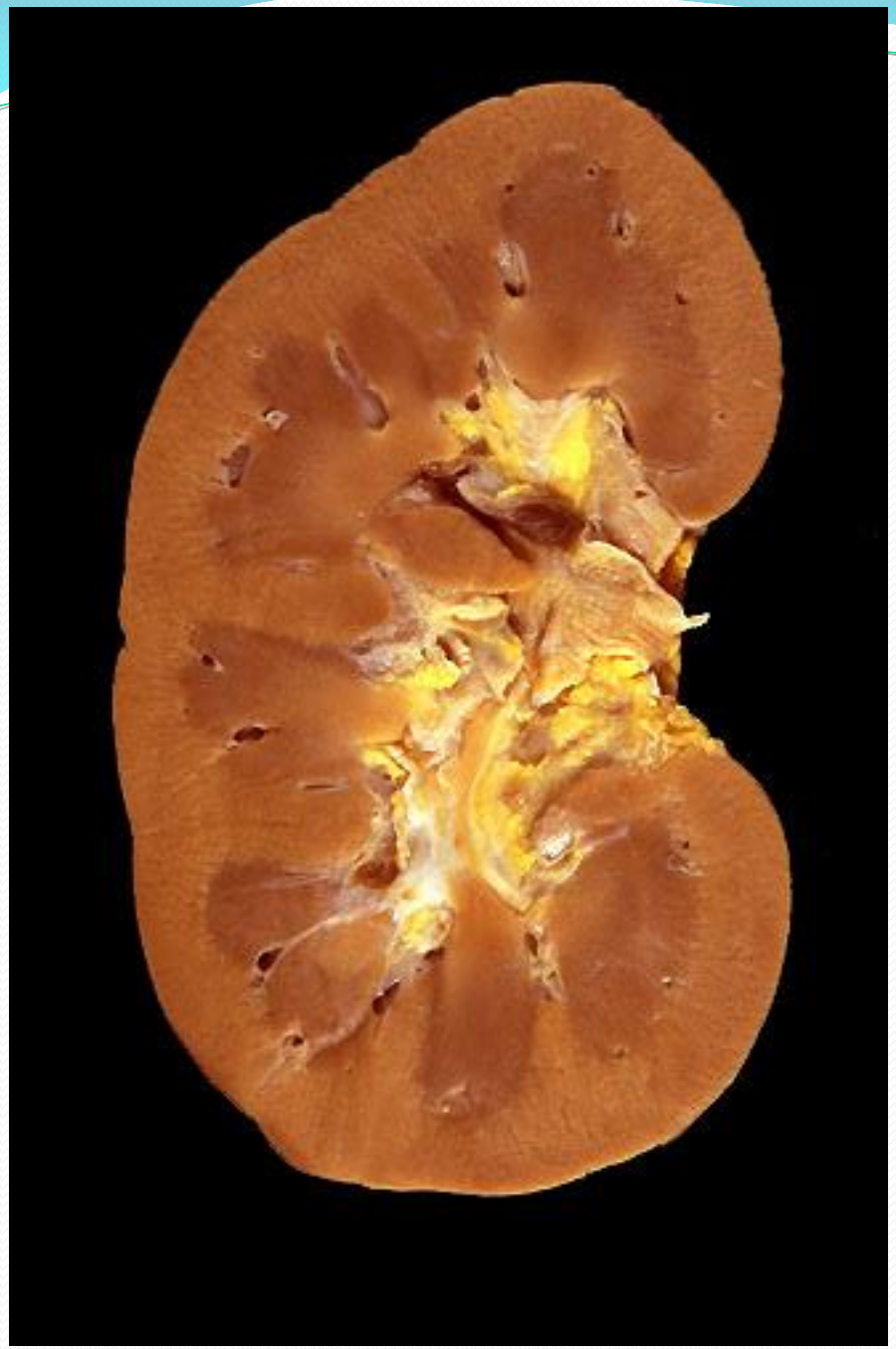
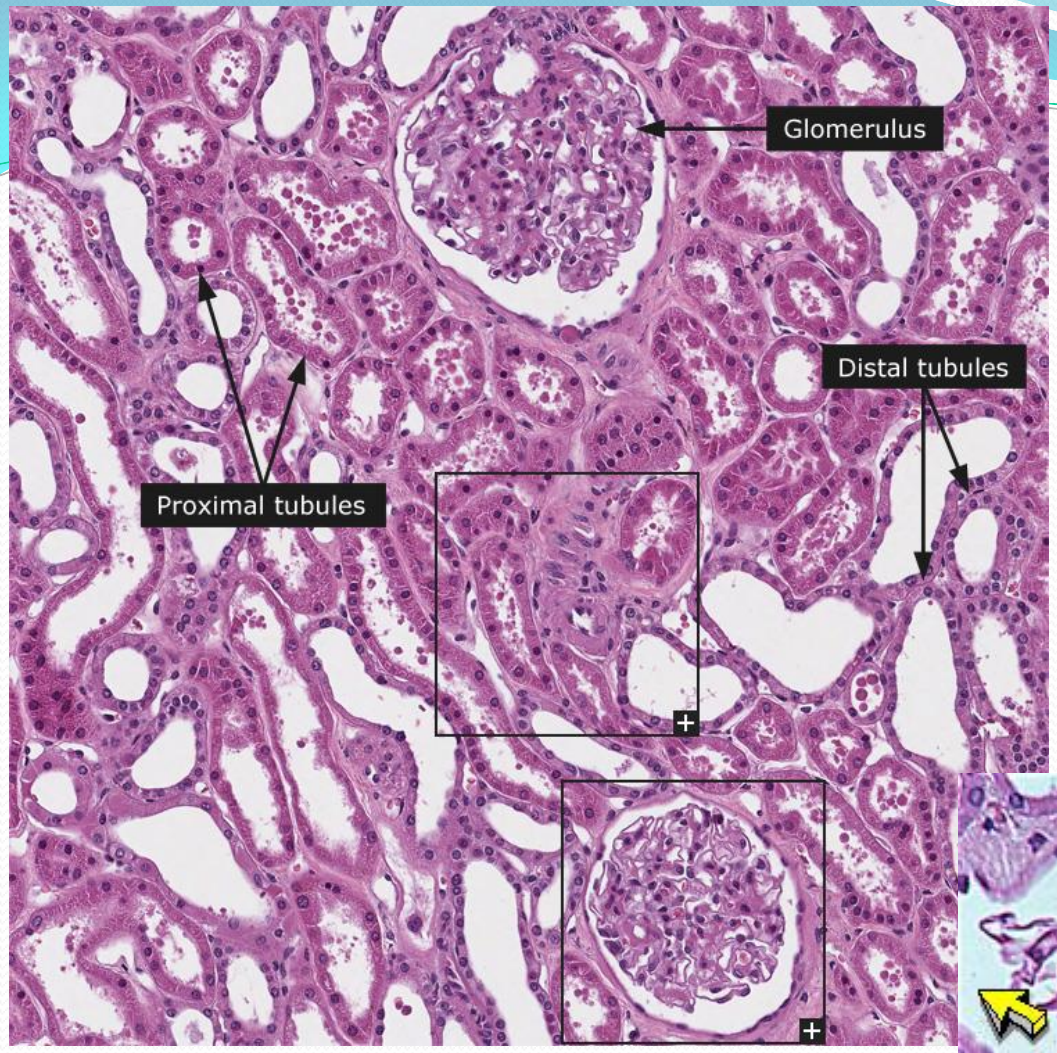
RENAL / KIDNEY PATHOLOGY

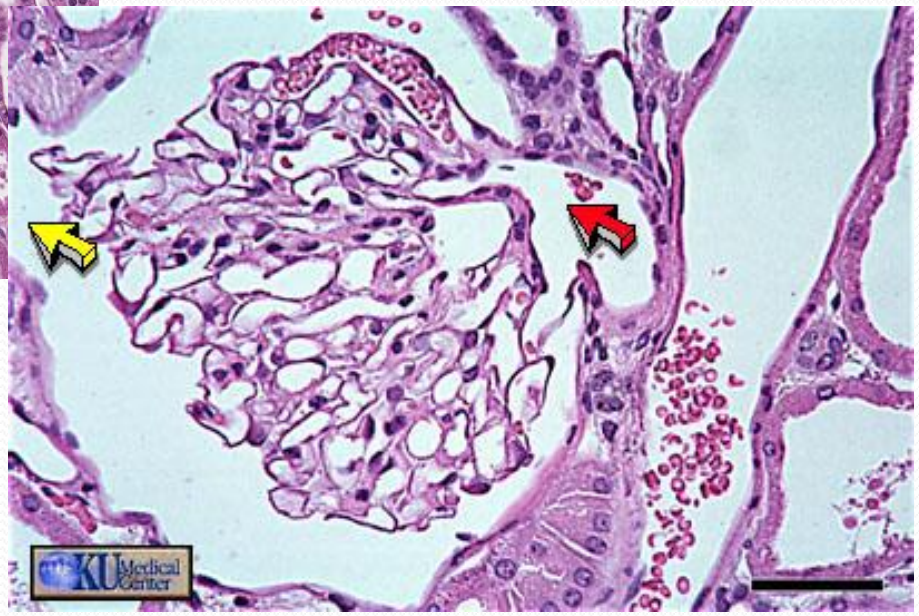
- **GLOEMRULAR**
- **TUBULAR**
- **VASCULAR**
- **INTERSTITIAL**

DISEASES

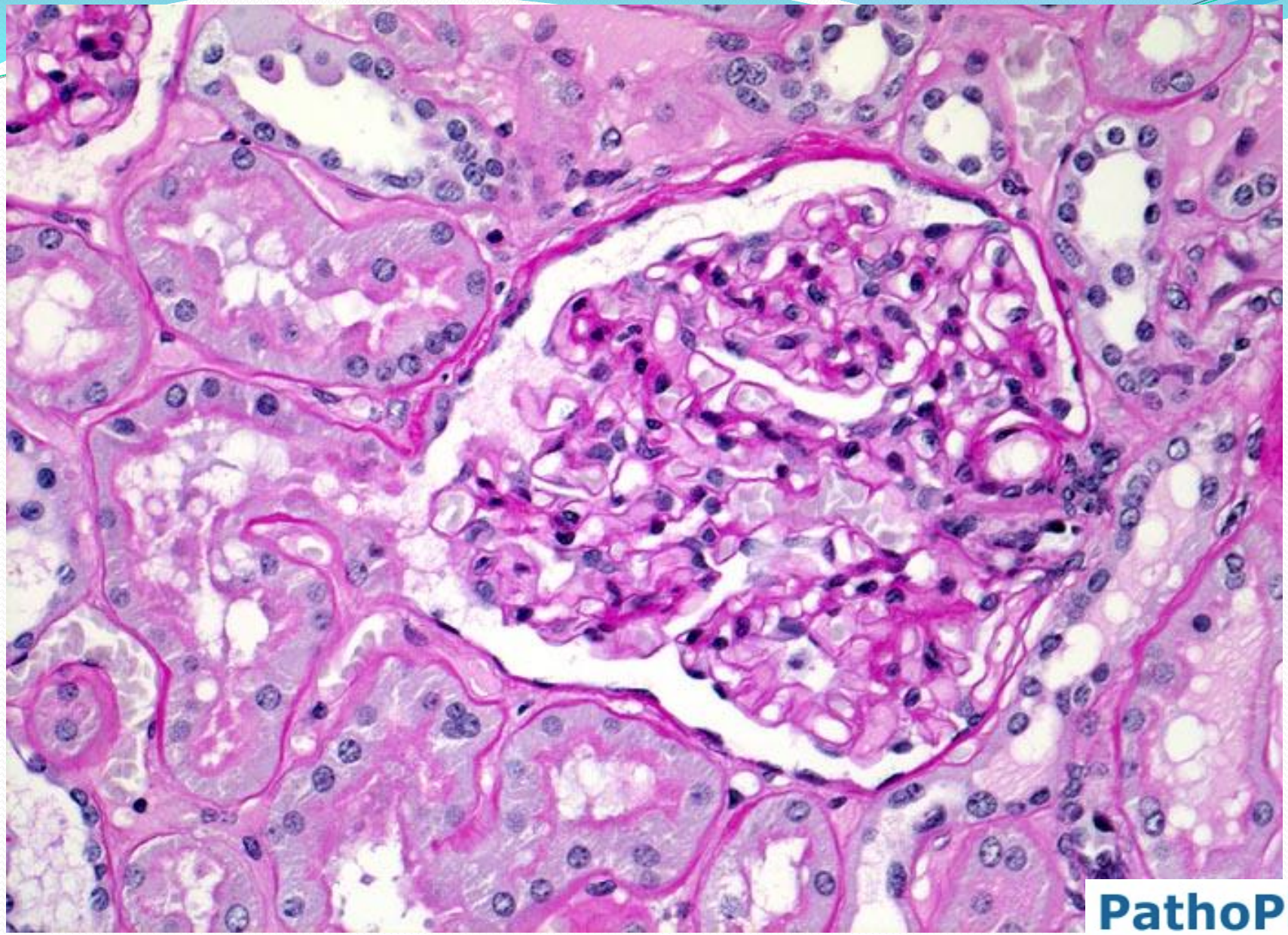


In cross section, this **normal adult kidney** demonstrates the lighter outer cortex and the darker medulla, with the renal pyramids into which the collecting ducts coalesce and drain into the calyces and central pelvis.

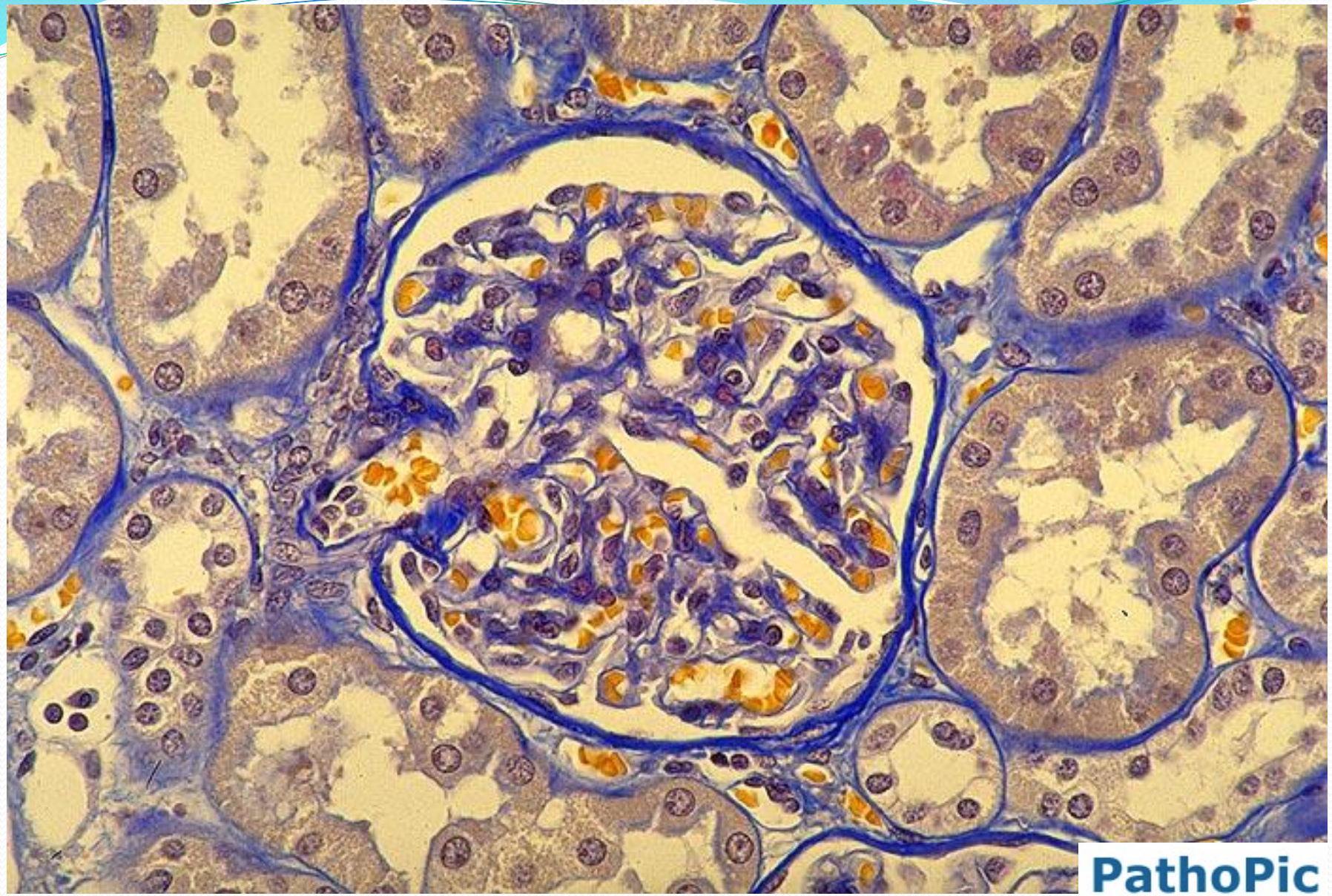




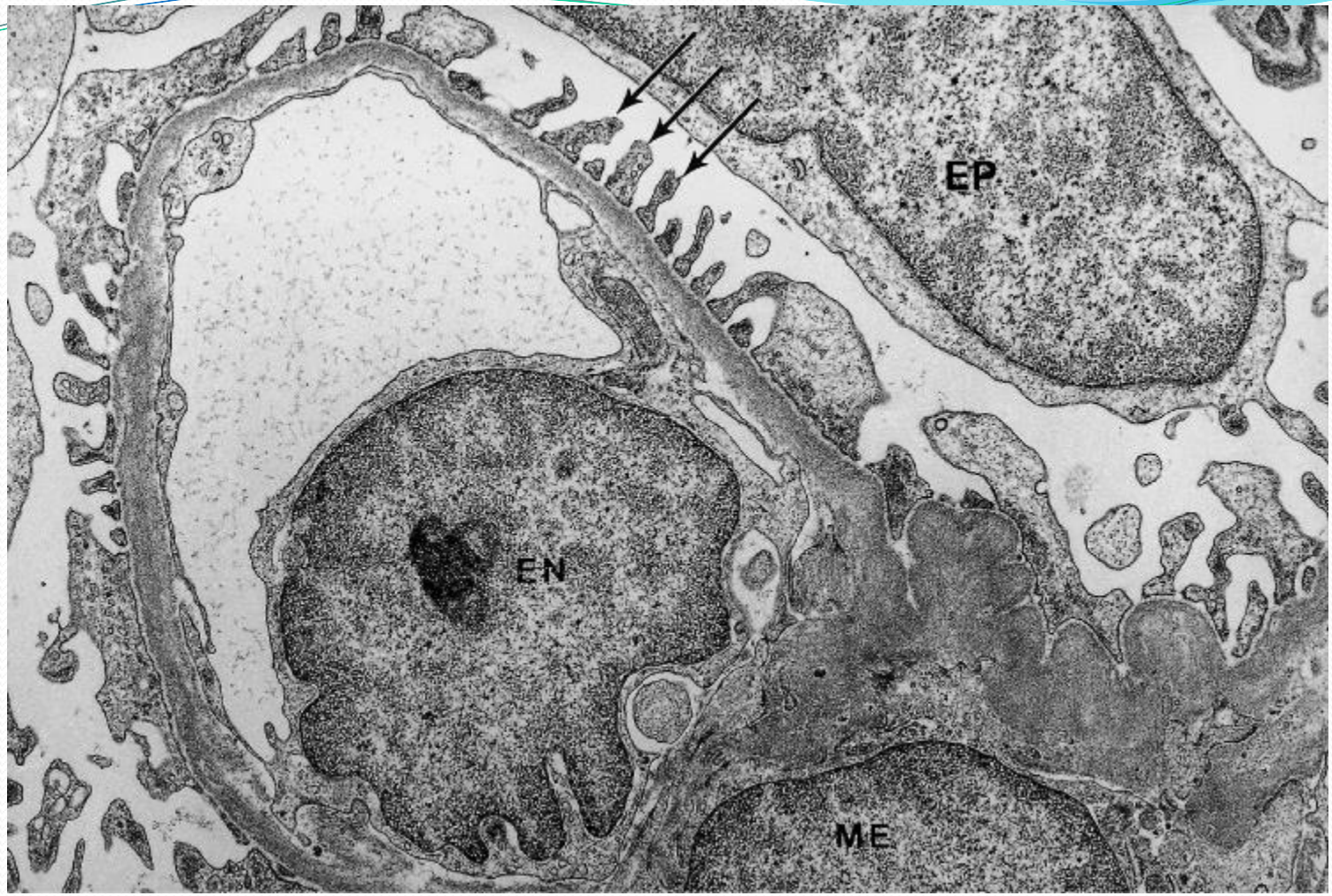
HE, normal glomerulus



PAS, normal glomerulus



Fuchsin Orange G, normal glomerulus



Electron micrograph of normal glomerulus showing the relationship of different cell types. The epithelial aspect of the basement membrane is covered by foot processes (arrows) and the capillary lumen is lined by attenuated endothelium. EP = epithelial cell; ME = mesangium; EN = endothelial cell.

Glomeruli injured *primary* or *secondary* = *glomerulopaties / GLOMERULAR DISEASES*

with clinical manifestation of:

- **Nephrotic syndrome**
  - **heavy proteinuria (more than 3.5 g / 24 hrs) leading to**
  - **hypoproteinemia (hypoalbuminemia)**
  - **peripheral edema**
  - **hyperlipidemia**
- **results from *noninflammatory glomerulopathies.***

- **Nephritic syndrome**
  - **hematuria**
  - **degrees of proteinuria (under 3.5 g/day)**
  - **oliguria, decreased glomerular filtration rate**
  - **hypertension**
  - **edema.**
- **is associated with *inflammatory glomerular disease* (*glomerulonephritis)***

- **Renal failure**

***Acute* decline GFR increase in blood urea nitrogen and serum creatinine values - results from damage of: glomeruli, tubules and interstitium.**

***Chronic* results from a variety of renal diseases glomerular, tubulointerstitial, and vascular.**

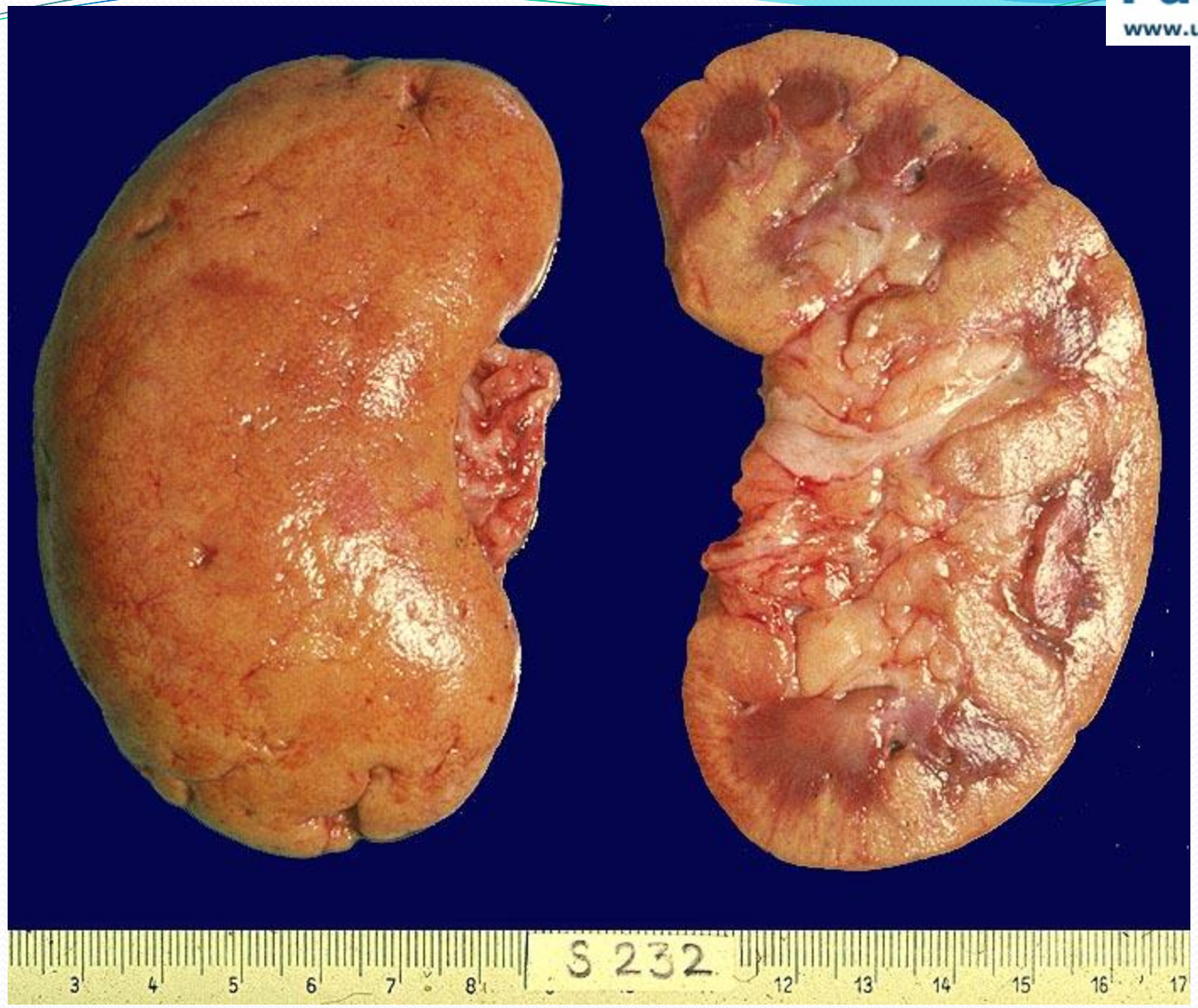
Non-inflammatory glomerular lesions

- glomeruli are normocellular or at most mildly hypercellular.
- proteinuria - nephrotic range
- loss of structural and functional integrity of any of the three components comprising the glomerular capillary wall: the endothelial cell, the basement membrane, and the epithelial cell (visceral podocytes).
- primary diseases involving only the kidney or components of a systemic disease

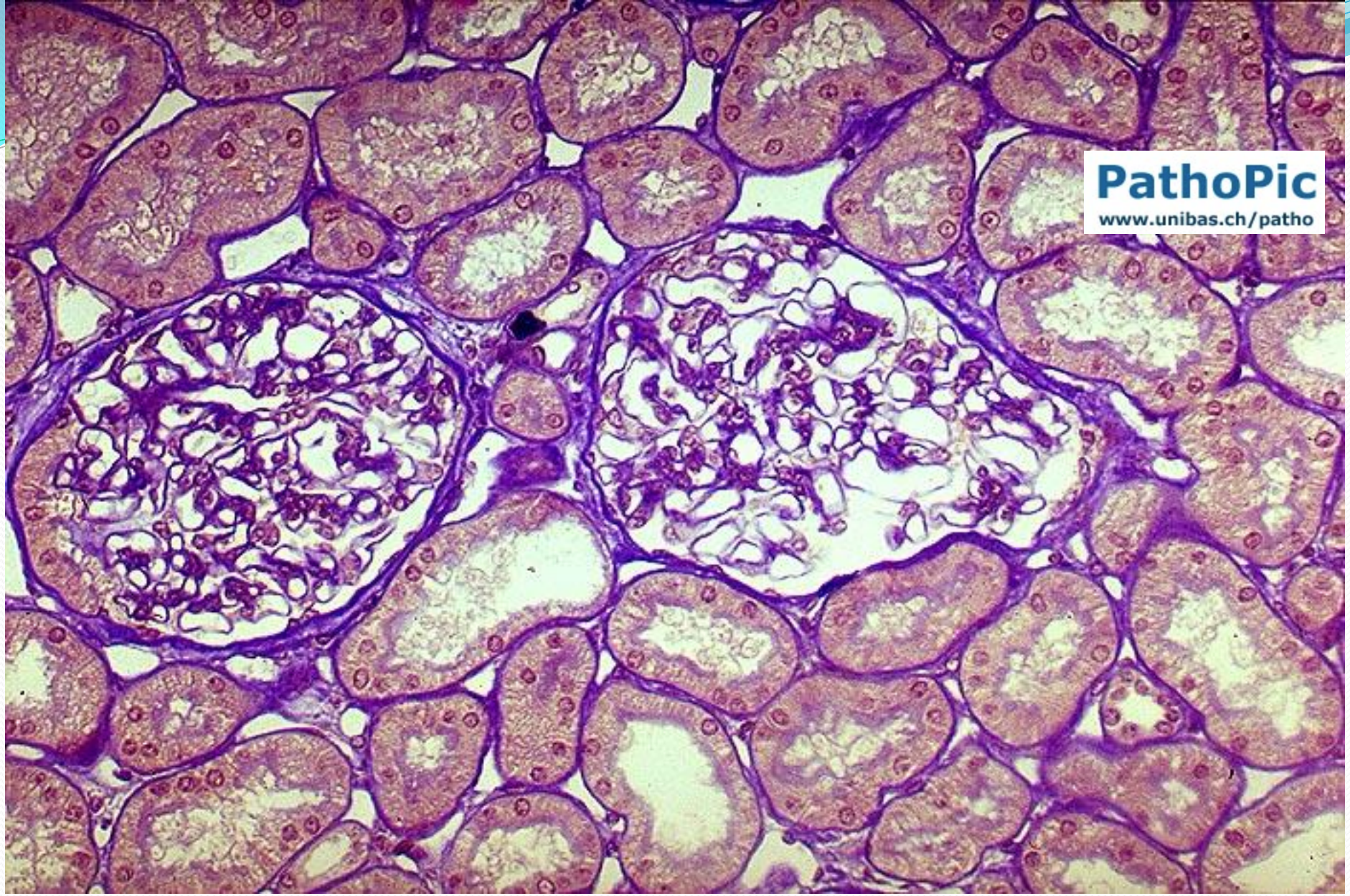
Minimal change nephrotic syndrome (lipoid nephrosis):

= a glomerular disorder characterized clinically by the nephrotic syndrome and pathologically by the fusion of epithelial foot processes (EM) + accumulation of lipid in the proximal tubular cells, which is reflected histologically in a foamy cytoplasm (lipoid nephrosis)

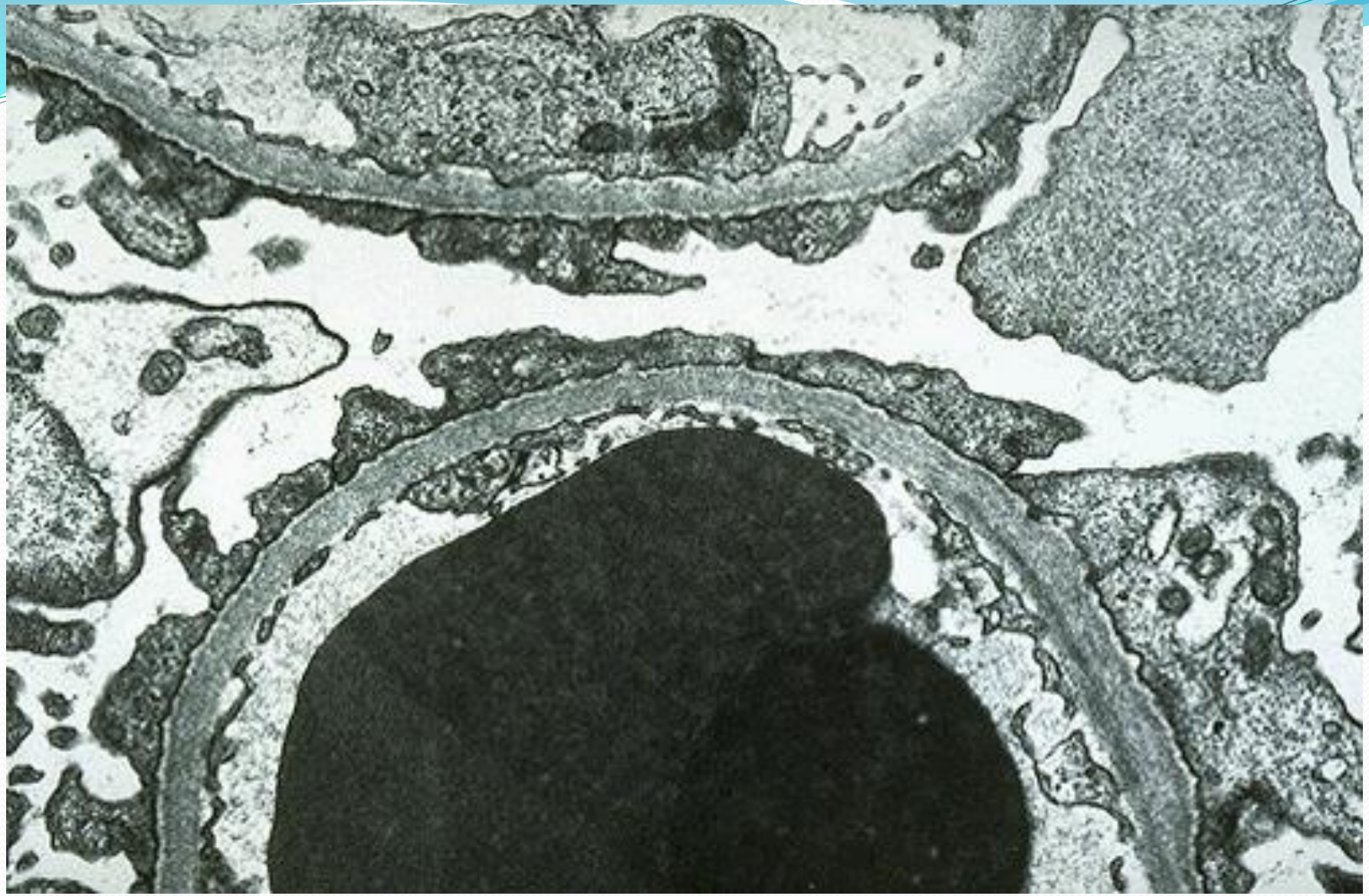
- disorder of childhood, being the major cause of the nephrotic syndrome
- the cause or the pathogenesis of minimal change nephrotic syndrome isn't understood
- light microscopic appearance of glomeruli is essentially normal
- EM: no electron-dense deposits are seen
- corticosteroid therapy efficient
- no tendency to progress into chronic renal failure



Minimal change disease / lipoid nephrosis - gross



Note normal basement membrane and absence of cell proliferation.



EM: Ultrastructural characteristics of minimal change disease: effacement of foot processes

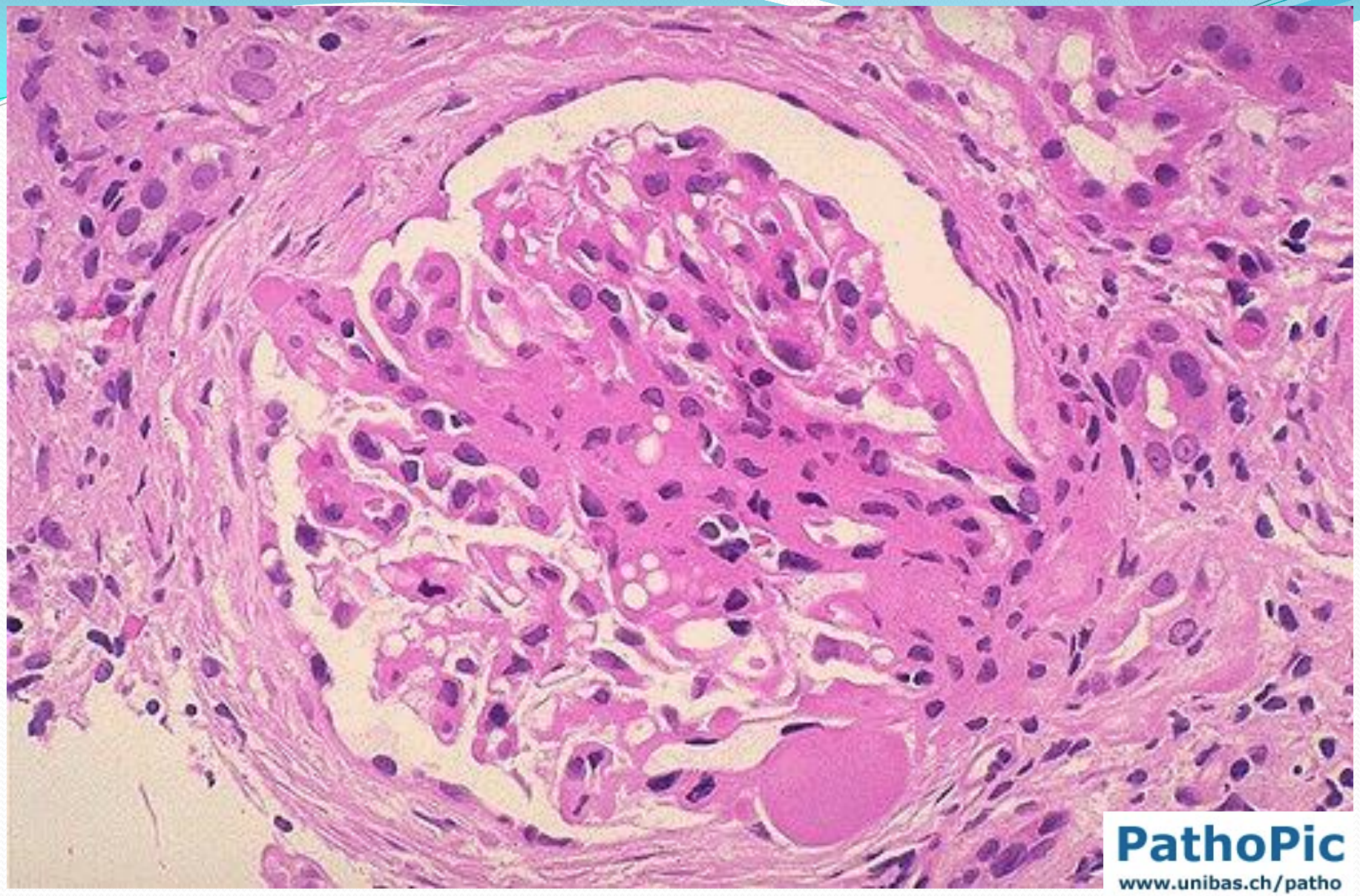
Focal segmental glomerulosclerosis

= *some* glomeruli exhibit *segmental* areas of sclerosis in the capillary tufts whereas others appear normal

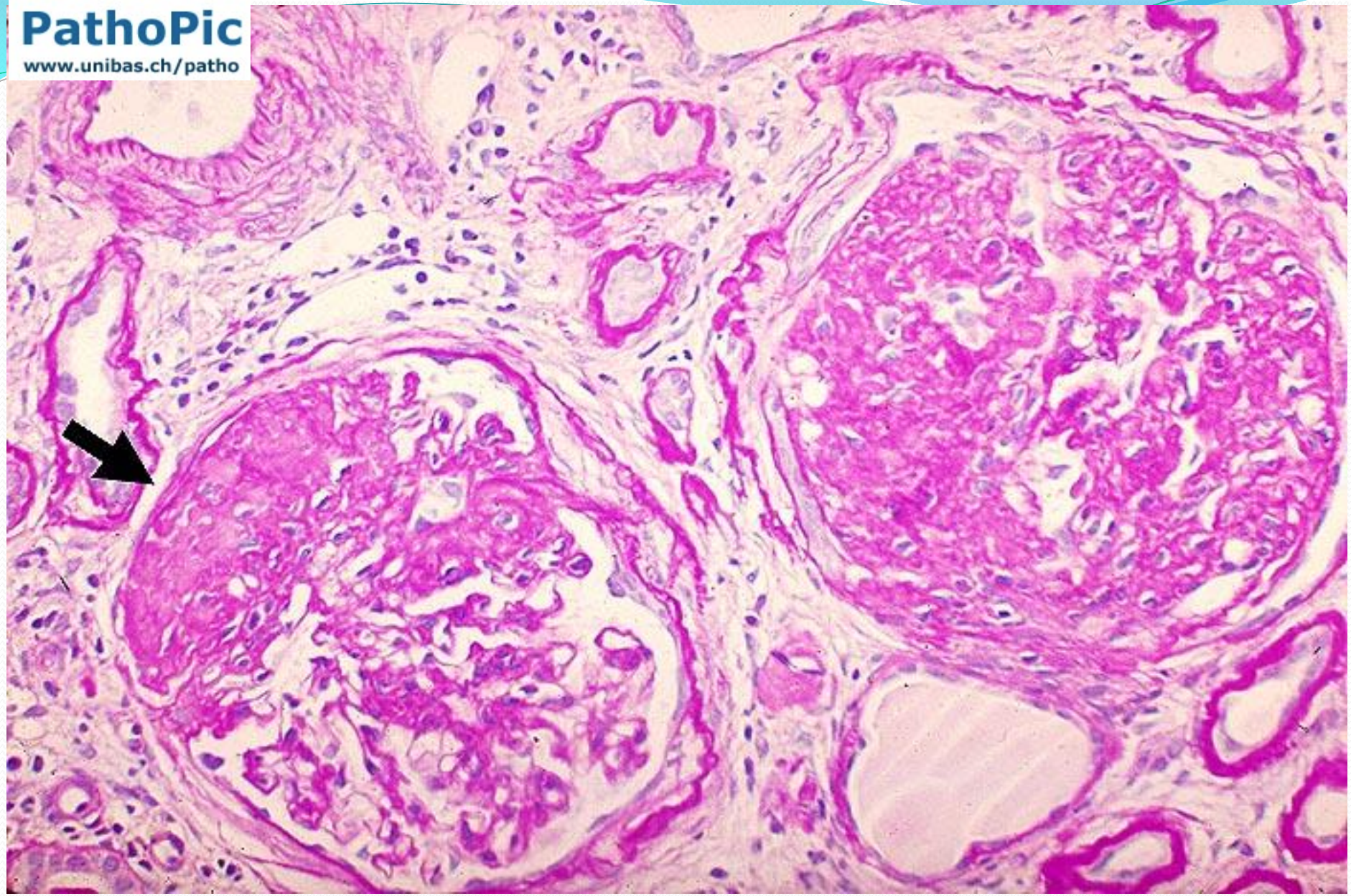
! Focal < 50% of glomeruli

! Segmental partial injury of glomerulus

- The majority of cases are of unknown etiology (idiopathic)
- LM: glomeruli show segmental areas of capillary loop obliteration PAS-positive material (*hyalinosis)* + adjacent glomeruli present adhesions to Bowman's capsule + the mesangium is hypercellular.
- EM: diffuse effacement of epithelial cell foot processes + folding and thickening of the basement membrane and capillary collapse.



Focal segmental glomerulosclerosis, hyaline insudation / hyalinosis.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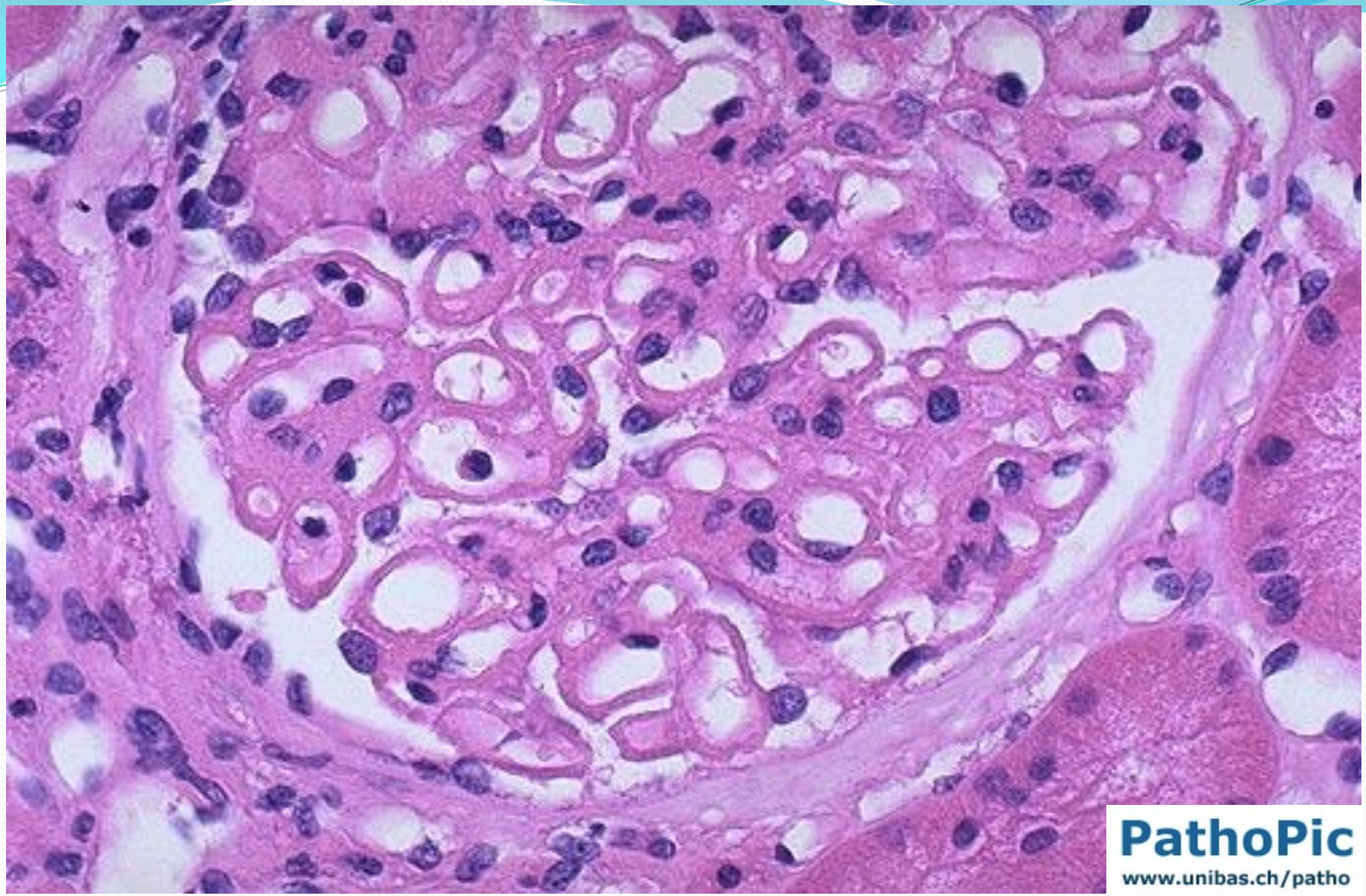
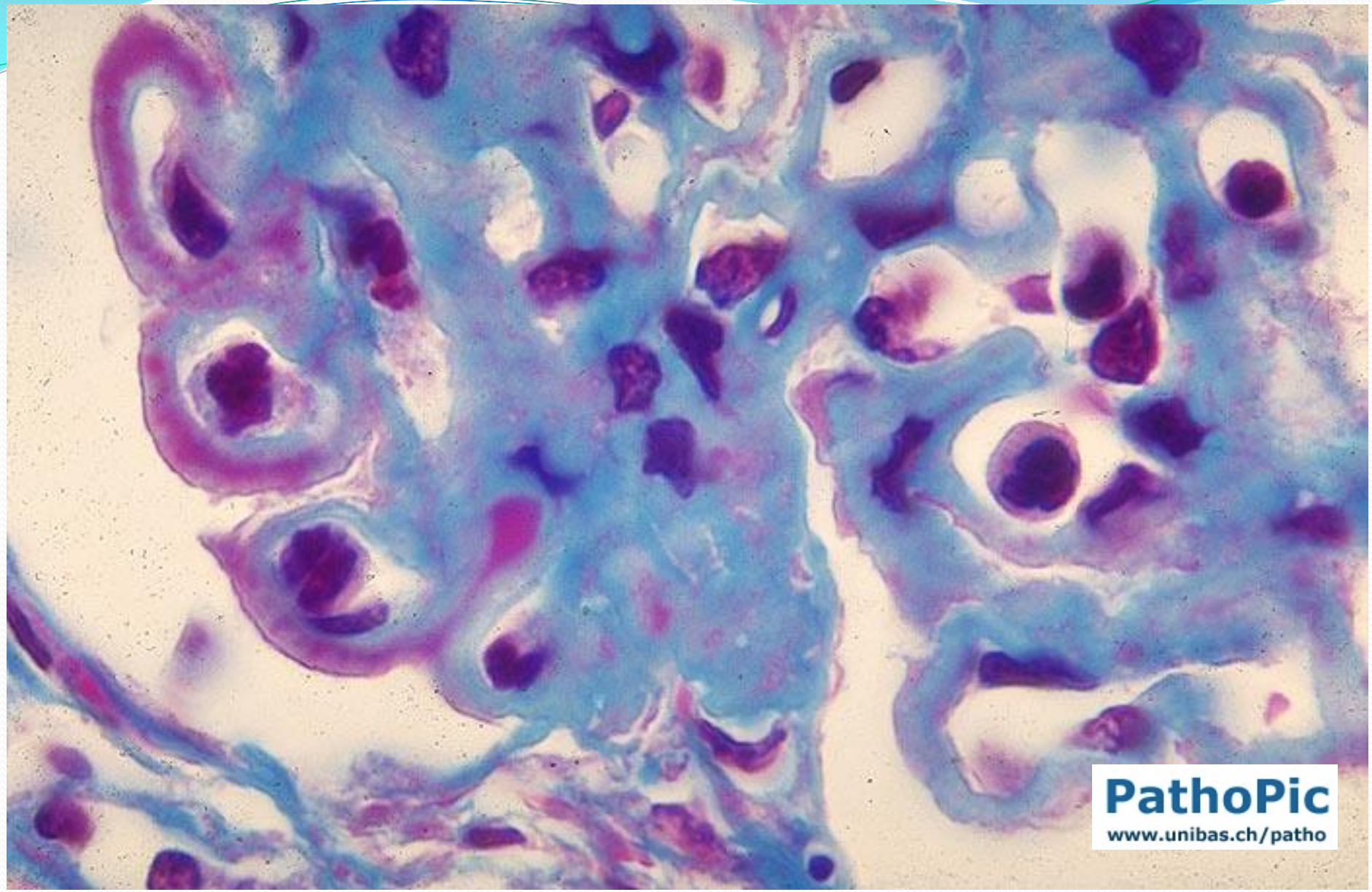
Membranous nephropathy

= diffuse thickening of the glomerular basement membrane

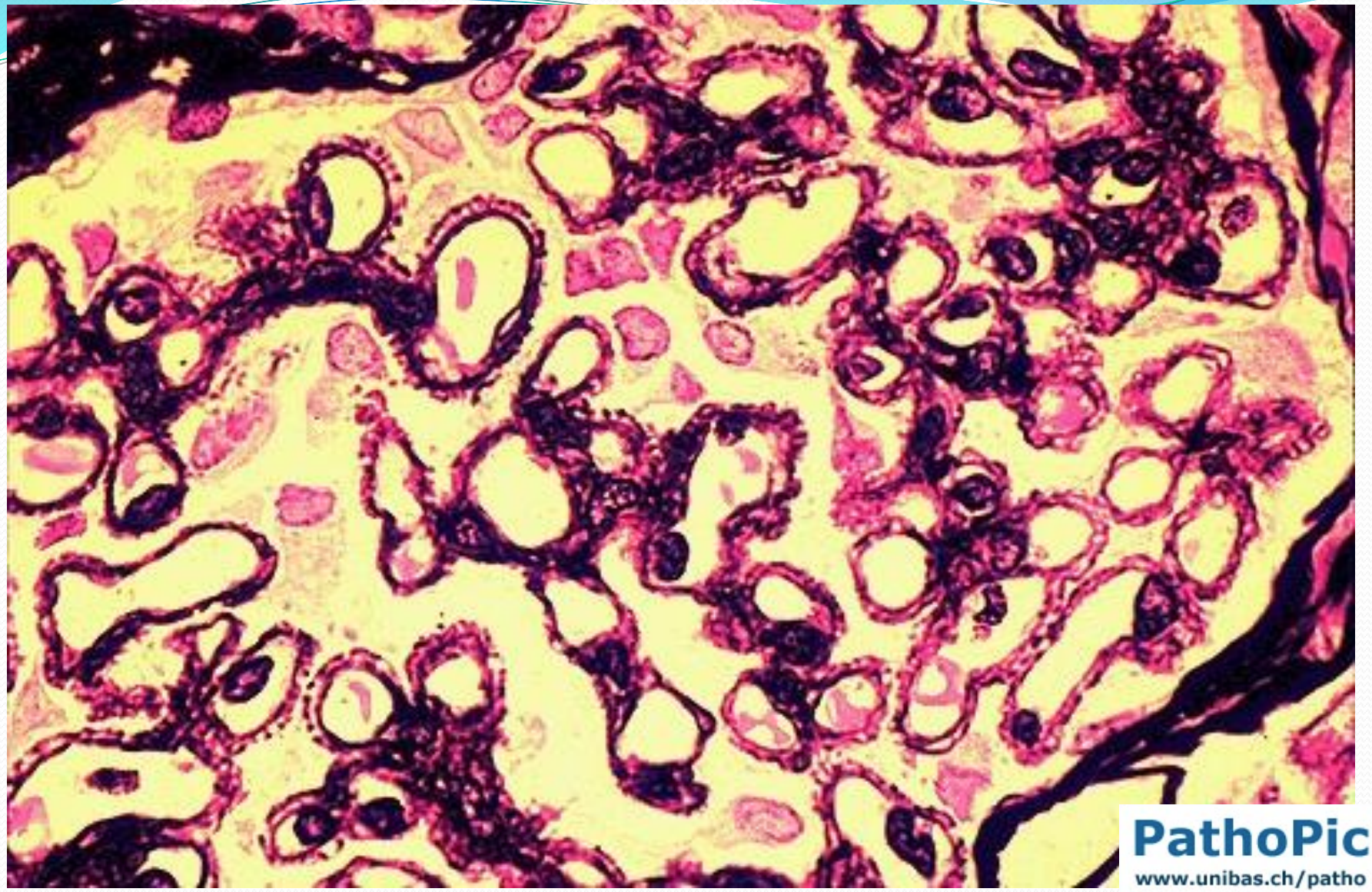
- is the most frequent cause of the nephrotic syndrome in adults (30% of the cases)
- most cases are idiopathic
- LM: the glomeruli are enlarged, but normocellular
- silver stain: “spikes” of argyrophilic material on the epithelial surface of the basement membrane around the immune complexes, which do not stain with silver; the capillary lumens are encroached upon and glomerular obsolescence ensues
- EM: 4 stages of disease progression



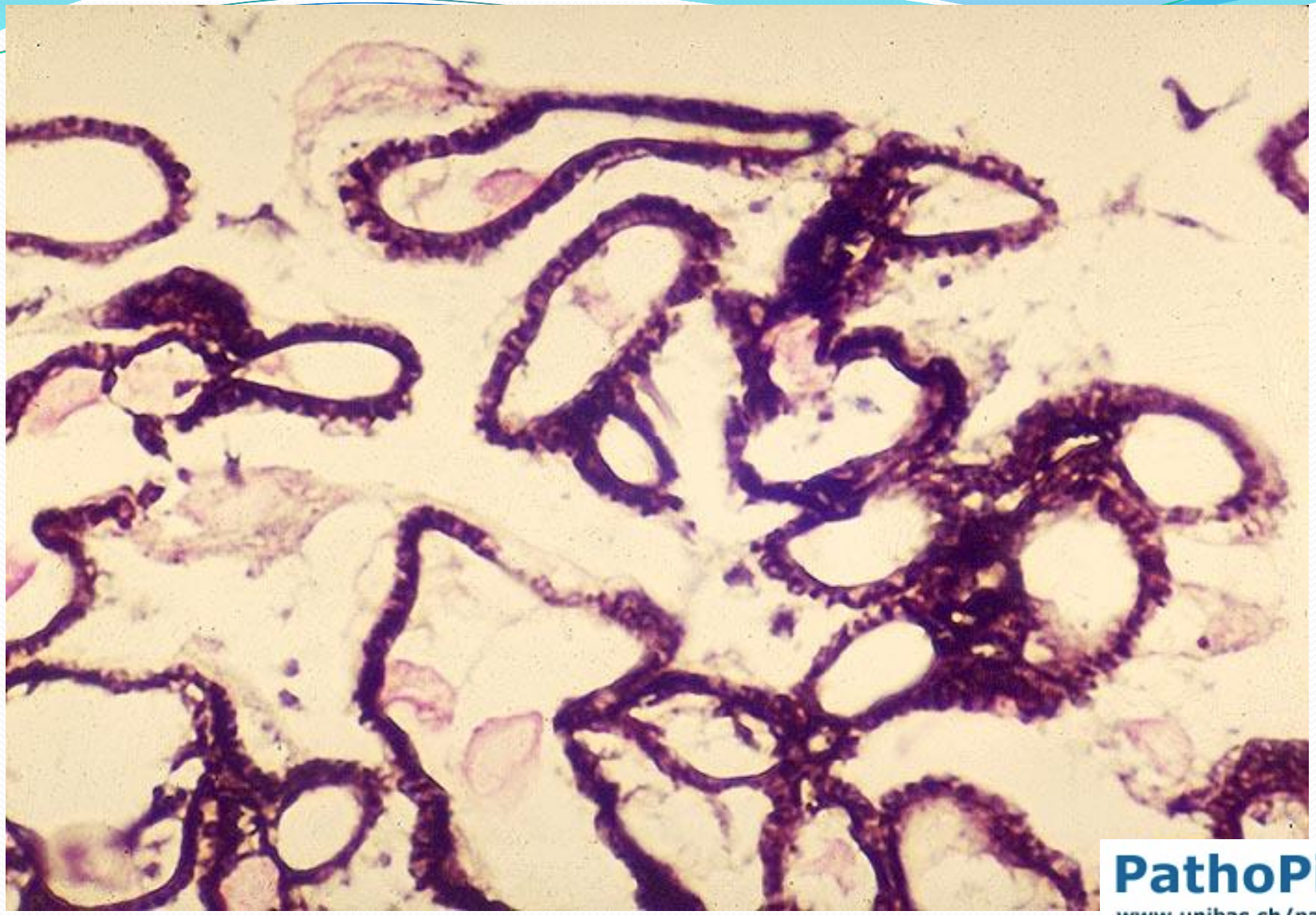
Membranous nephropathy. Note the marked diffuse thickening of the capillary wall without an increase in the number of cells.



Membranous nephropathy: subepithelial immune complexes deposits



Membranous nephropathy: silver preparation showing spike formation along the thickened basement membrane



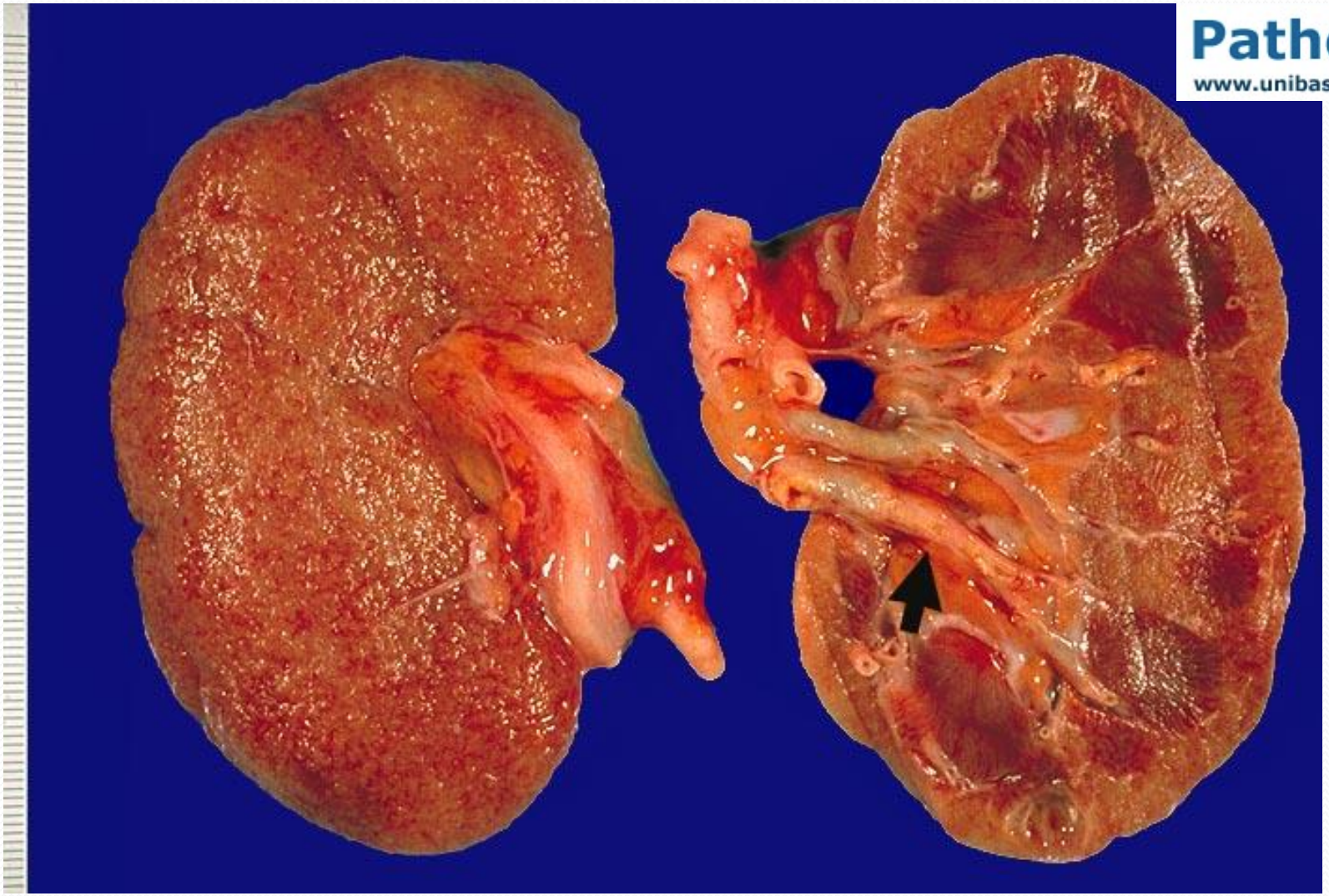
Membranous nephropathy: silver impregnation.

Diabetic glomerulosclerosis

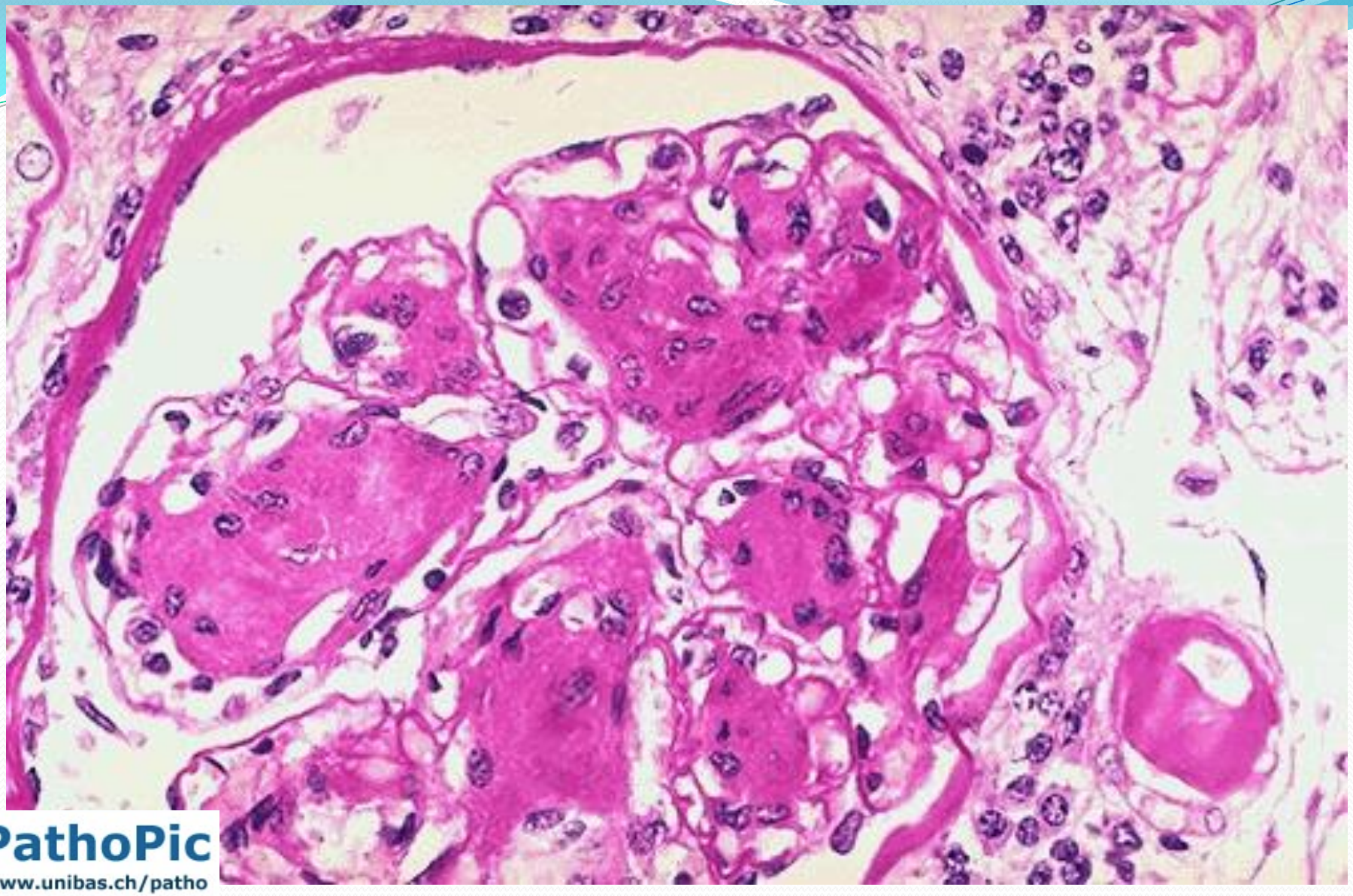
an expression of the *diabetic microangiopathy* that occurs in many systemic small arteries, arterioles and capillaries

glomerular sclerosis is caused by the progressive accumulations of basement membrane material

- proteinuria initially mild to nephrotic range
- thickening of the glomerular basement membrane + diffuse widening of mesangial areas, with the accumulation of a PAS-positive matrix = *diffuse glomerulosclerosis*
- multiple nodules in the glomeruli - rounded, homogenous, eosinophilic masses with time the nodules become acellular, silver stains reveal a pattern of concentric lamination = *nodular glomerulosclerosis*
- mixed: diffuse & nodular



Diabetic glomerulosclerosis gross



Nodular glomerulosclerosis (Kimmelstiel-Wilson disease) in a patient with long-standing diabetes mellitus.

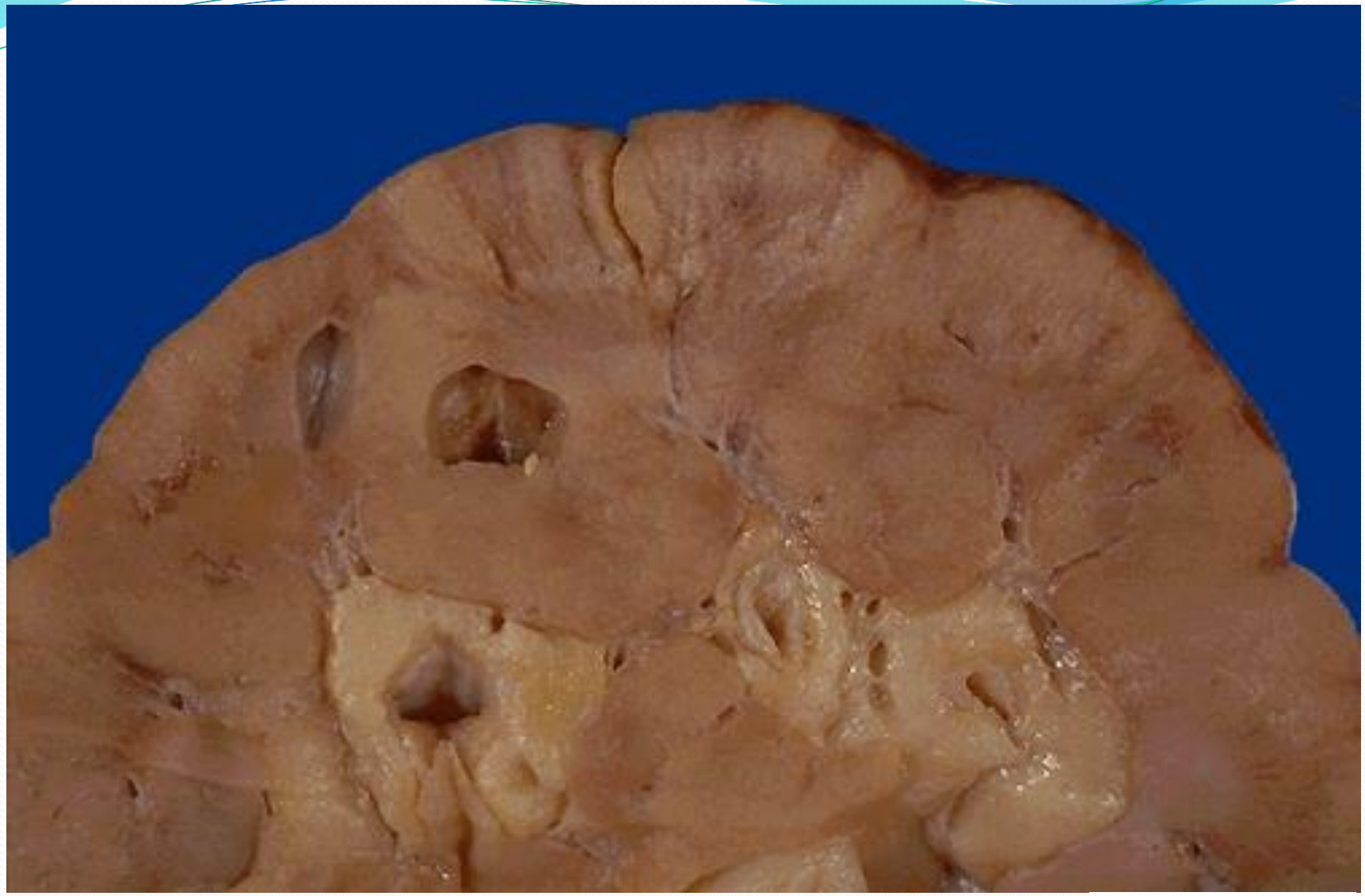
Renal amyloidosis

prominent feature of most cases of systemic amyloid

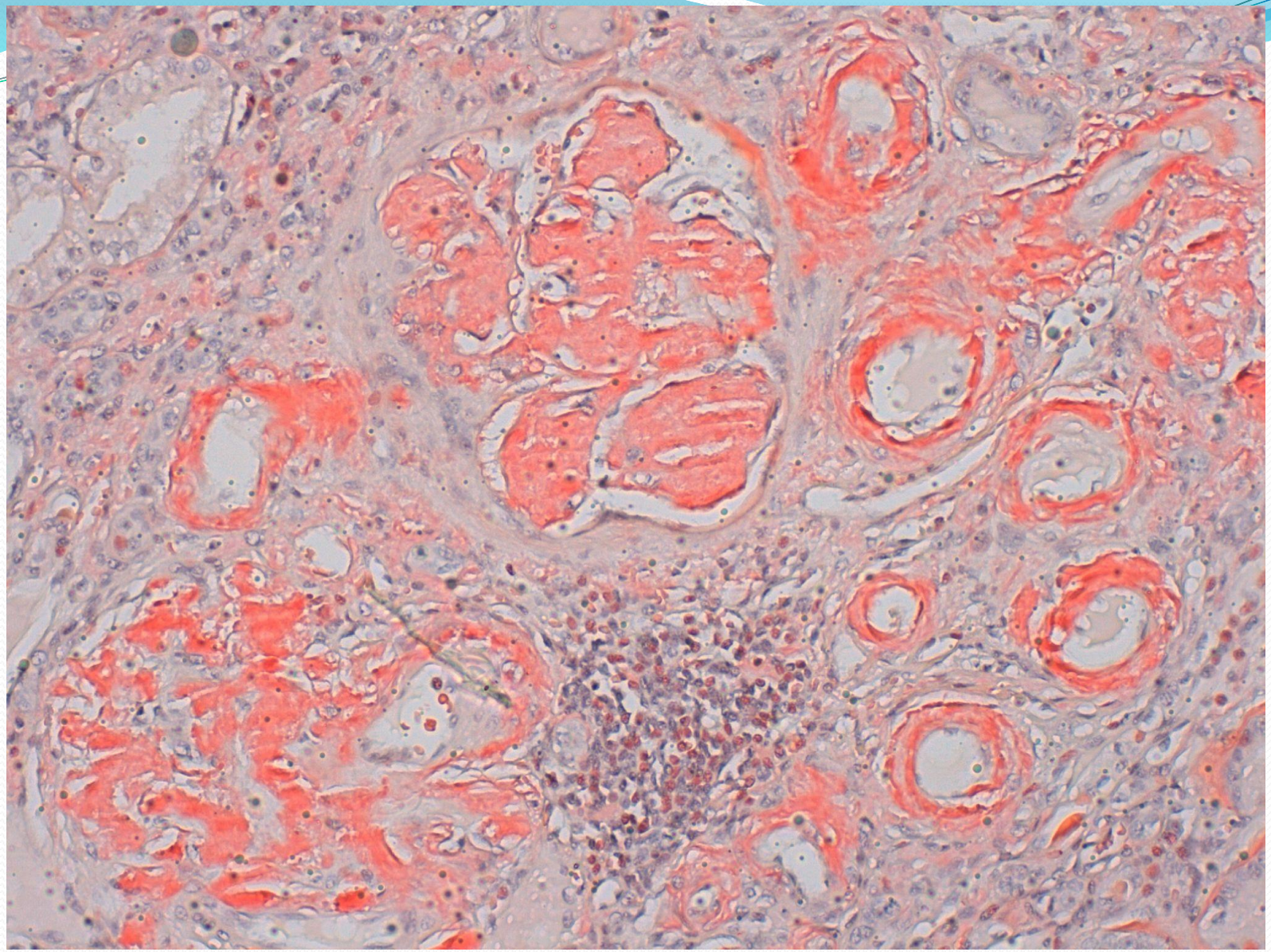
eosinophilic (H&E stain) amorphous material

apple-green color in sections with Congo red and examined under polarized light

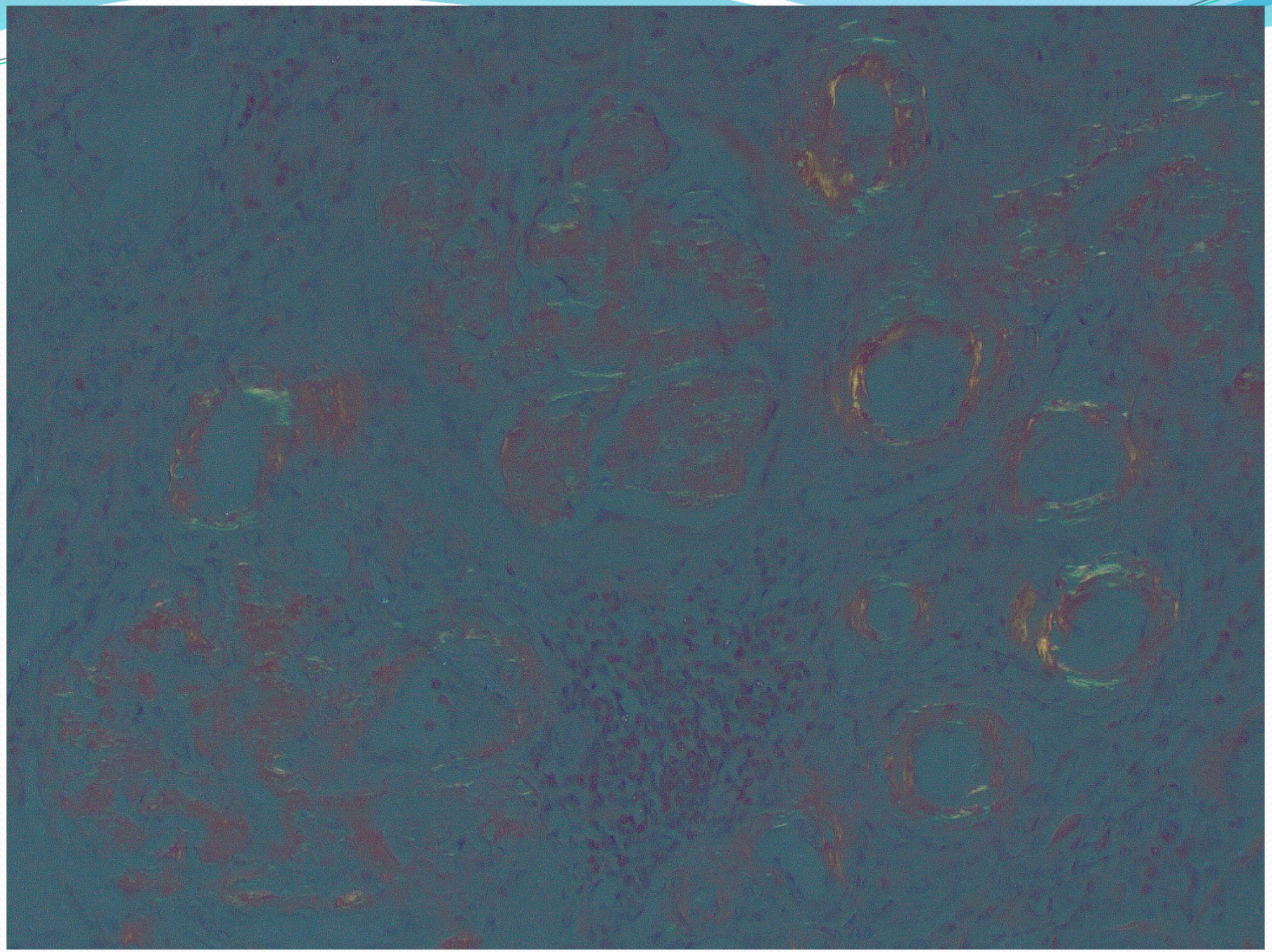
- initially mesangial amyloid deposition produces diffuse mesangial widening without hypercellularity
- it spreads to obliterate capillary lumens
- glomeruli become enlarged with nodular deposits
- finally, glomeruli appear as large, amorphous, eosinophilic balls
- EM: non-branching fibrils



Gross, *kidney amyloidosis*.



Kidney amyloidosis: glomeruli with prominent mesangial and vascular deposition of **amyloid,** Congo red stain.



Deposits of amyloid exhibiting birefringence under polarized light (Congo red stain).

Inflammatory glomerular lesions / glomerulonephritis

- *diffuse* or *focal* hypercellularity of the glomeruli injuries may be global (entire glomerulus) or segmental
- nephritic syndrome complete / monosymptomatic - hematuria
- pathogenetic mechanisms can be:
  - immunologic,
  - thrombotic,
  - toxic,
  - unknown

Immunologic injury types:

- trapping of circulating immune complexes in a subepithelial location; EM: subepithelial “humps”
- in situ immune complex formation by the binding of circulating antibody to an antigen that has already deposited in the glomerular basement membrane
- activation of the alternative pathway of complement
- cell-mediated processes

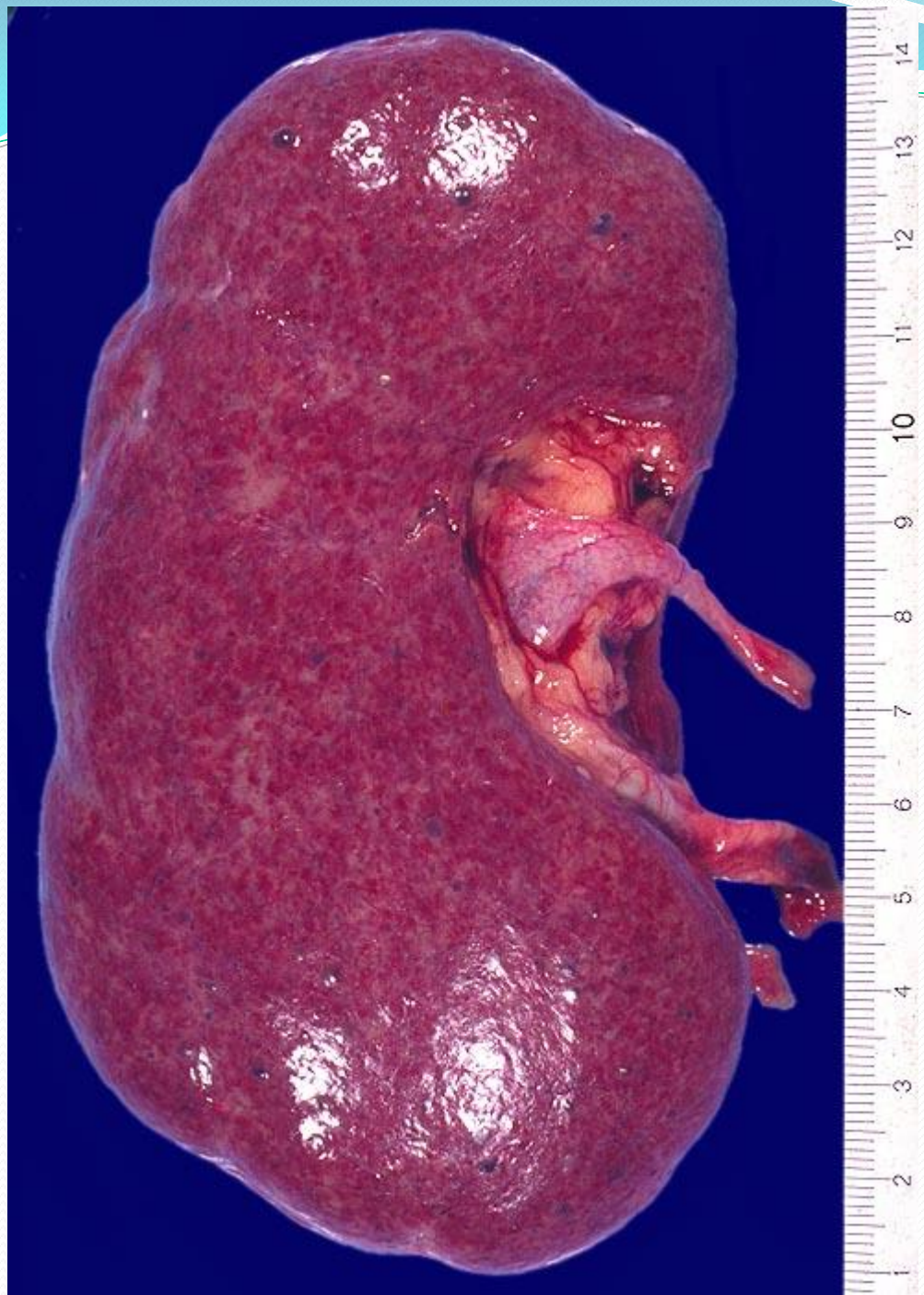
Acute glomerulonephritis (postinfectious)

is a sequel to infection with a variety of agents, but the most frequent association is group A beta-hemolytic streptococci

primary infection may be in the pharynx or the skin

most commonly affects children

- LM: diffuse enlargement and hypercellularity of the glomeruli due to proliferation of both endothelial and mesangial cells leukocytic infiltration of capillary loops: neutrophils and monocytes
- EM: subepithelial “humps”
- long-term prognosis: most data suggest complete recovery, particularly in children



Acute glomerulonephritis, gross.

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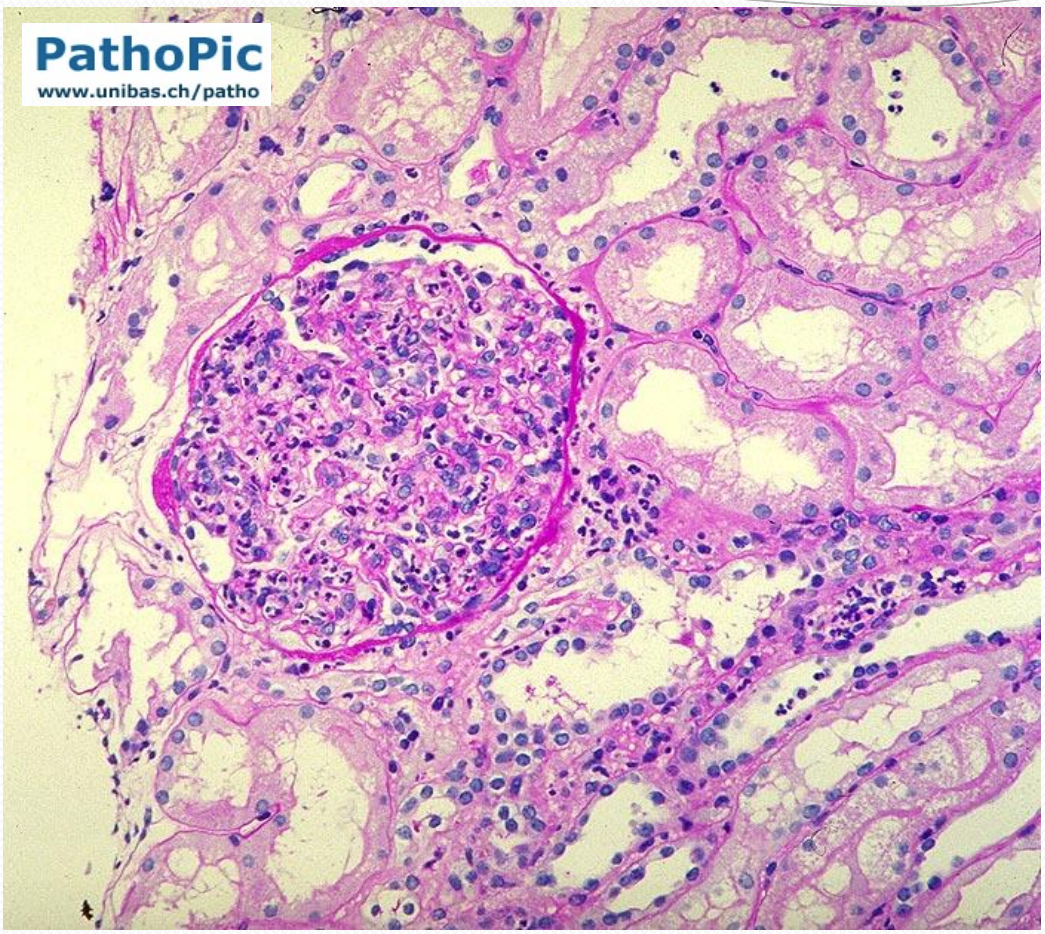
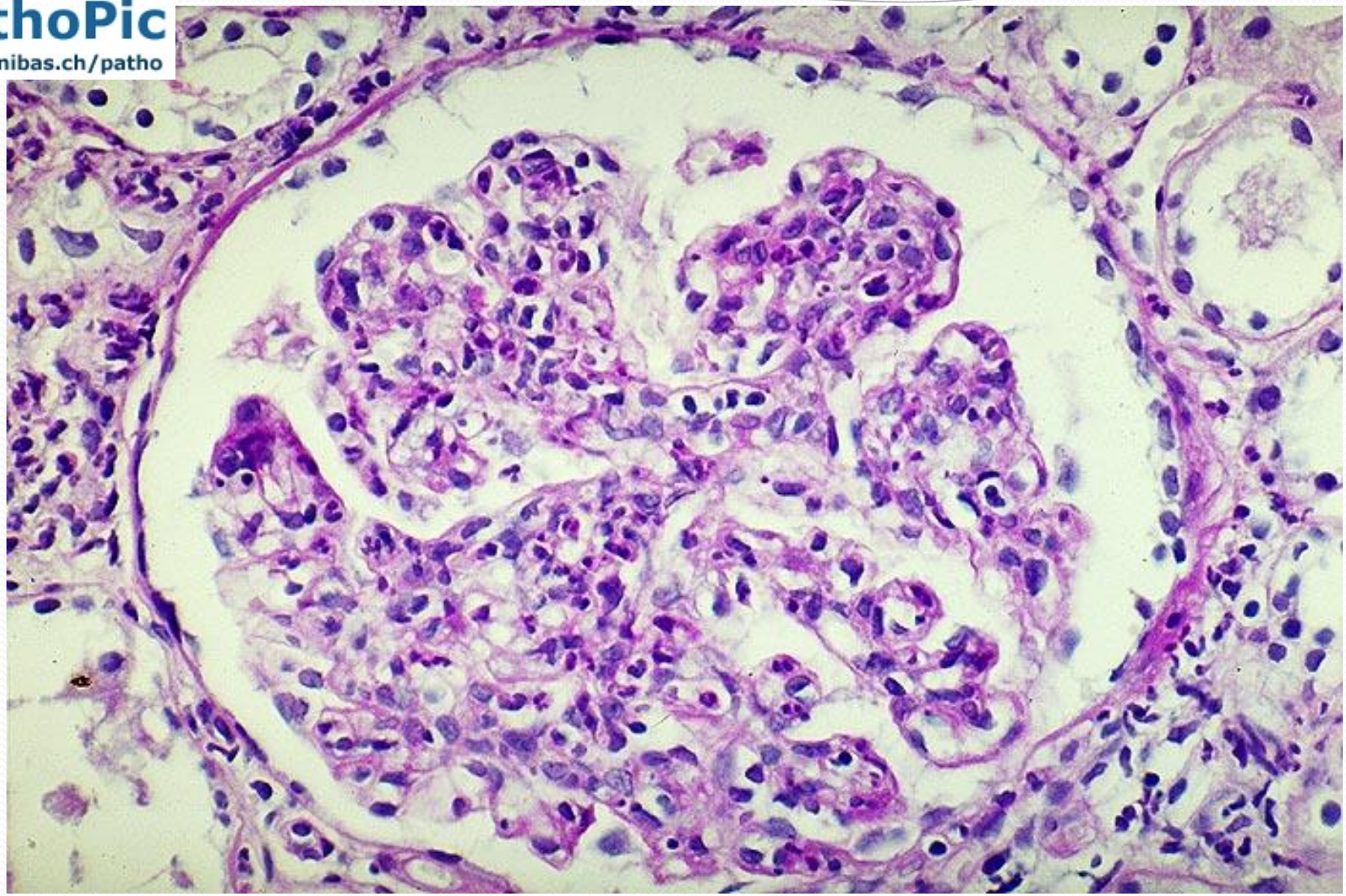
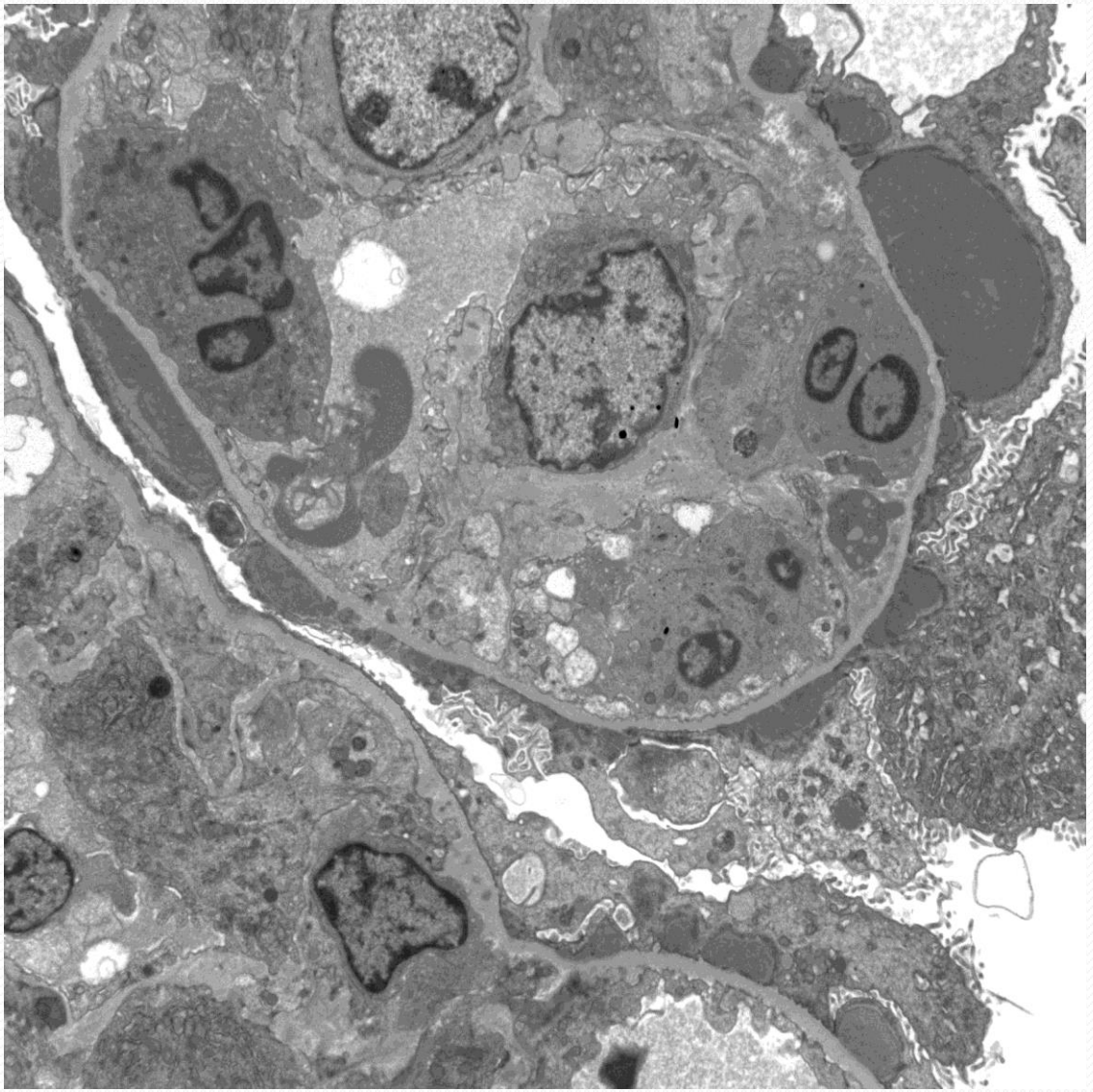


Acute proliferative glomerulonephritis. Glomerular hypercellularity is due to intracapillary leukocytes and proliferation of intrinsic glomerular cells.



Acute proliferative glomerulonephritis. Glomerular hypercellularity, prominent number of intra-capillary neutrophils.

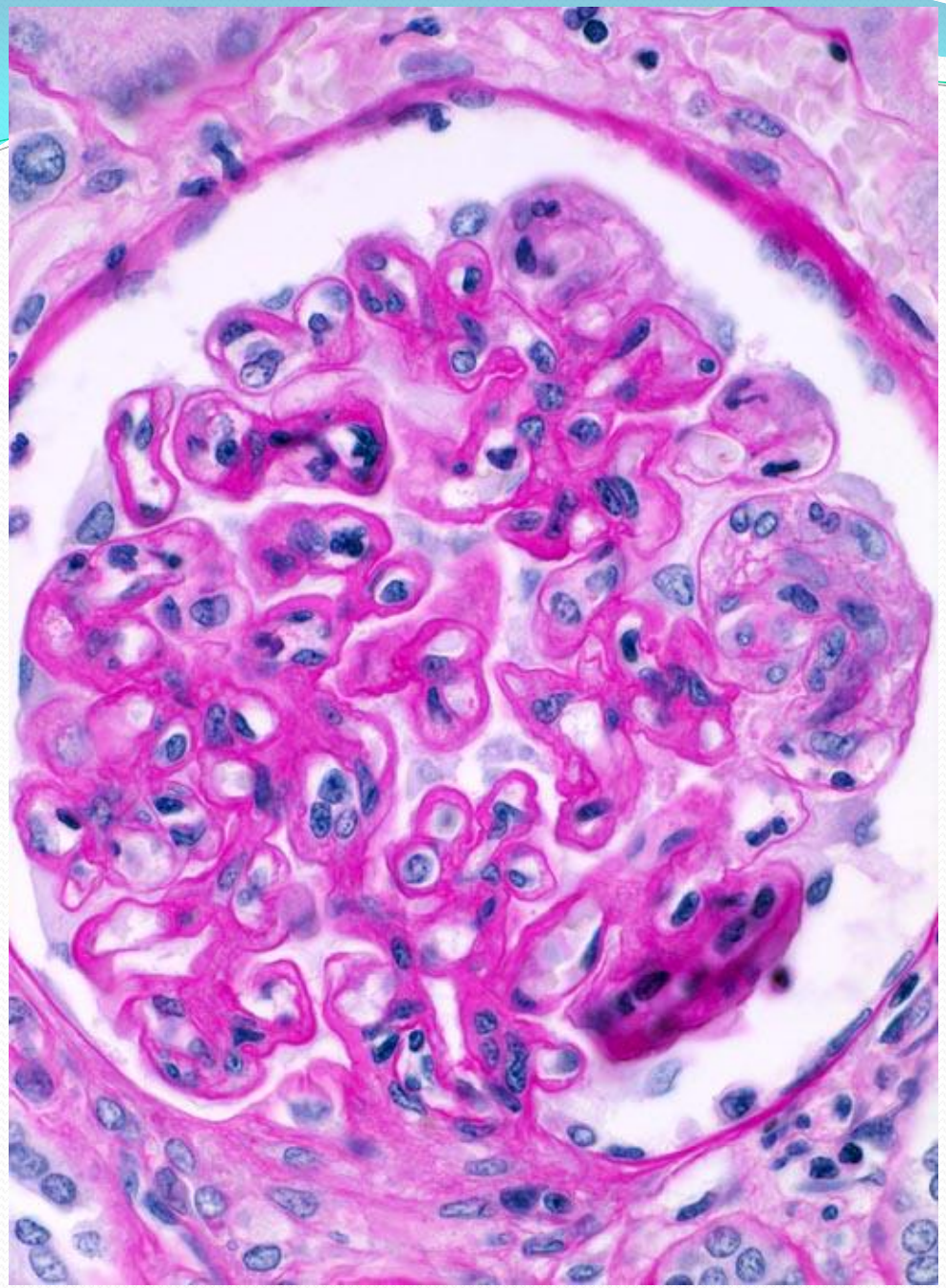


EM: Typical electron-dense subepithelial "hump"

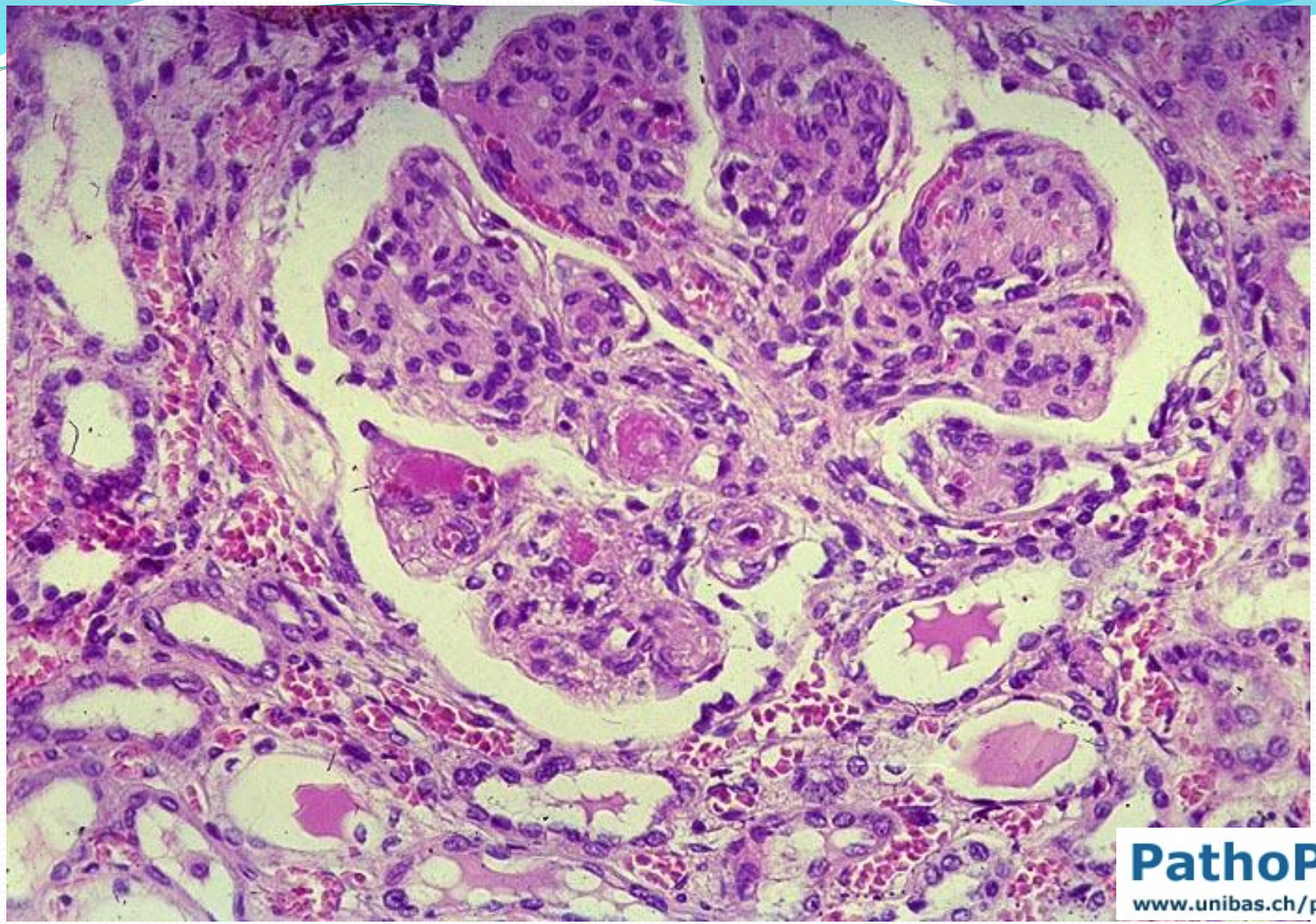
Membranoproliferative glomerulonephritis:

- the combination of glomerular basement membrane thickening (“membrano”) and mesangial cell proliferation (“proliferative”)
- older children and young adults
- either the nephrotic or nephritic syndrome or a combination of both
- vast majority of patients progress to end-stage renal failure, regardless of treatment

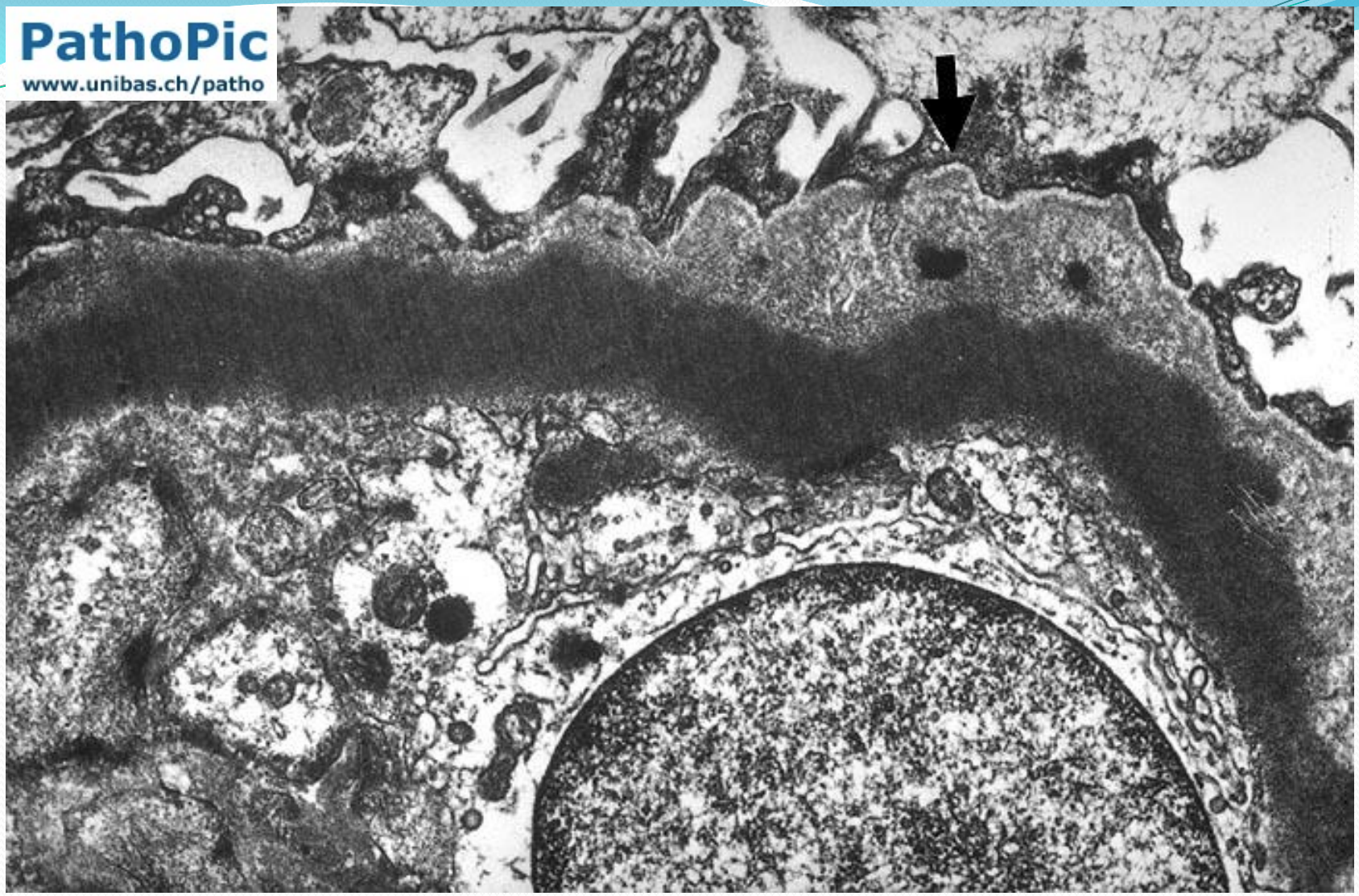
- glomeruli are hypercellular due to mesangial cell proliferation
  - type I: LM cells and matrix of the mesangium insinuate themselves between the endothelial cells and the basement membrane = *mesangial interposition;* silver stain: double contour of the basement membrane; EM: subendothelial and mesangial electron-dense deposits;
  - type II LM simiar; EM ribbon-like zone of increase density within the thickened basement membrane;
- variable infiltration by leucocytes
- glomeruli show prominent lobulation



Membranoproliferative glomerulonephritis: hypercellular glomerulus, double contour of the basement membrane, PAS stain.



Membranoproliferative glomerulonephritis: glomerulus showing prominent lobulation



Type II membrano-proliferative glomerulonephritis, dense-deposit disease. There are markedly dense homogeneous deposits within the basement membrane proper / BM lamina densa.

Lupus nephritis

variety of renal lesions in SLE focused on glomeruli (wide range of involvement) + interstitial involvement + necrotizing arteriolitis

variable clinical manifestations, including the nephritic and nephrotic syndrome

the renal involvement is one of the major prognostic determinants in patients with SLE

!SLE = systemic lupus erythematosus

LM:

- Mild lesions: diffuse mesangial expansion with or without hypercellularity + segmental endothelial cell proliferation
- severe inflammation is manifested by enlarged, hypercellular glomeruli, mesangial cellular proliferation, enhanced lobulation, segmental areas of tuft necrosis & karyorrhexis „hematoxylin bodies”, polys infiltration and crescent formation, marked thickening of the involved capillary wall “wire loop” & hyaline thrombi

EM: immune complexes localized in mesangial, subendothelial, or subepithelial areas

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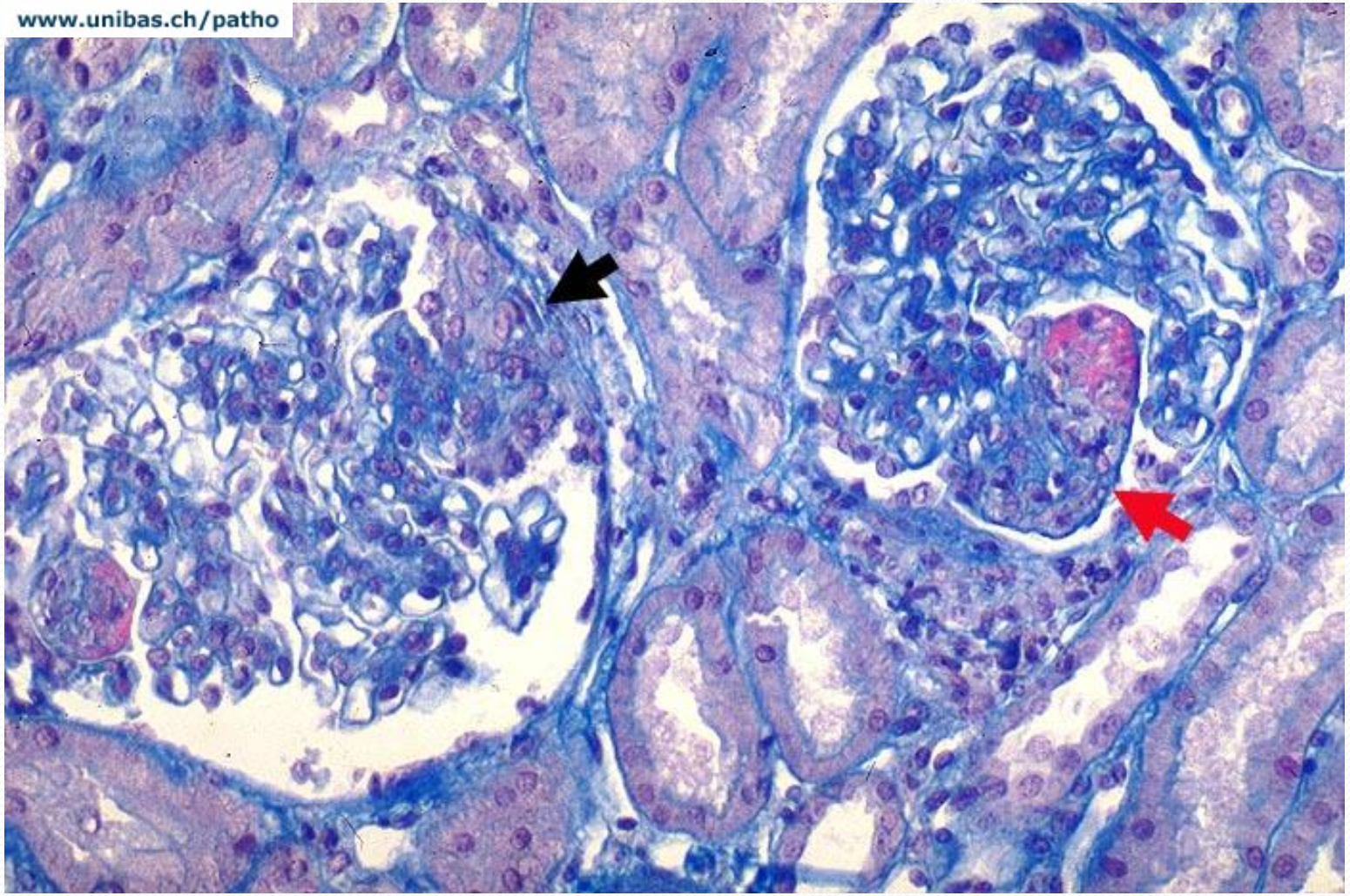
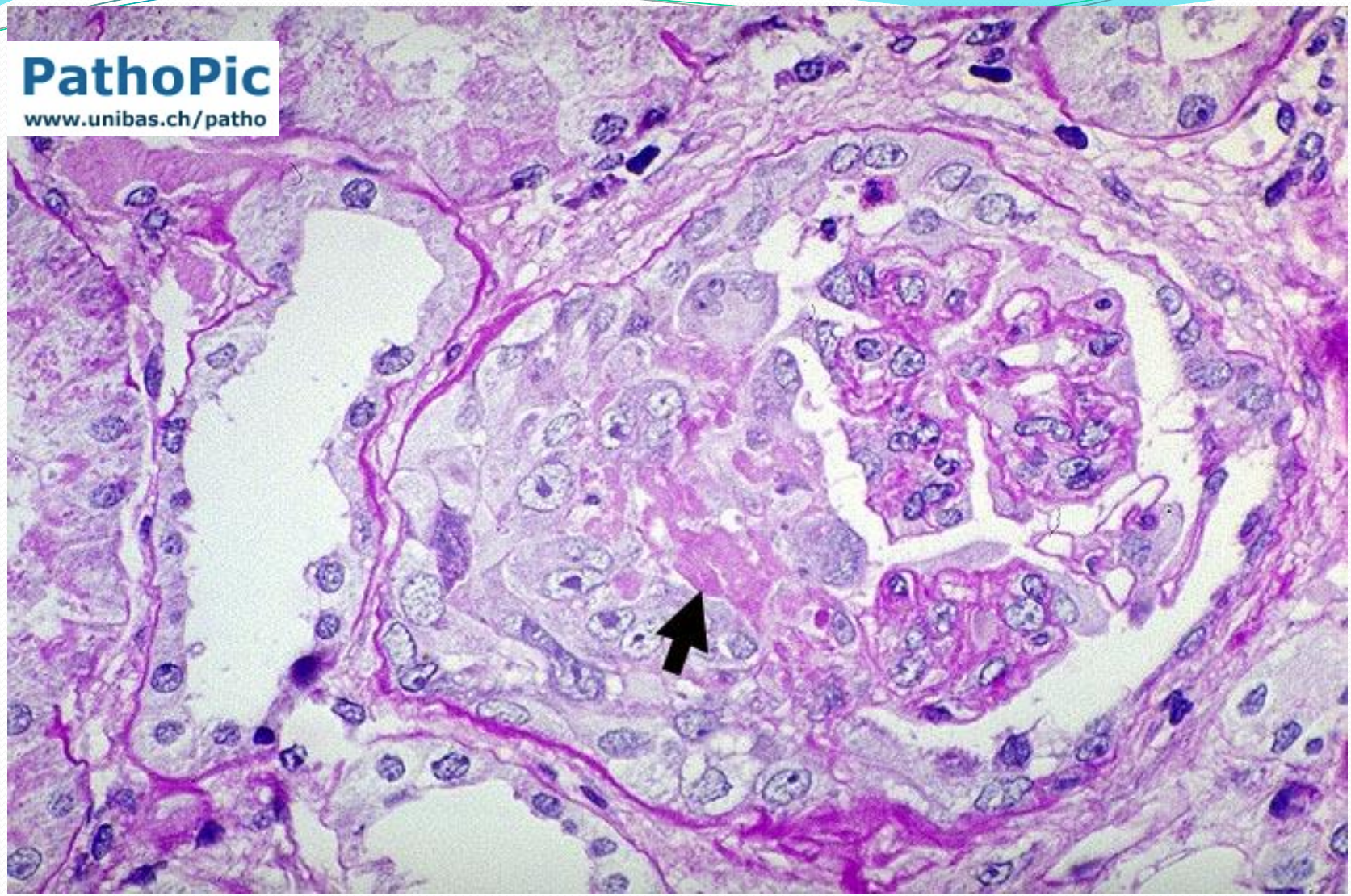
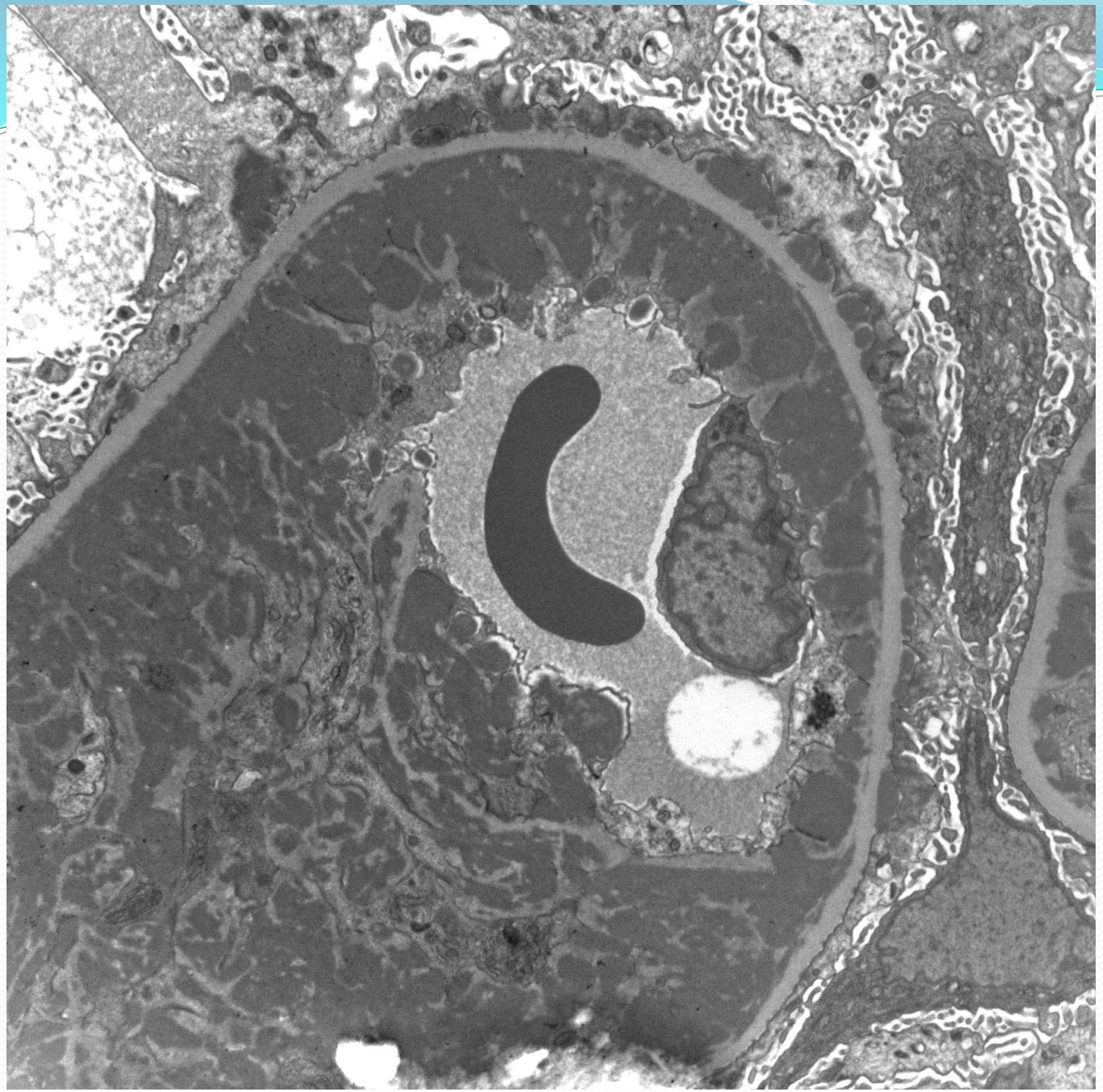


Lupus nephritis. There is focal and segmental glomerulonephritis characterized by segmental necrosis (red arrow), adhesions to Bowman's capsule (black arrow) and leukocytic infiltration.



Lupus nephritis: focal and segmental glomerulonephritis, epithelial crescent, fibrin within filtration space (arrow).



Lupus nephritis: EM Capillary loop showing marked accumulation of deposits in the mesangium subepithelial and subendothelial regions.

Focal glomerulonephritis

segmental portions of *some* glomeruli are involved

only or primarily the kidney (**IgA nephropathy**) **Berger disease**

part of systemic diseases Henoch-Schönlein purpura, SLE (lupus nephritis – WHO class III), systemic vasculitis, bacterial endocarditis

Ig A nephropathy:

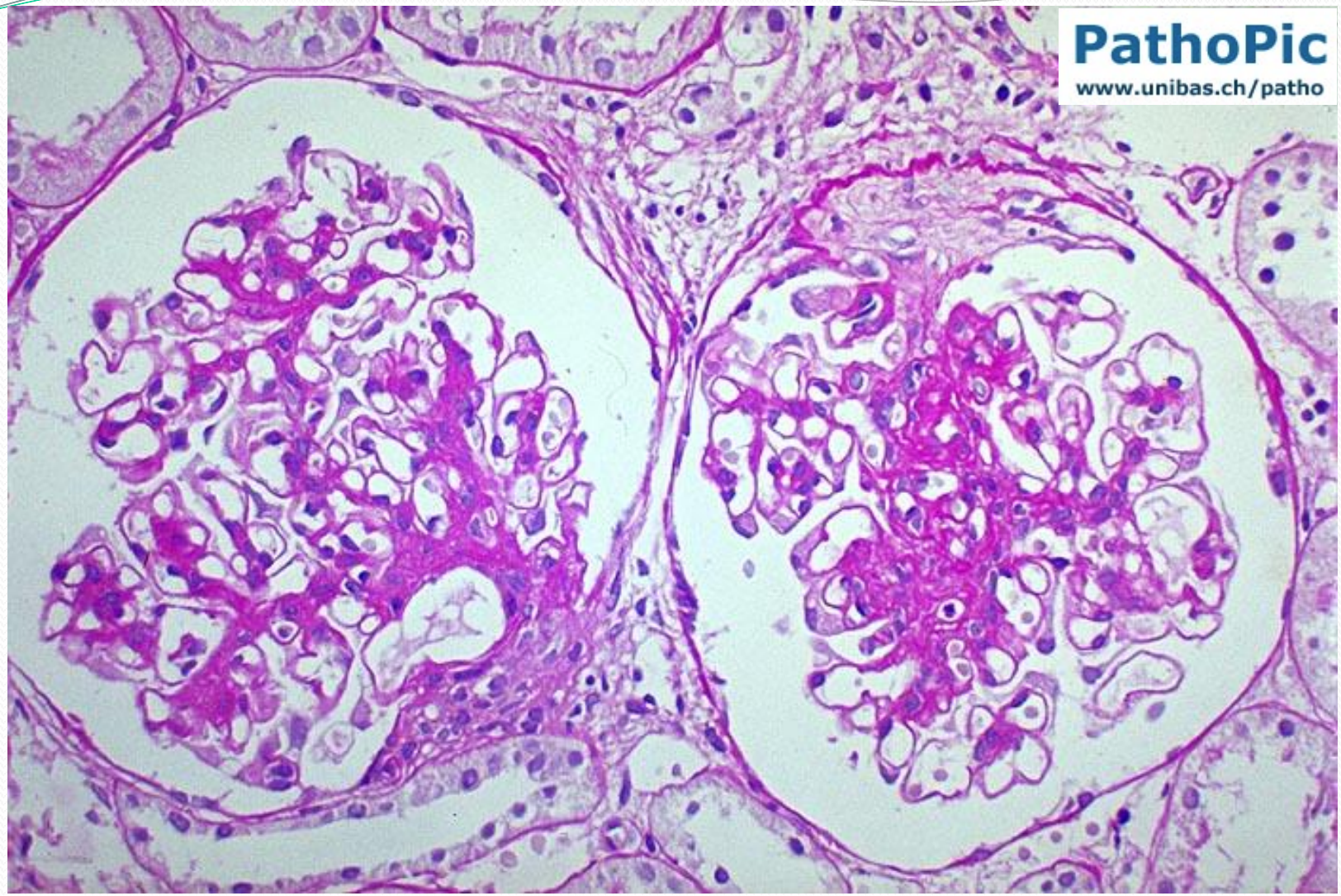
- young men (15 to 30 years)
- hematuria
- up to 20% of patients with IgA nephropathy progress to end-stage renal failure
- does not spontaneously resolve and is not responsive to therapy

LM:

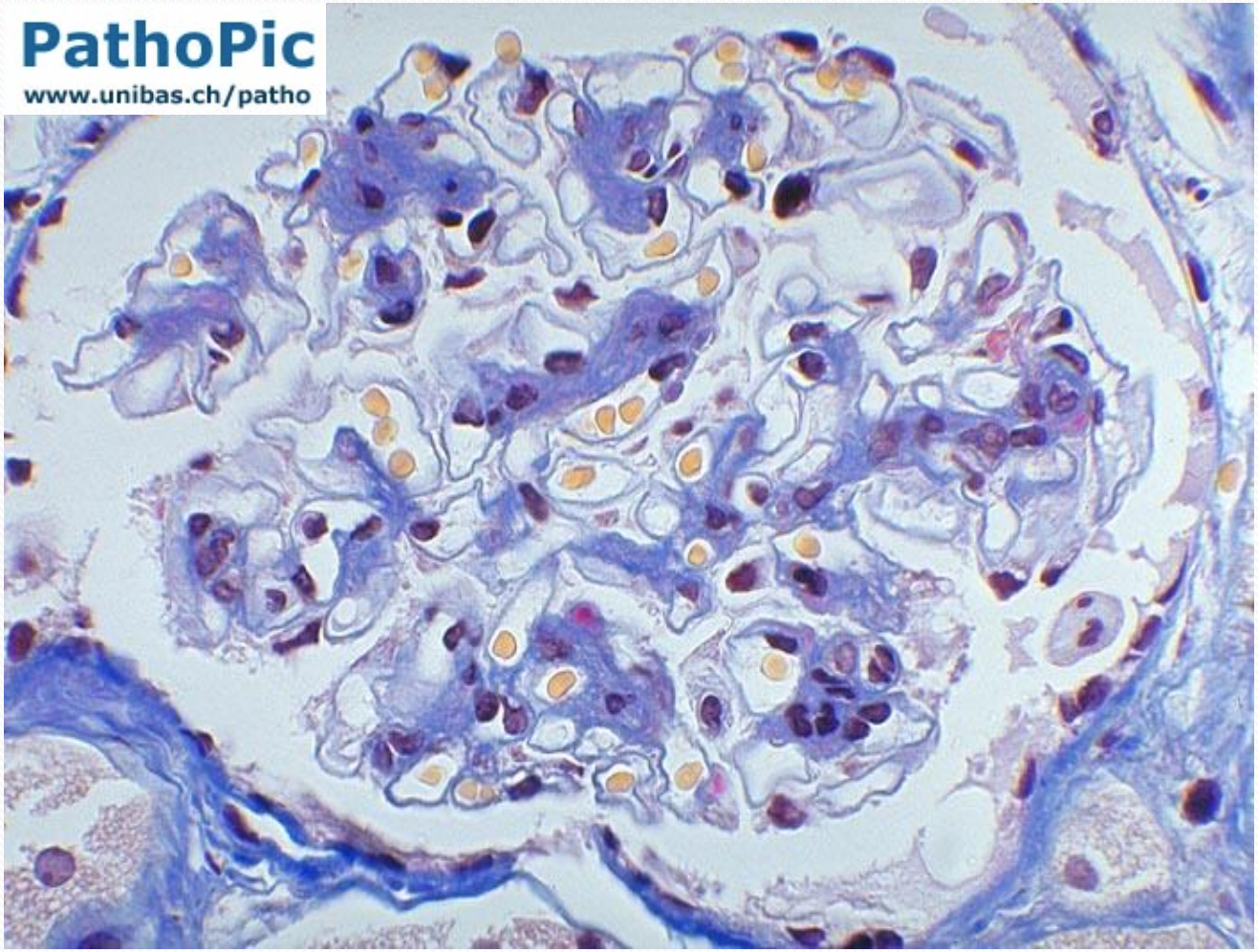
- focal mesangial proliferative lesion + widening of the matrix mild injuried glomeruli
- segmental necrosis of the glomerular tufts, crescents, hyaline material in mesangium = severe injuries / progression to renal failure

EM:

- mesangial cellularity and increased mesangial matrix



IgA nephropathy. Light microscopy showing mesangial proliferation and matrix increase.



IgA nephropathy: mesangial proliferation and matrix increase.

Crescentic (rapidly progressive) glomerulonephritis

majority of glomeruli are surrounded by an accumulation of cells (crescents) in Bowman's space

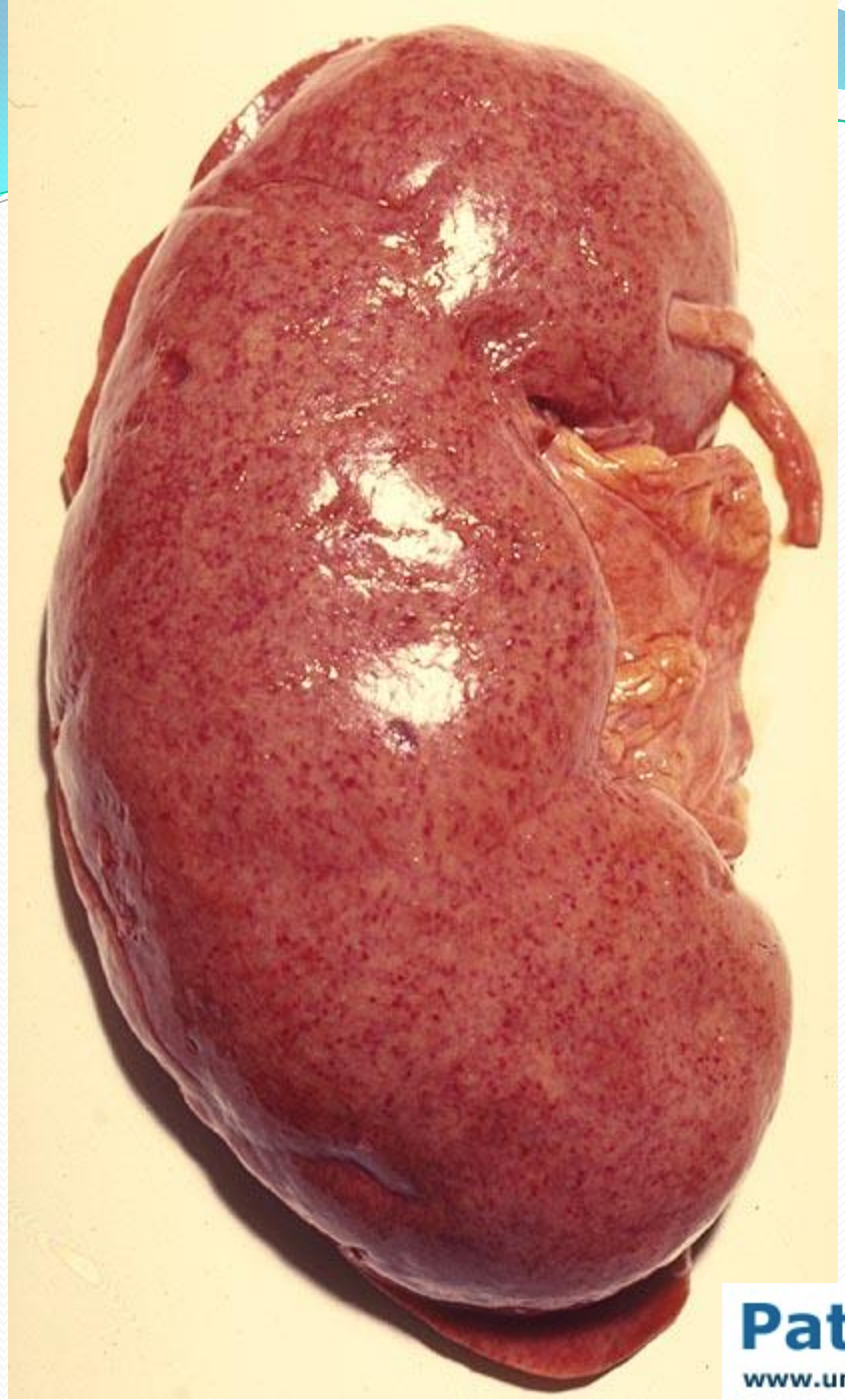
crescents = fulminant glomerular damage

escape of fibrin into Bowman's space seems to be the most important trigger for glomerular crescent formation

rapid and progressive decline in renal function

idiopathic crescentic glomerulonephritis = diagnosis of exclusion, otherwise are specific primary glomerular and systemic diseases that can cause crescentic glomerulonephritis

- crescents range from cells filling a segment of Bowman's space to circumferential masses of cells that completely surround the glomerulus.
- they evolve from a cellular to a fibrocellular form, and eventually scar to create a fibrous crescent
- circumferential crescents result in globally scarred glomeruli



Crescentic (rapidly progressive) glomerulonephritis, gross

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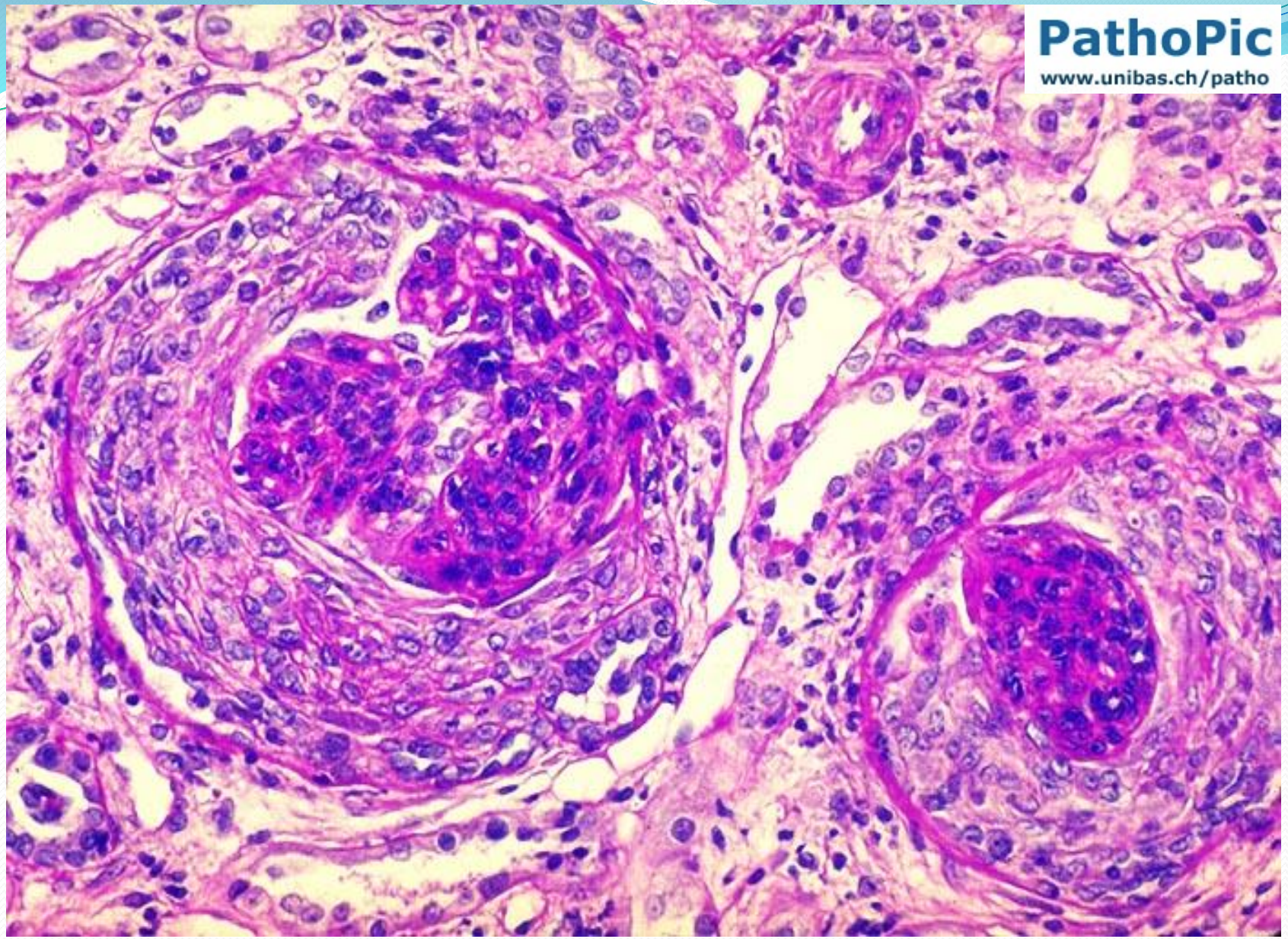
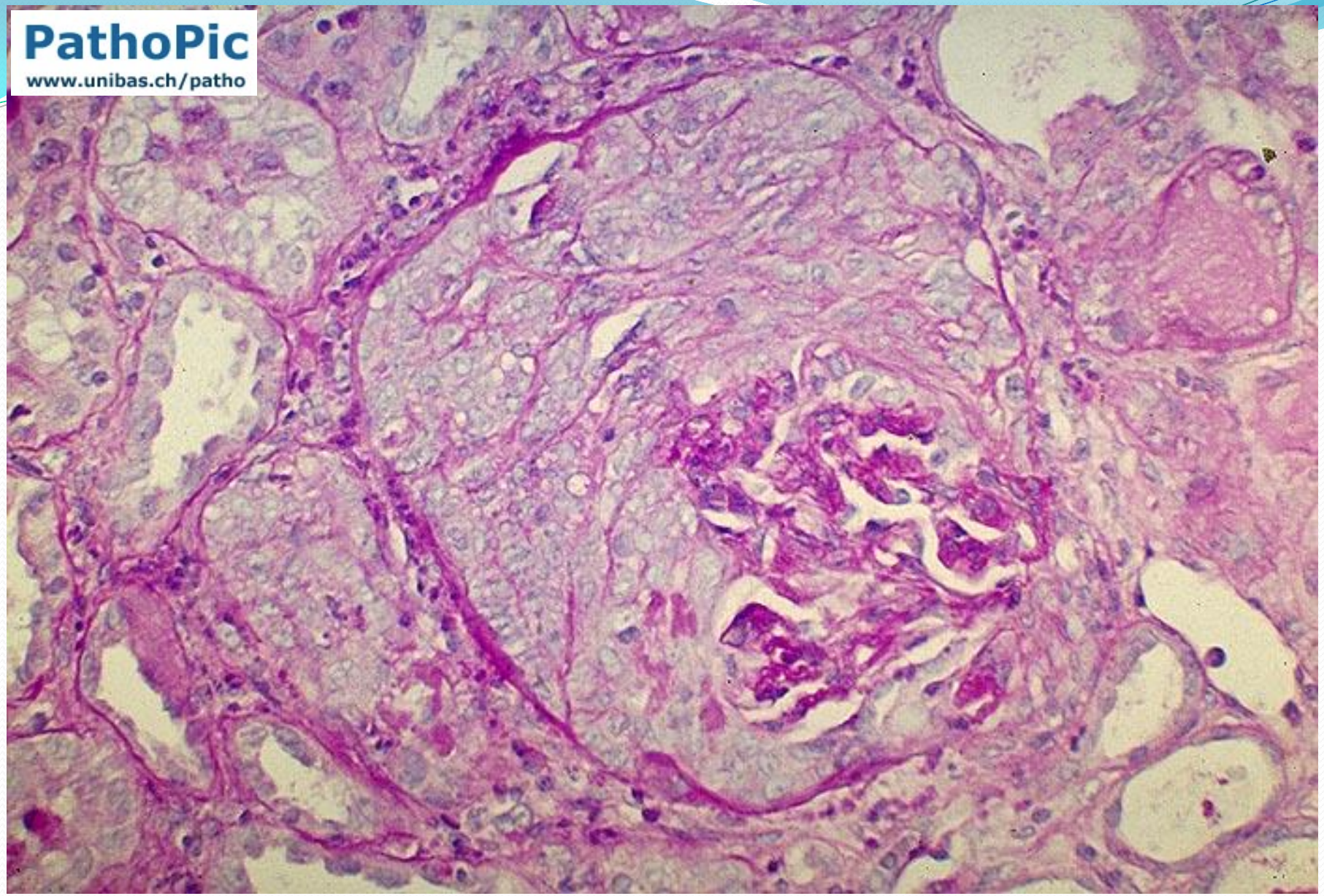


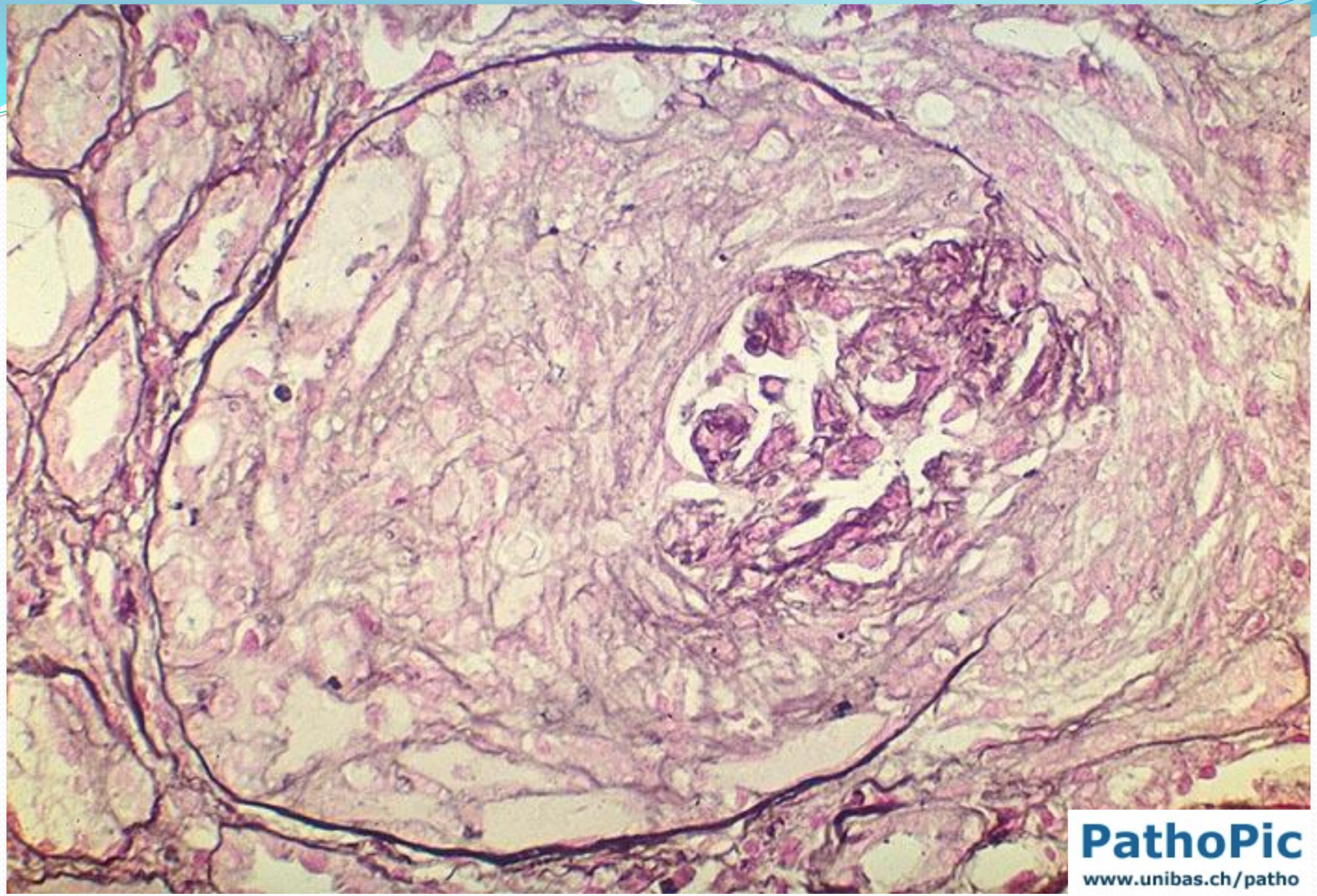
Crescentic (rapidly progressive) glomerulonephritis

Cellular crescents, PAS stain.



Crescentic (rapidly progressive) glomerulonephritis

Fibro-cellular crescent, PAS stain.



Crescentic (rapidly progressive) glomerulonephritis

Fibrous crescent, silver impregnation.

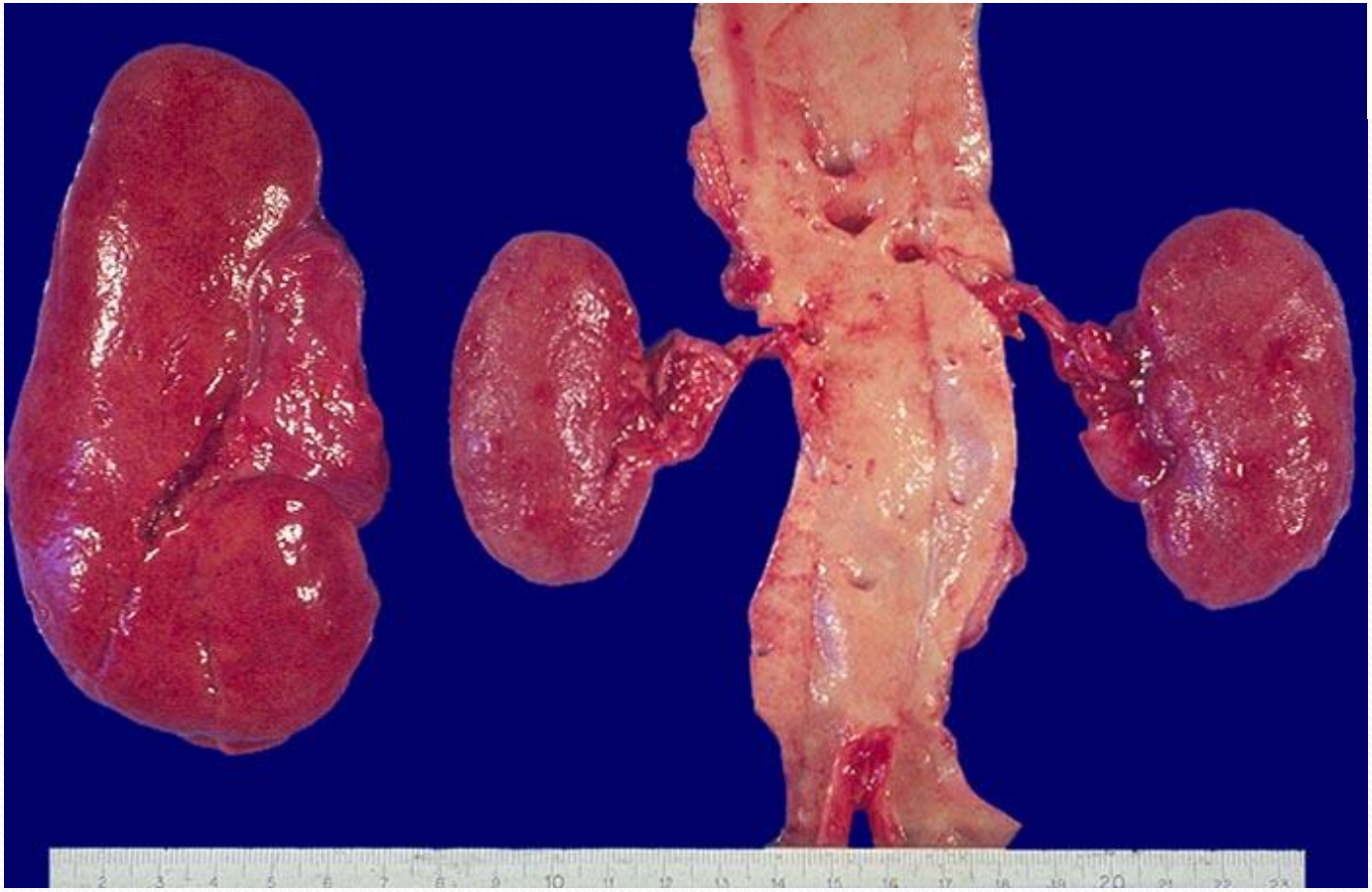
Chronic glomerulonephitis

an *end-stage pool* of primary or secondary *glomerular disease*

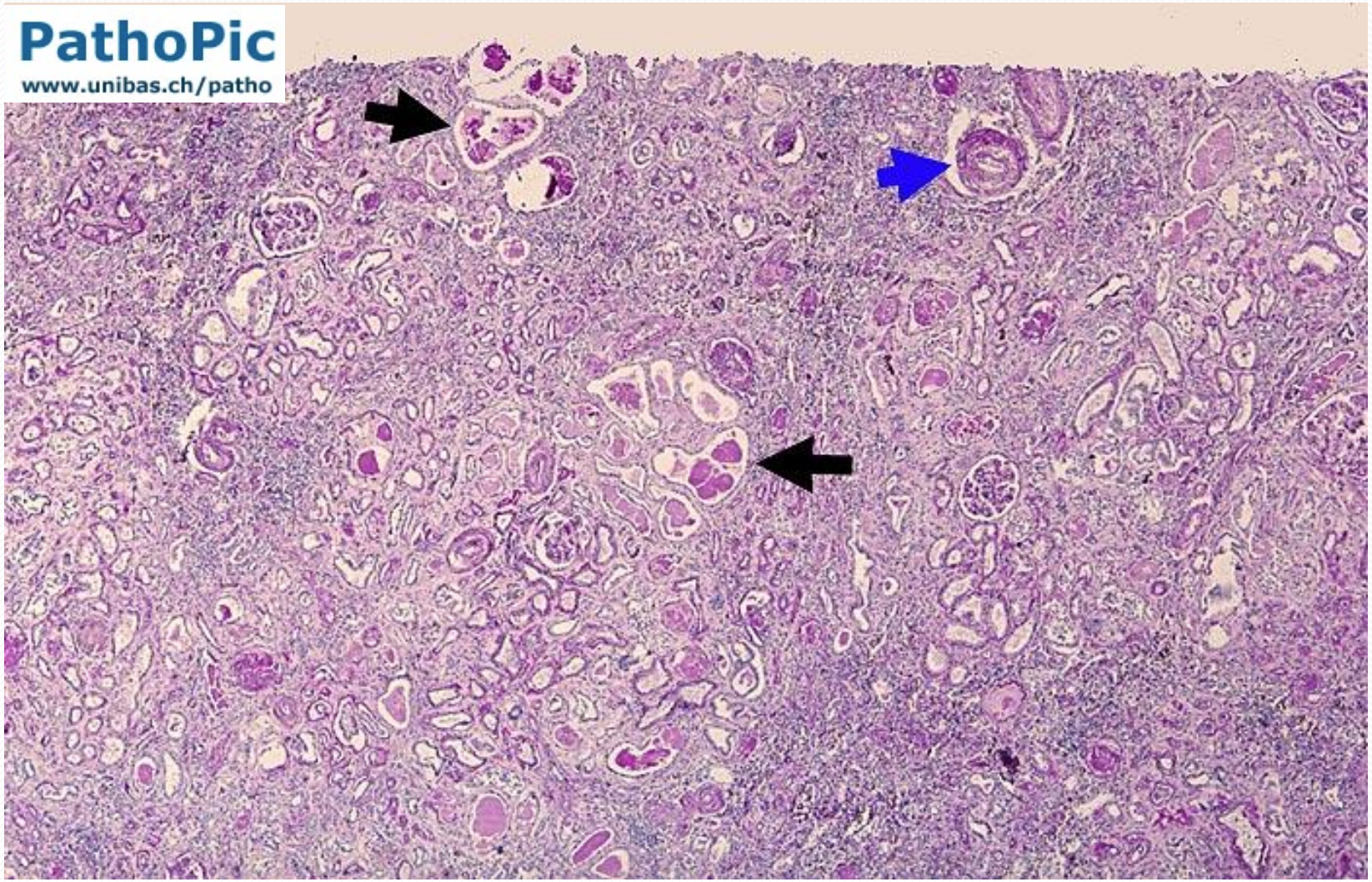
relentlessly progressive

dialysis until renal transplant

- kidneys are symmetrically contracted and have diffusely granular, pale cortical surfaces
- on section, the cortex is thinned, and there is an increase in pelvic fat
- hyaline obliteration of glomeruli, transforming them into acellular eosinophilic, PAS-positive masses
- atrophy of associated tubules (to the sclerotic glomeruli)
- arterial and arteriolar sclerosis
- interstitial fibrosis and lymphocytic infiltration



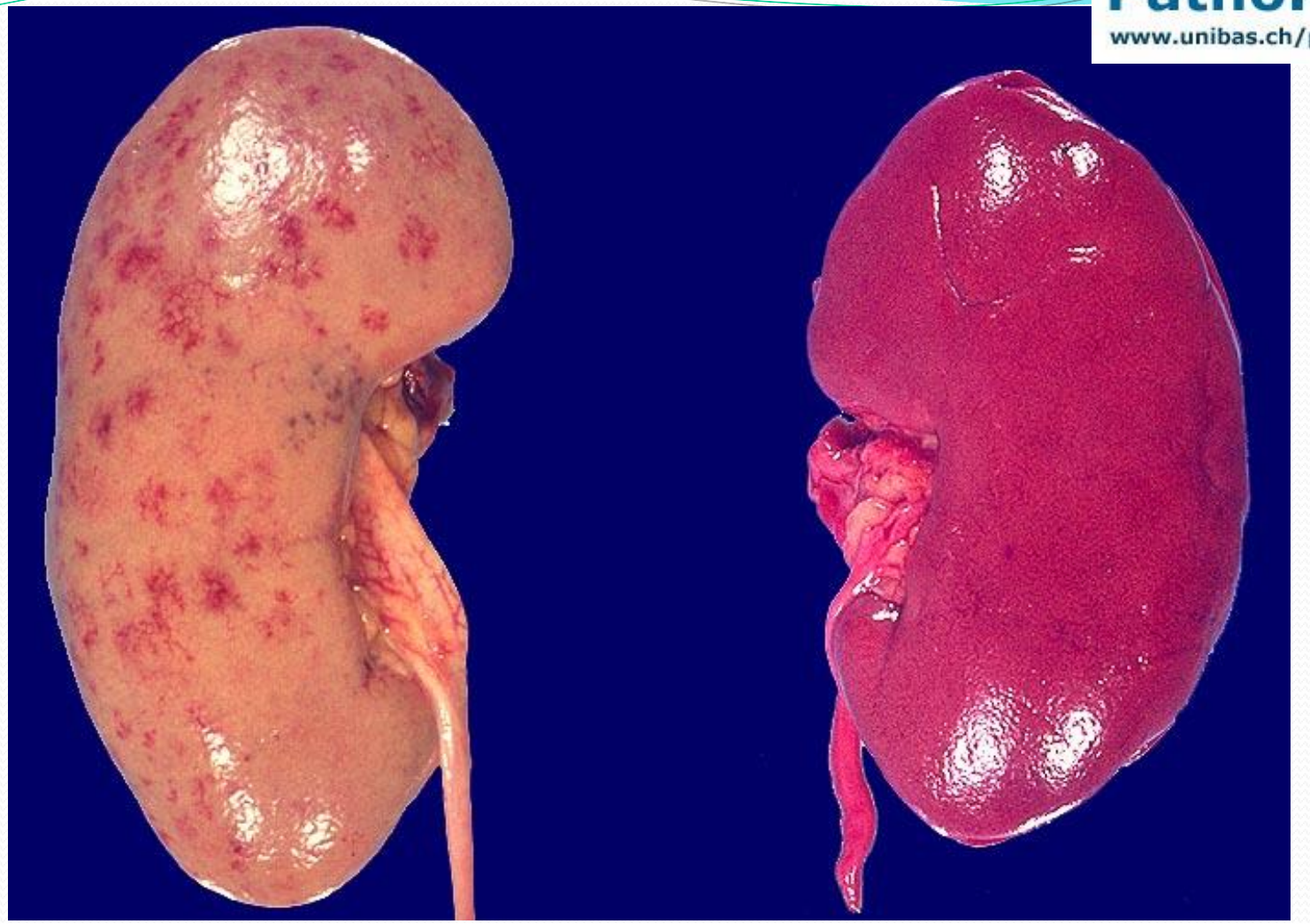
Chronic glomerulonephritis: Seen here are atrophic kidneys, pale and fine granular surface. A normal-sized kidney (left side) to compare.



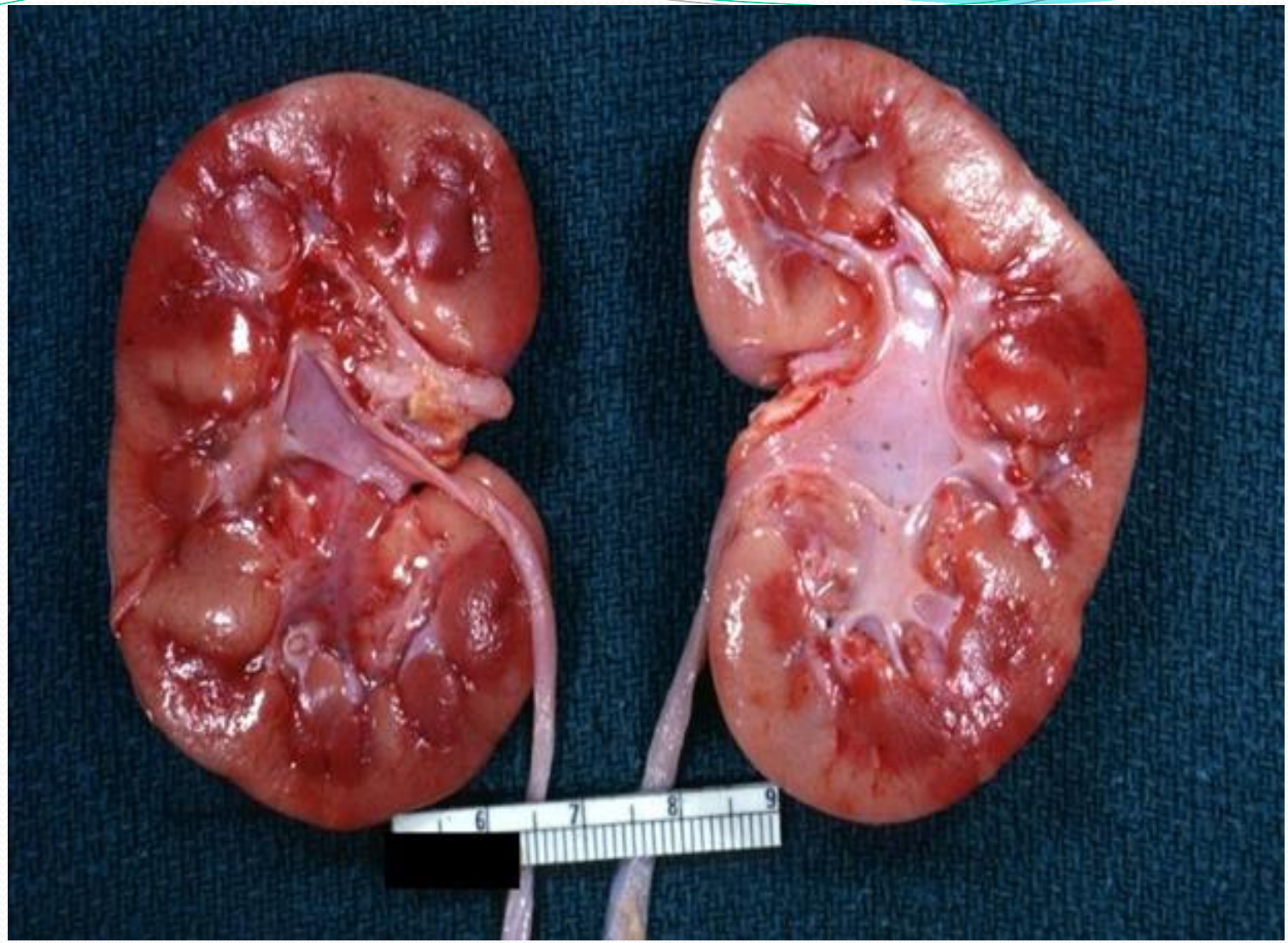
Chronic glomerulonephritis There is marked interstitial inflammation and fibrosis; tubular atrophy; glomerular sclerosis

ACUTE TUBULAR NECROSIS acute injury of the renal tubules that results in acute renal failure

- **Ischemic ATN**
  - **Causes:** shock, dehydration, hepatorenal syndrome, sepsis, complications of renal transplantation, intravascular hemolysis, myoglobinuria secondary to crush injuries
  - **Gross:** swollen, pale cortex and congested medulla
  - **LM:** proximal tubules are dilated, with flattening of the epithelium, patchy "necrosis", distal tubules are dilated and contain hyaline casts
  - recovery phase
- **Toxic ATN**
  - heavy metals, antibiotics, organic solvents
  - varying degrees of epithelial cell damage extremes: complete necrosis of all proximal tubular cells (Hg) no morphologic changes in tubular epithelium (Li)



Ischemic acute tubular necrosis, (left side), compare with kidney normal gross aspect (right)



http://www.wikidoc.org/images/d/da/Burn16.jpg

Ischemic acute tubular necrosis, gross

PathoPic
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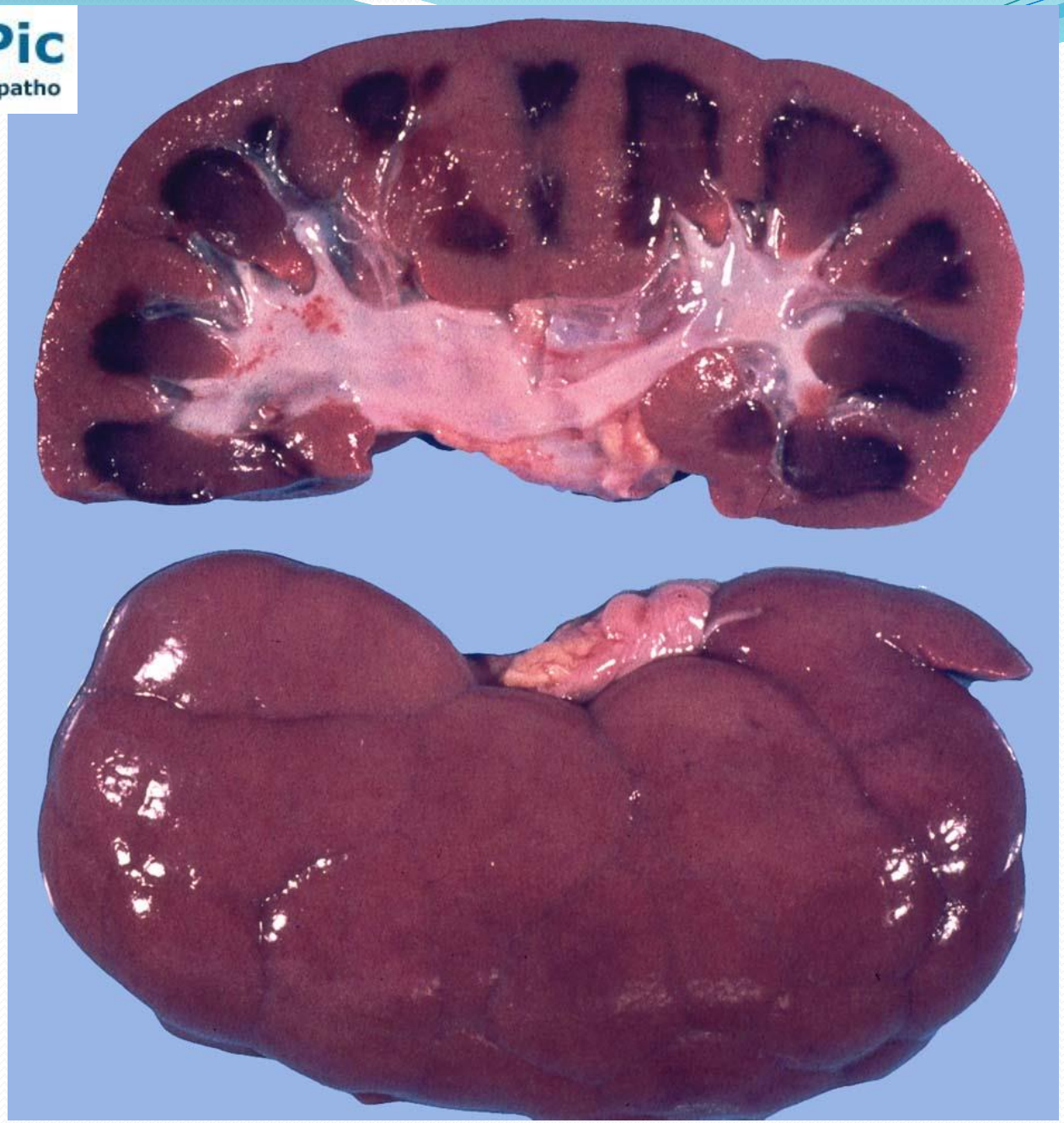
Ischemic acute tubular necrosis, gross cut surface: haemorrhagic streaking in the medulla and renal papillae.



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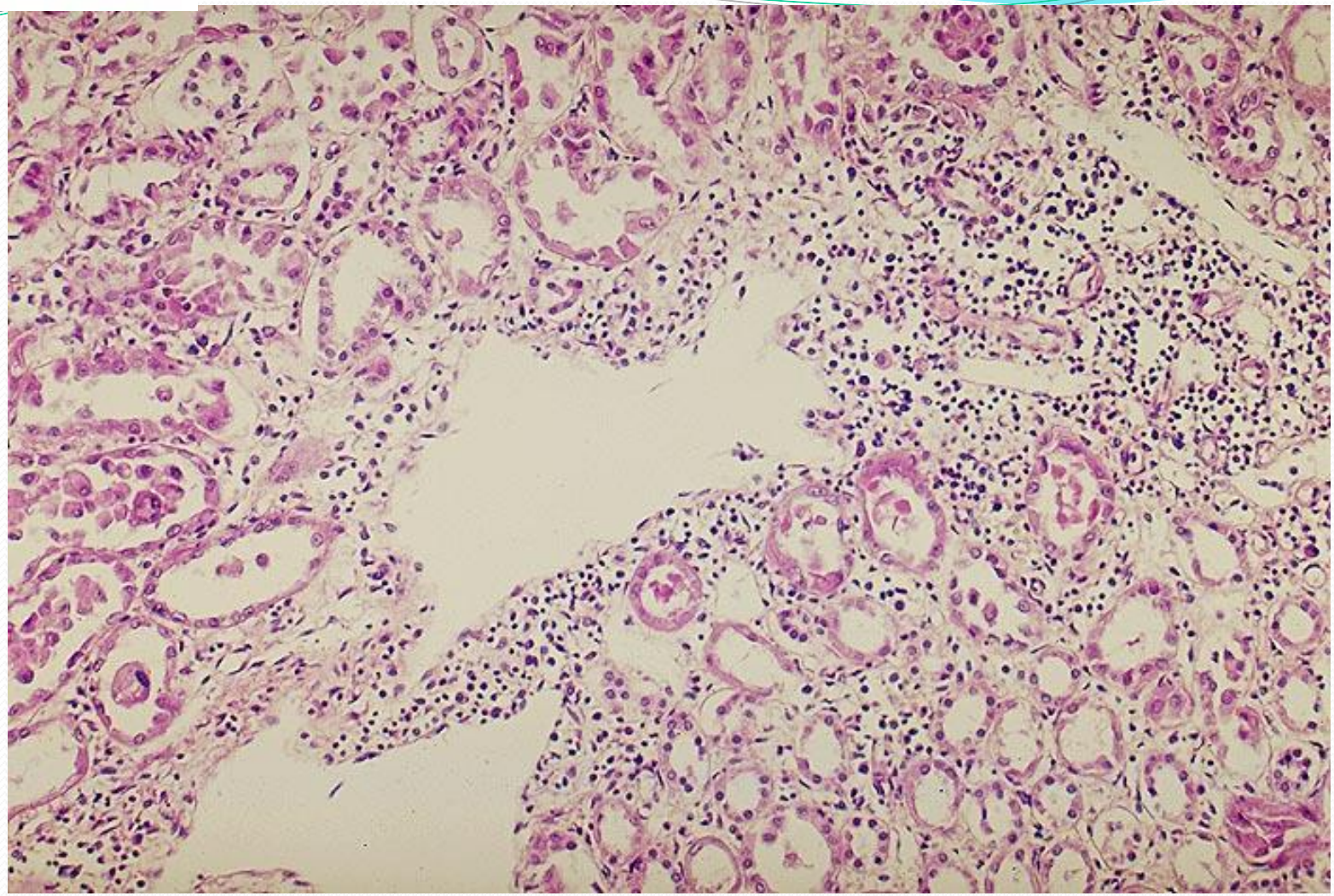

Ischemic acute tubular necrosis. There is focal necrosis and desquamation of the cells into the tubular lumen.

PathoPic
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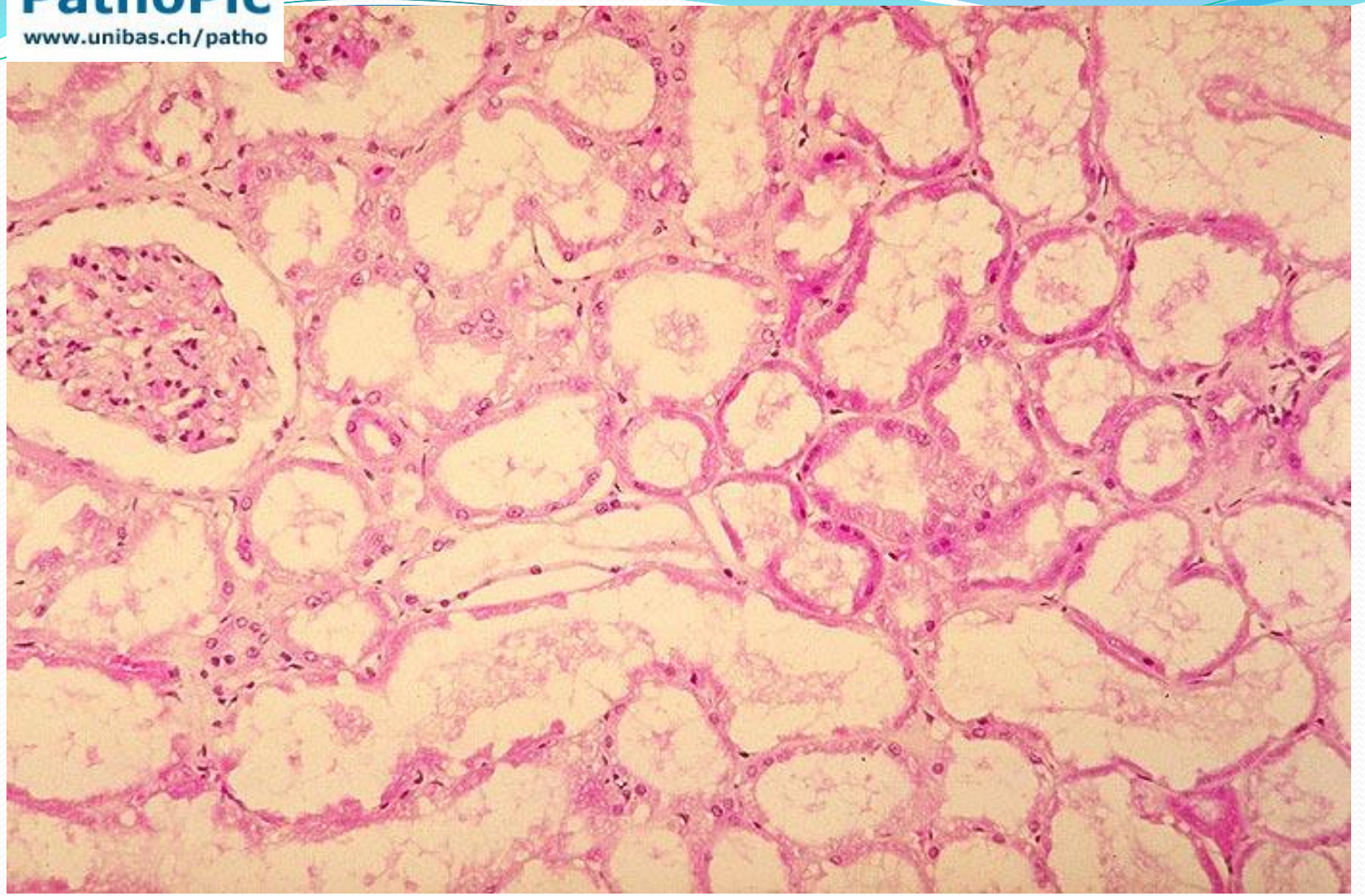

Ischemic acute tubular necrosis. The tubules are dilated and lined by flattened epithelium.

PathoPic
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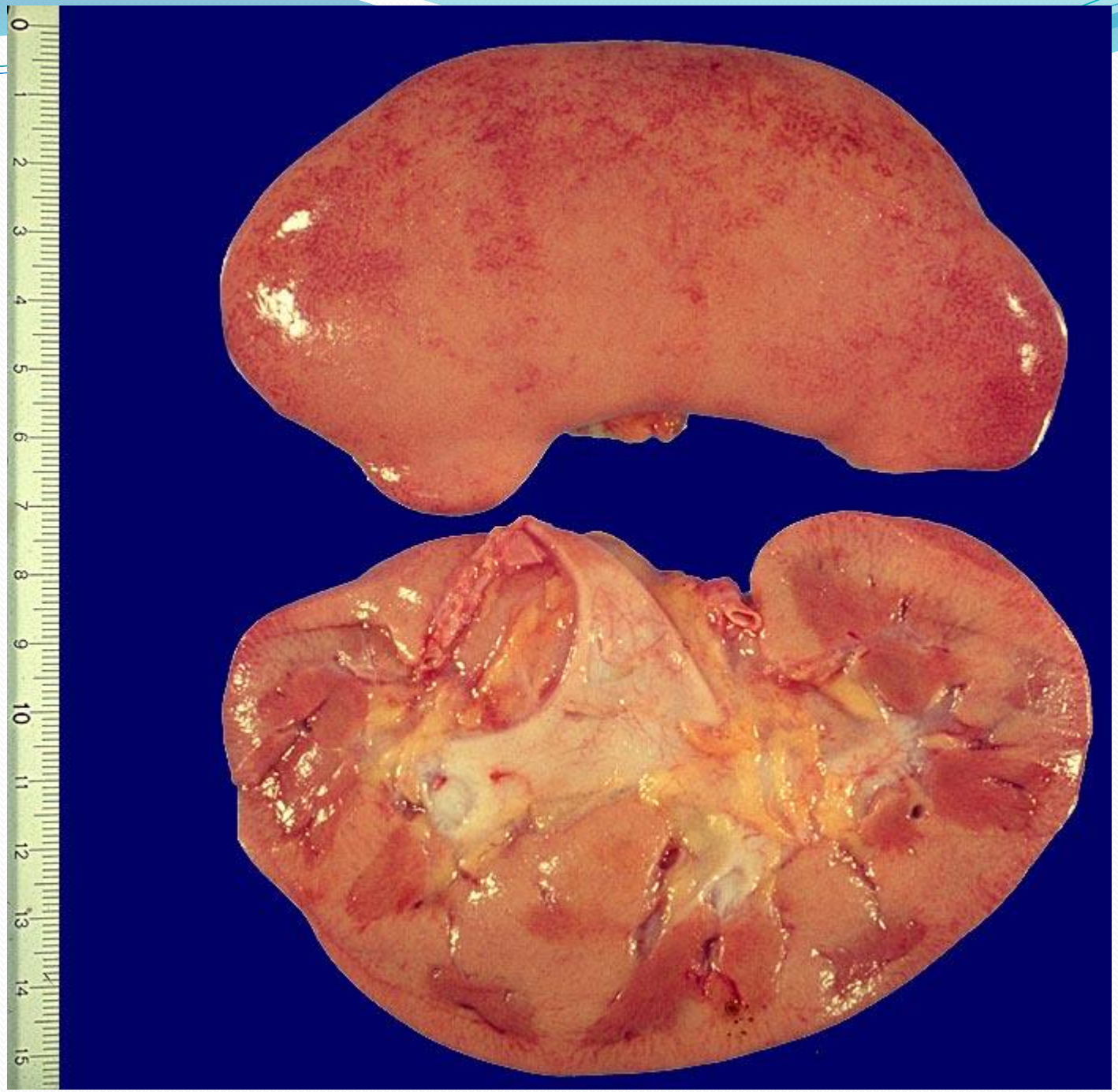
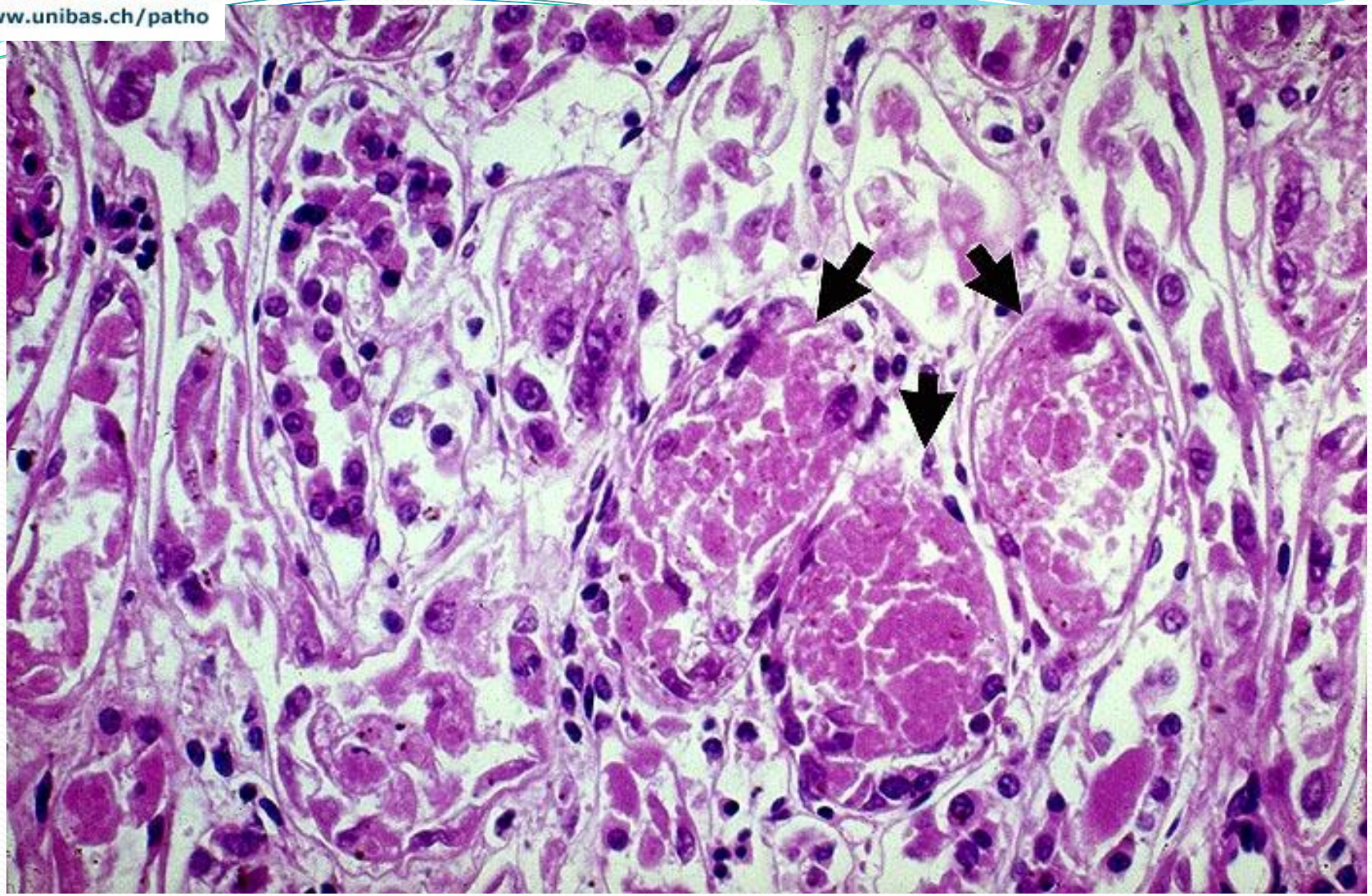
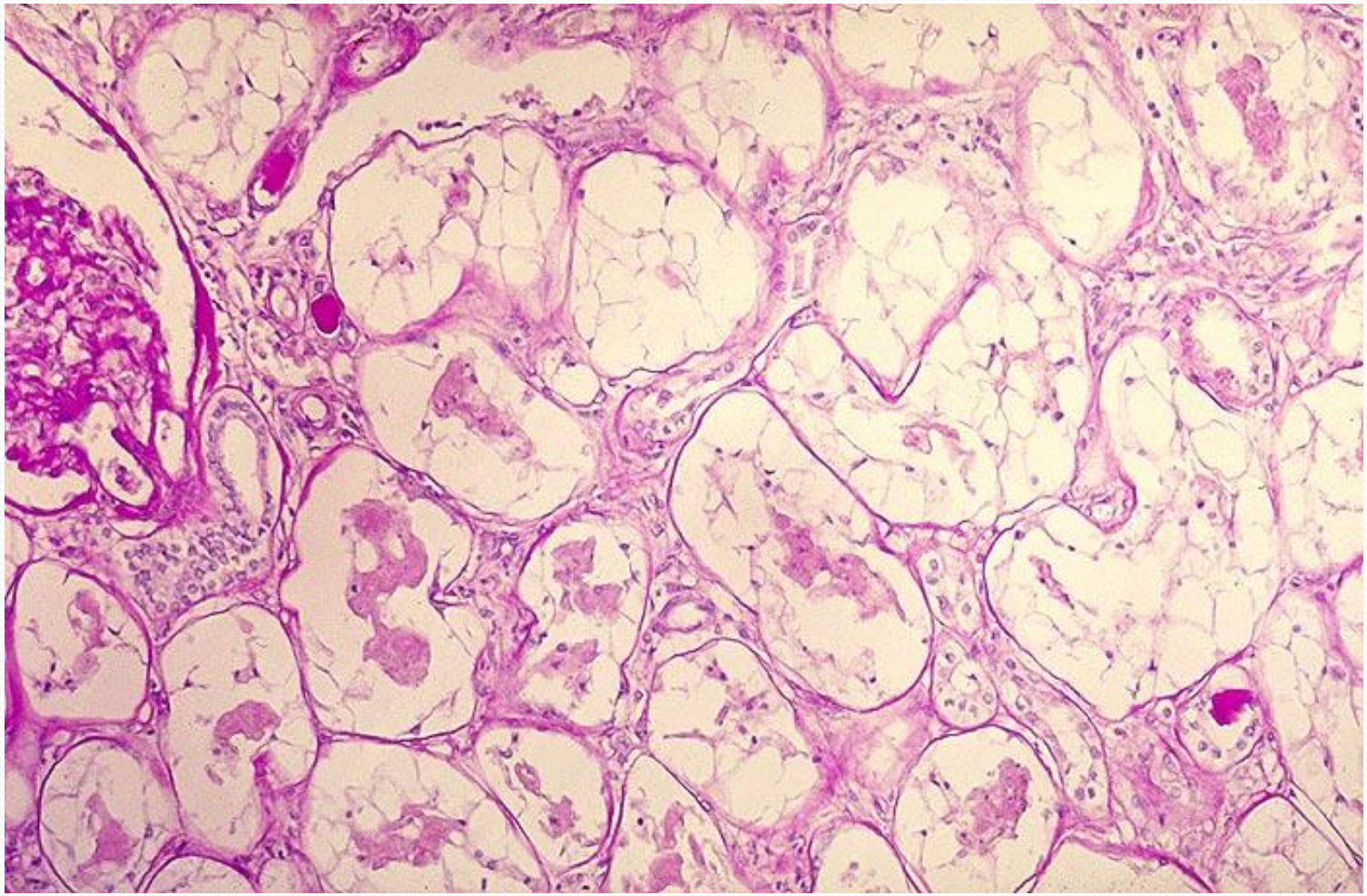


Toxic acute tubular necrosis, gross



Toxic acute tubular necrosis: early phase, patchy epithelial cell damage.



Toxic acute tubular necrosis: The tubular epithelium vacuolization and tubular dilation is a result of the **nephrotoxic** effect, PAS stain.

VASCULAR DISEASES

Benign nephrosclerosis is a consequence of renal ischemia

- Gross: kidneys are smaller than normal and affected bilaterally, the cortical surface exhibits fine granularity, on cut section, the cortex is thinned
- LM: larger arteries - replication of the internal elastic lamina and partial replacement of the muscular coat with fibrous tissue, arterioles - hyaline arteriolosclerosis …

Malignant nephrosclerosis = renal changes associated with *malignant hypertension* (DP ≥ 125 mmHg)

- Gross: the kidneys are small to enlarged, cortex displays petechiae "flea-bitten" kidney; the cut surface is mottled red and yellow
- LM: larger arteries narrowed lumen by profuse medial thickening - cellular proliferation “onion-skining” and the accumulation of a collagen matrix (hyperplastic arteriolosclerosis); arterioles exhibit fibrinoid necrosis

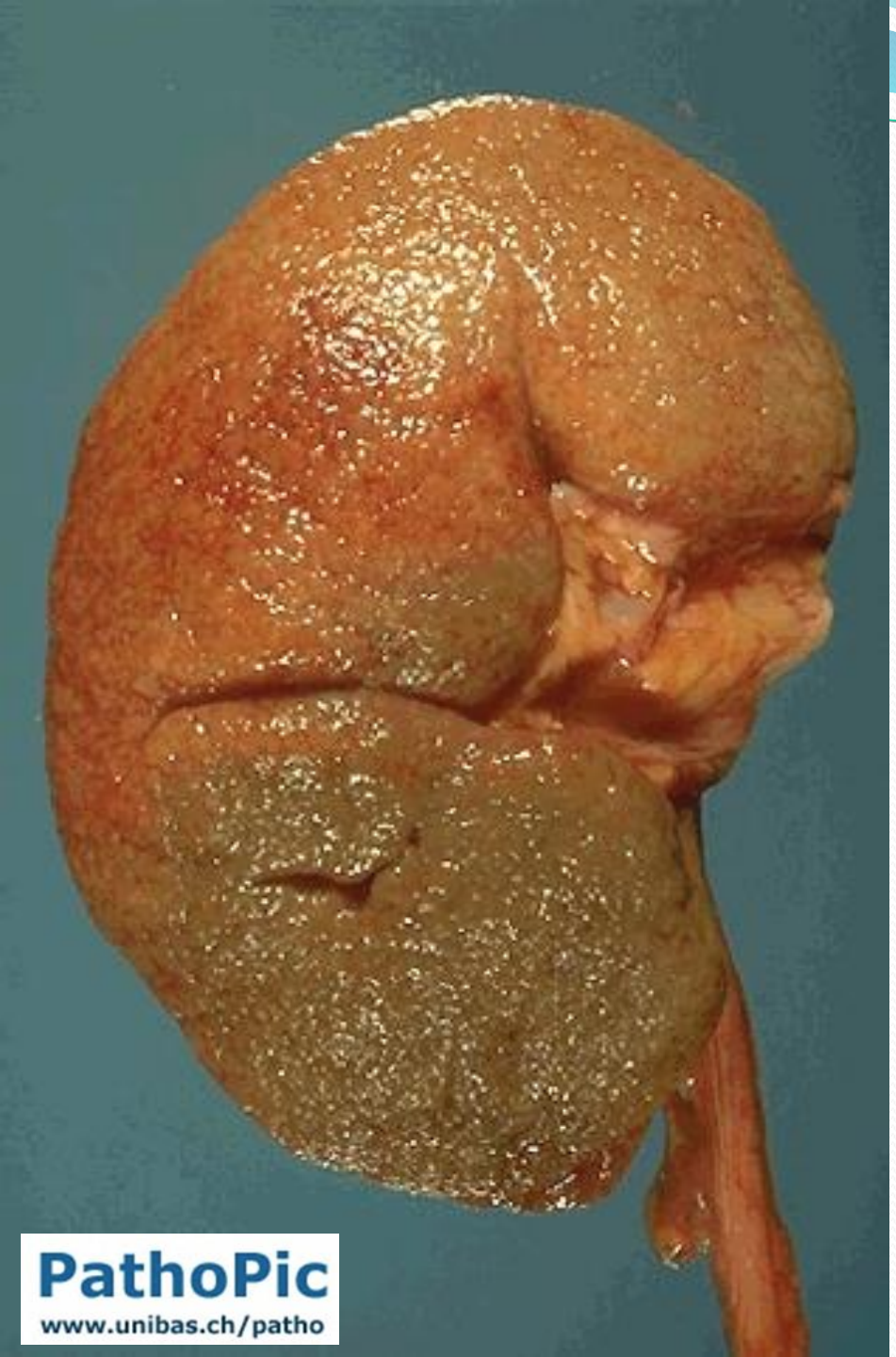
VASCULAR DISEASES

Benign nephrosclerosis

- glomerular capillaries are thickened, collagen and matrix material are deposited within Bowman's until glomerular obliteration by a dense, eosinophilic globular mass (scar)
- tubular atrophy
- fibrosis of the interstitium
- "benign" hypertension has such a high prevalence, even the small proportion of these patients who develop renal insufficiency amounts 1/3 of all patients with end-stage renal disease

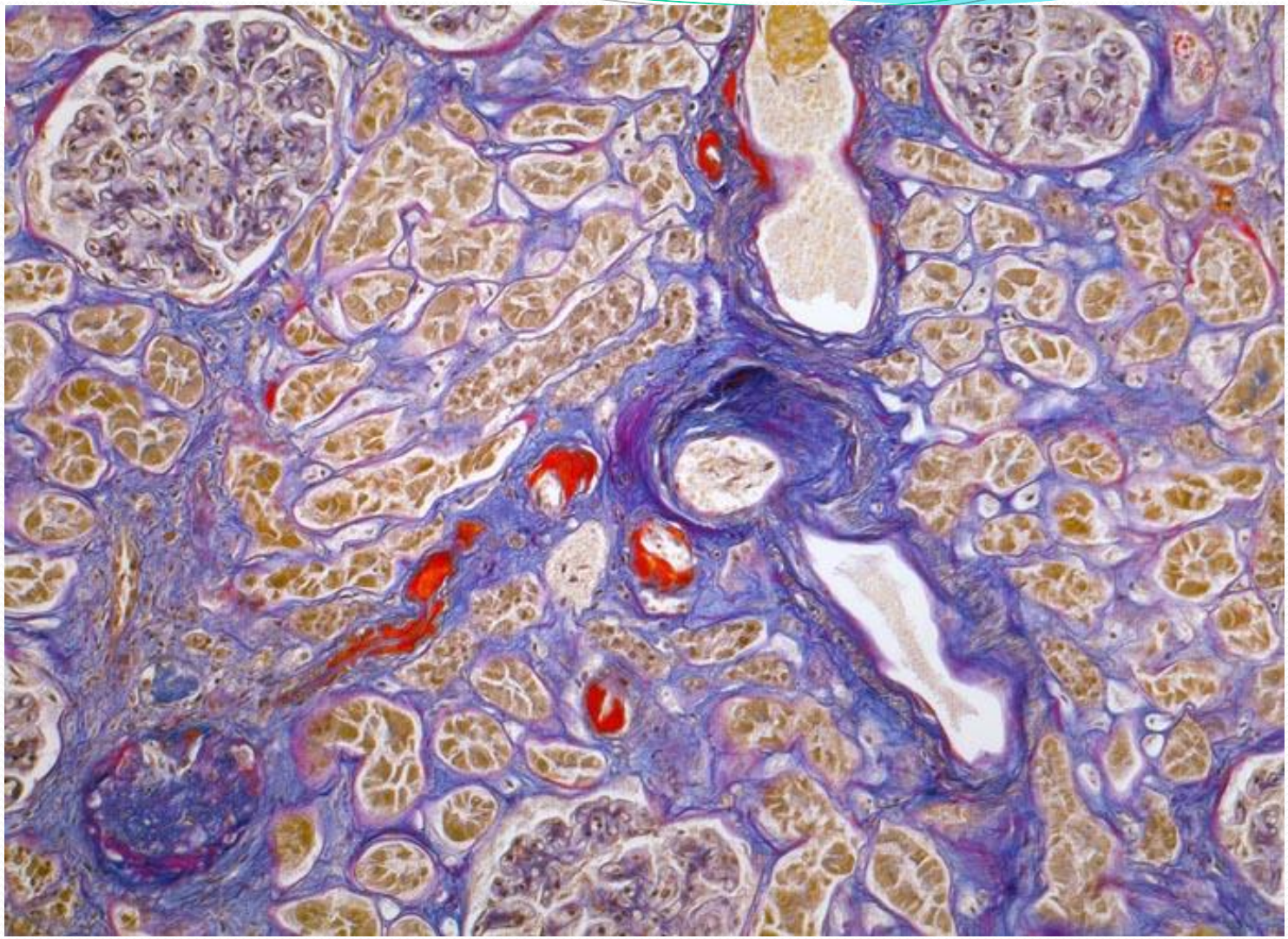
Malignant nephrosclerosis

- glomeruli frequently show fibrinoid necrosis, sometimes in continuity with the same process in the afferent arterioles
- subtotal infarction of glomeruli, with dilated capillaries stuffed with erythrocytes
- progressive deterioration of renal function eventually leads to uremia

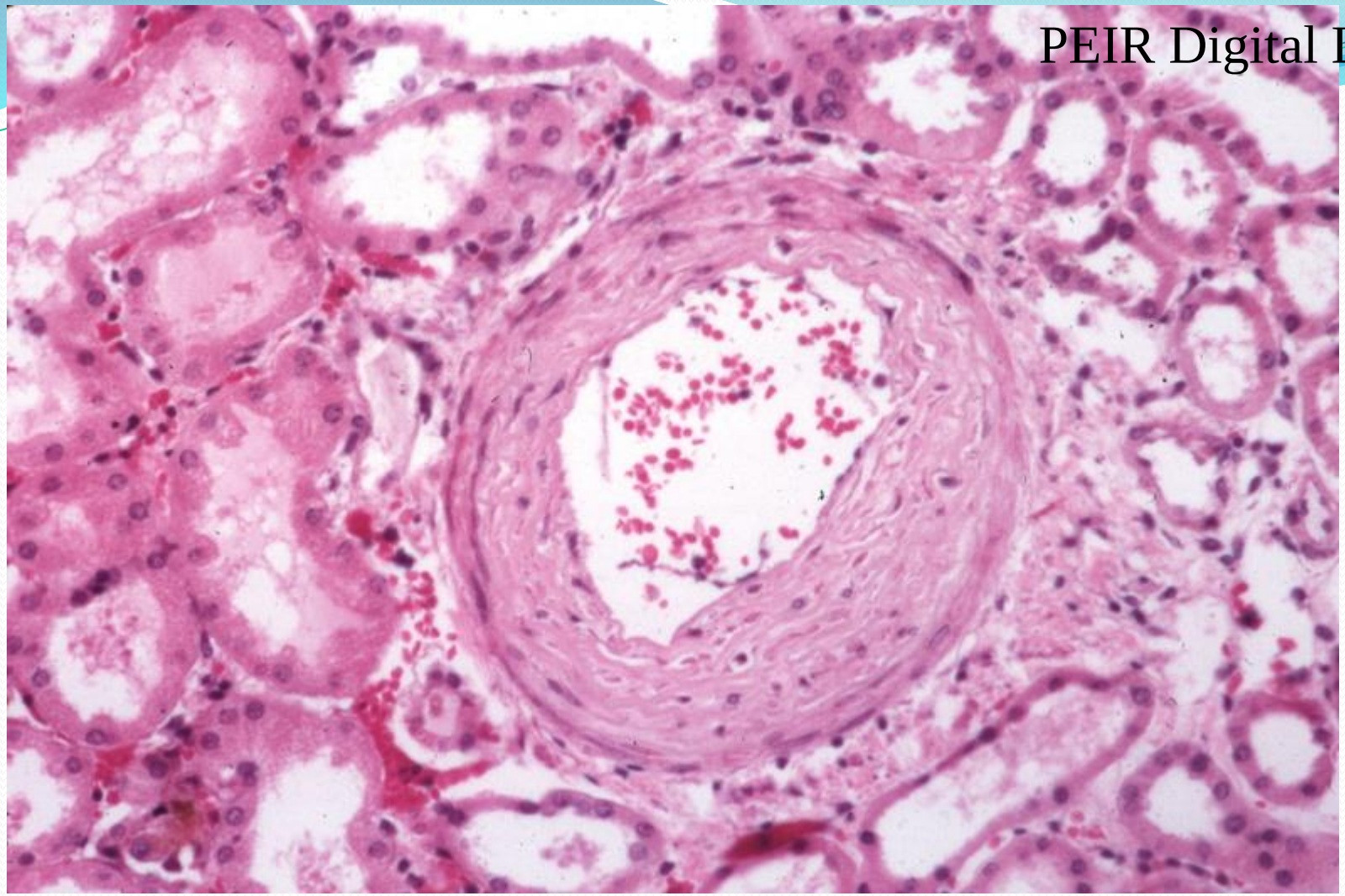


Benign nephrosclerosis. Patchy ischemic atrophy with focal loss of parenchyma that gives the surface of the kidney the characteristic granular appearance as seen here.

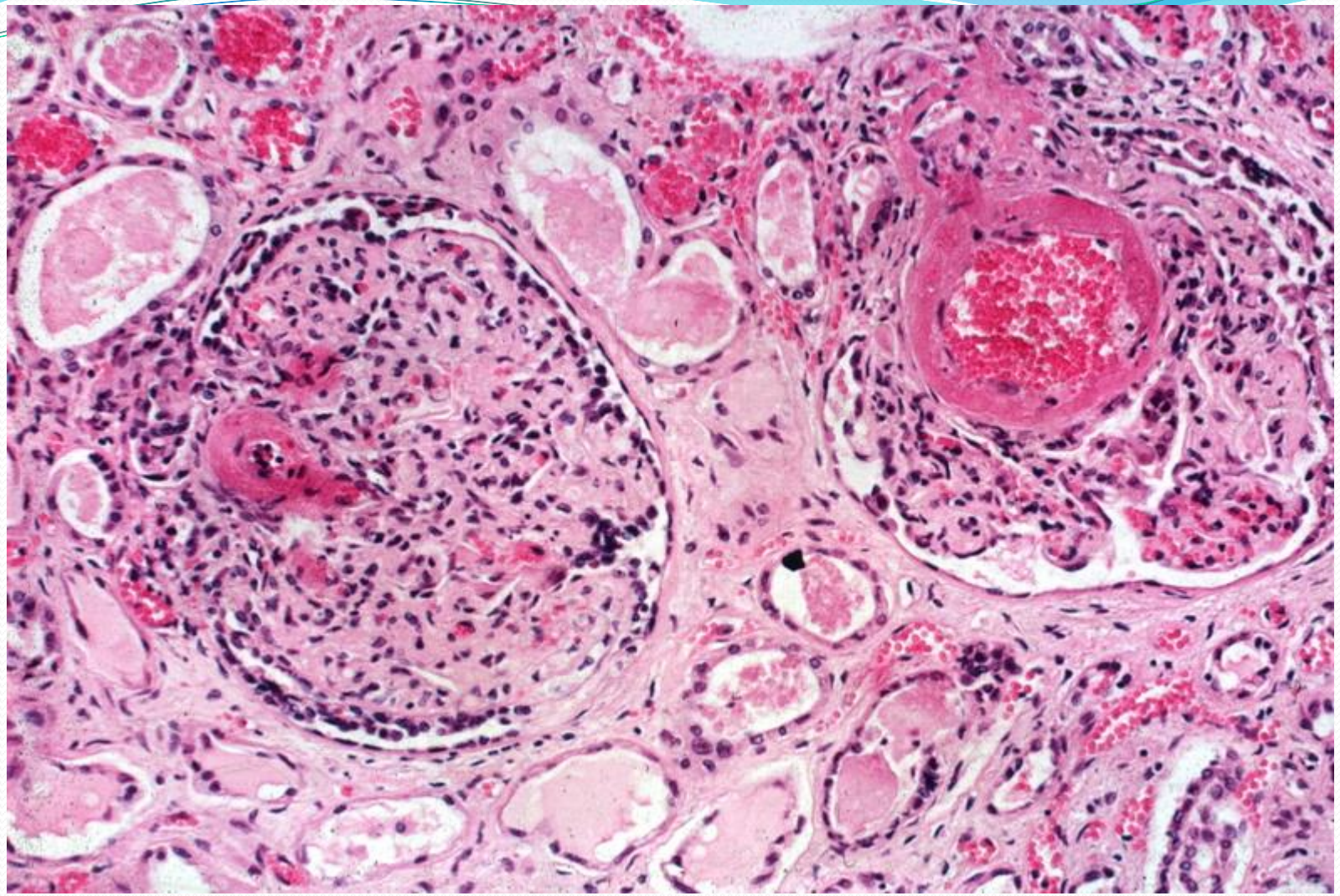
PathoPic
www.unibas.ch/patho



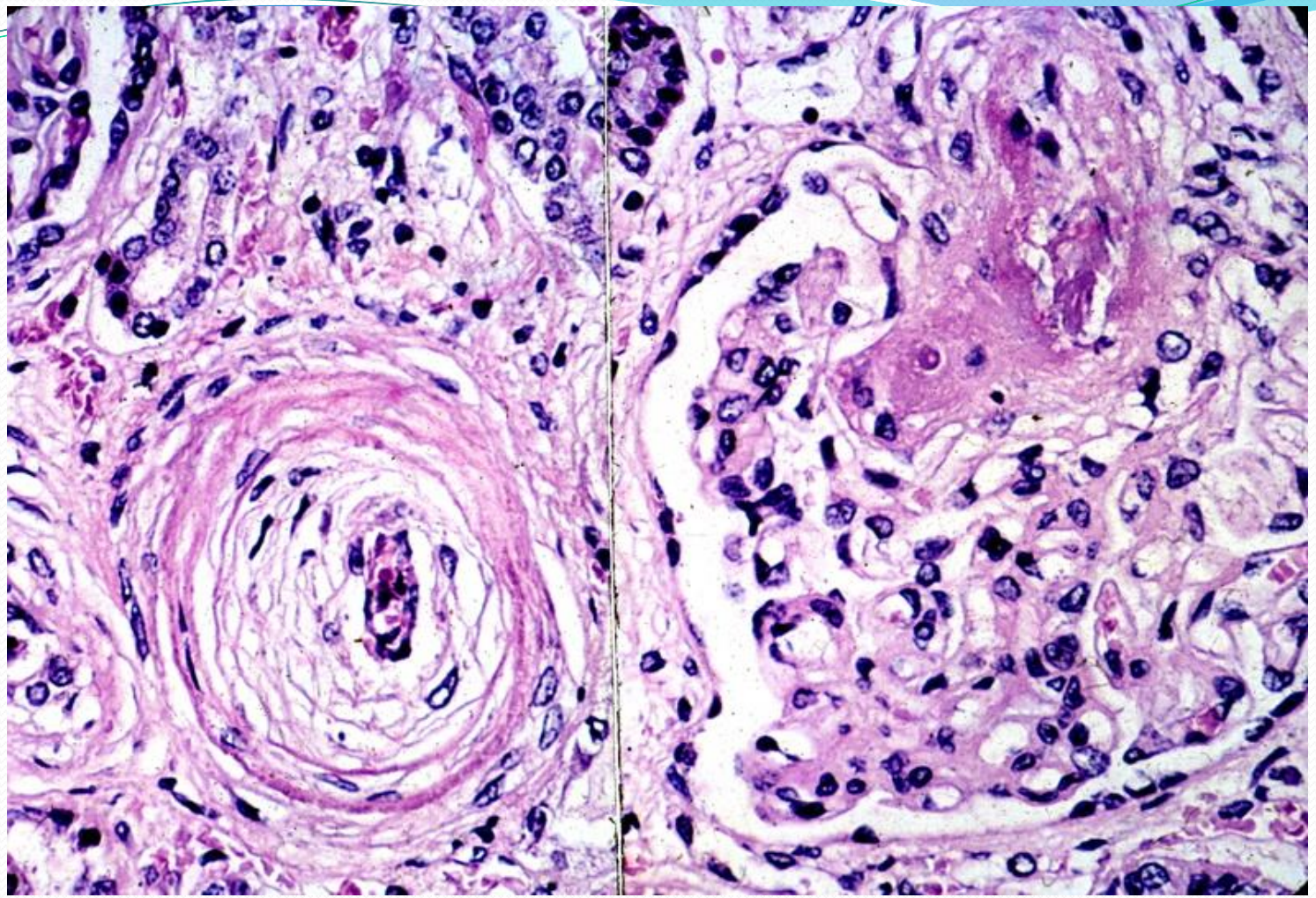
Benign nephrosclerosis: Narrowing of small arteries and arterioles caused by wall thickening



Benign nephrosclerosis: larger arteries - partial replacement of the muscular coat with fibrous tissue



Malignant hypertension leads to fibrinoid necrosis of small renal arteries (afferent and efferent arterioles) with extension to capillary tuft of the glomeruli.



Malignant nephroangiosclerosis. Fibrinoid necrosis of an afferent arteriole with mono- and polymorphonuclear inflammatory cells = necrotizing arteriolitis (right side) and an arterial narrowed lumen by profuse medial thickening - cellular proliferation “onion-skinning” and the accumulation of a collagen matrix = hyperplastic arteriolosclerosis (left side)