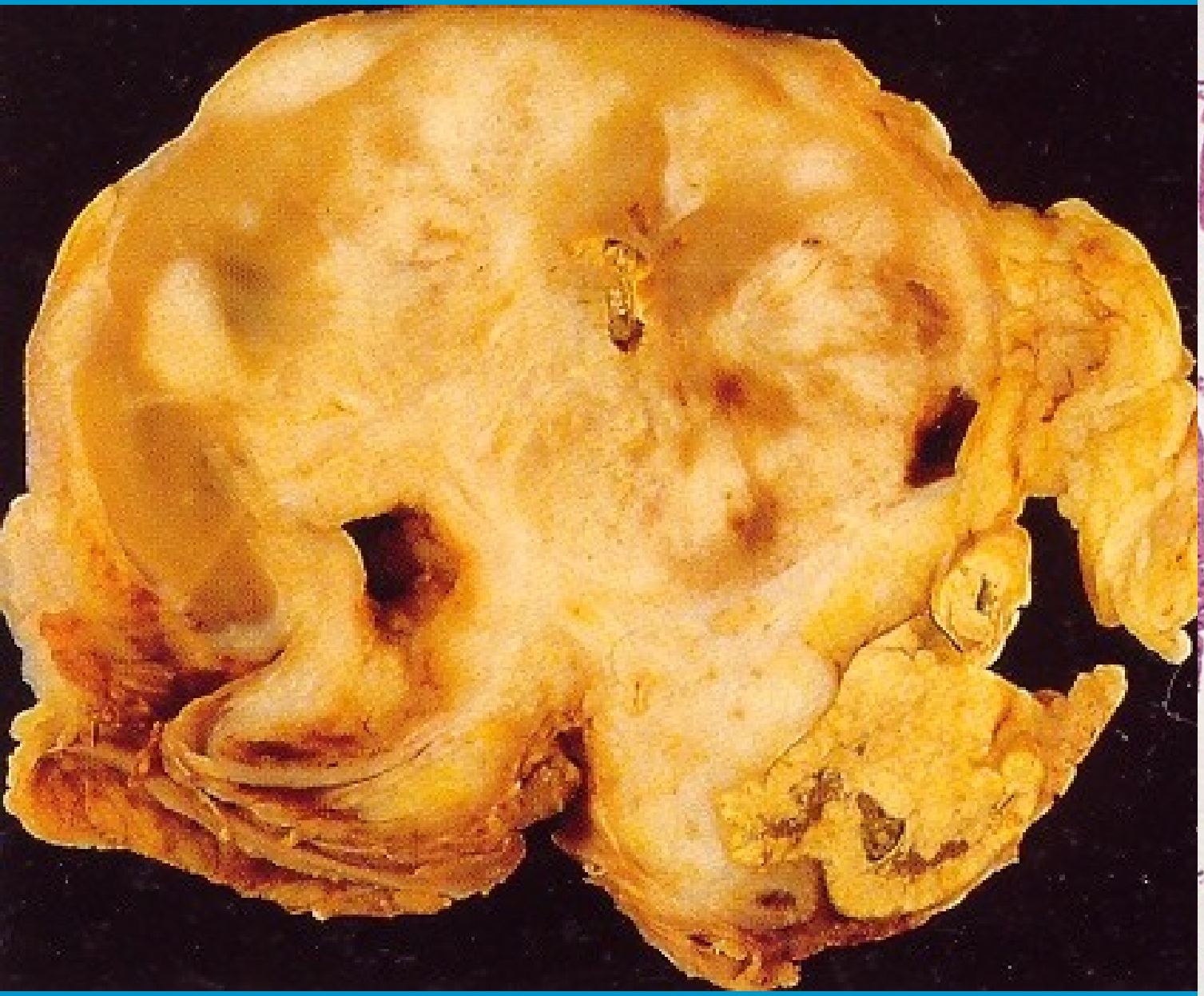



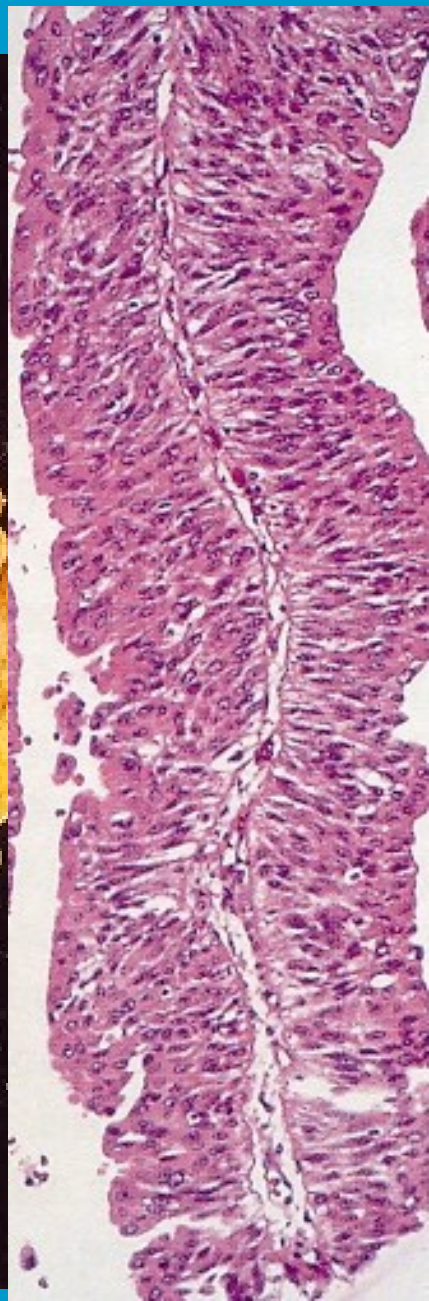


# Transitional cell ca of the renal pelvis



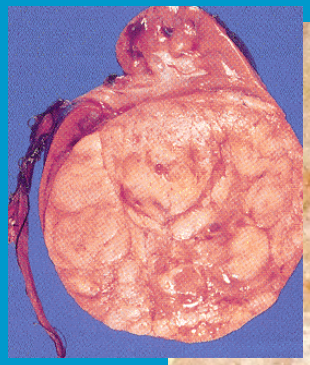
# Transitional cell ca of the renal pelvis

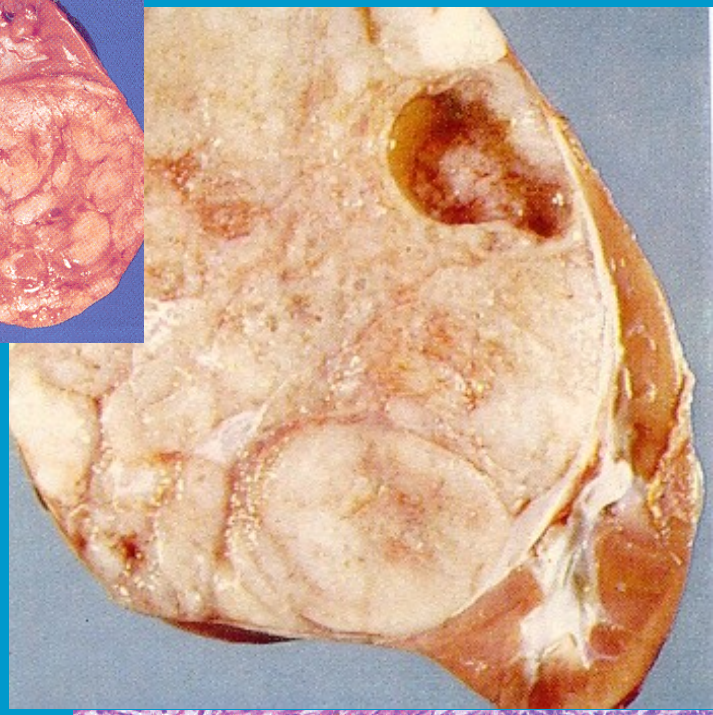


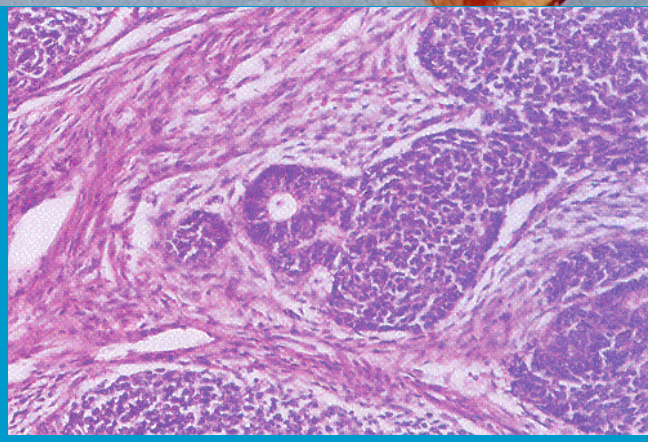


# Wilms' tumor - nephroblastoma

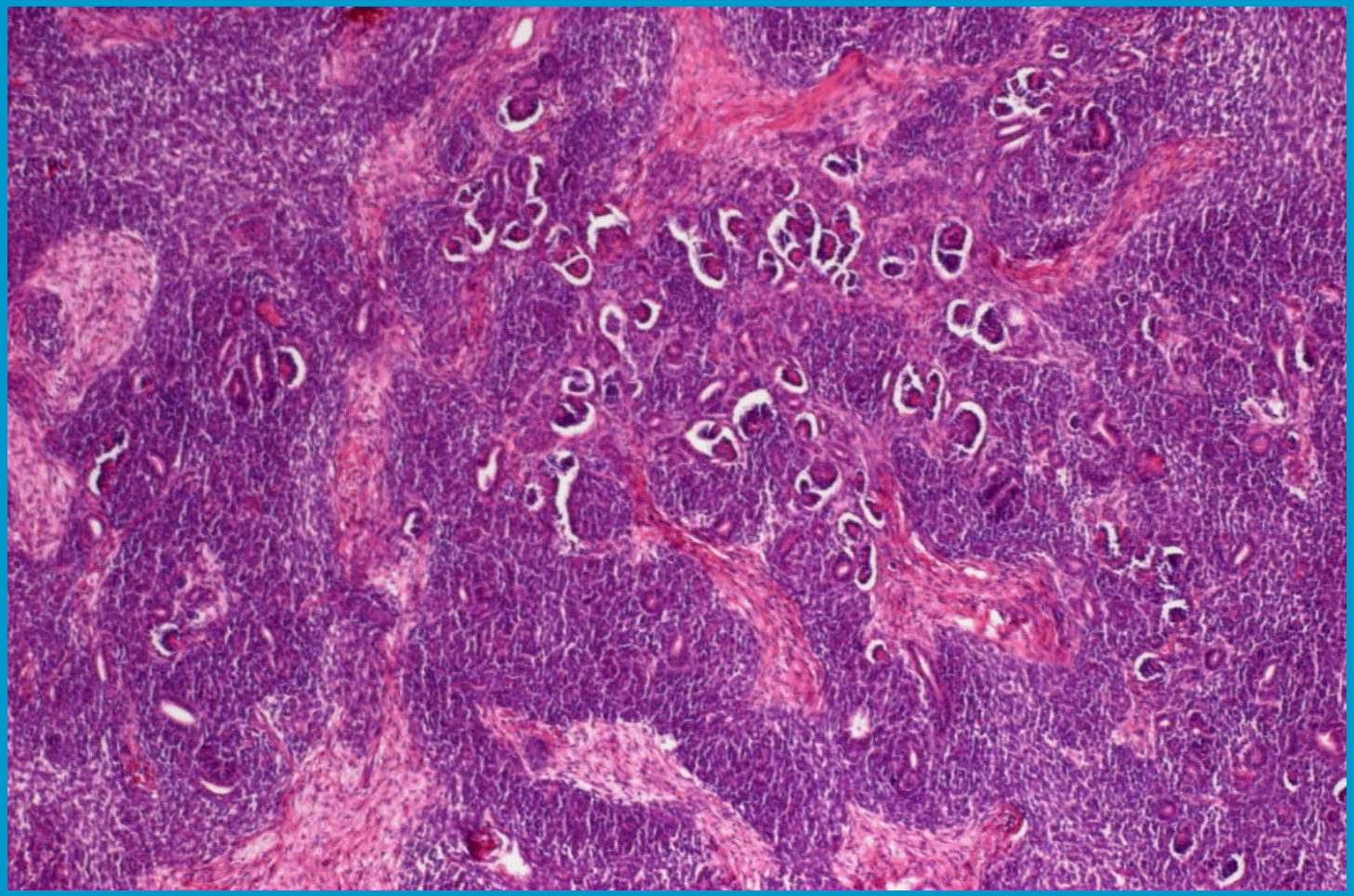
- Malignant embryonal tu metanefrogenous blastema
- Peak incidence 1-4 yrs
- 3rd most common ch. malignancy, treatable
- hematuria, local compression
- Suppresoric gene WT1 (11p13), WT2 (11p15)
- MACRO: large, soft
- MICRO blastic cells, immature **epithelial, mesenchymal** differentiation







# Wilms' tumor - nephroblastoma



# Secondary tumors

- Local spread (adrenals, pancreas, liver)
- Lung carcinoma
- Malignant lymphoma
- Others