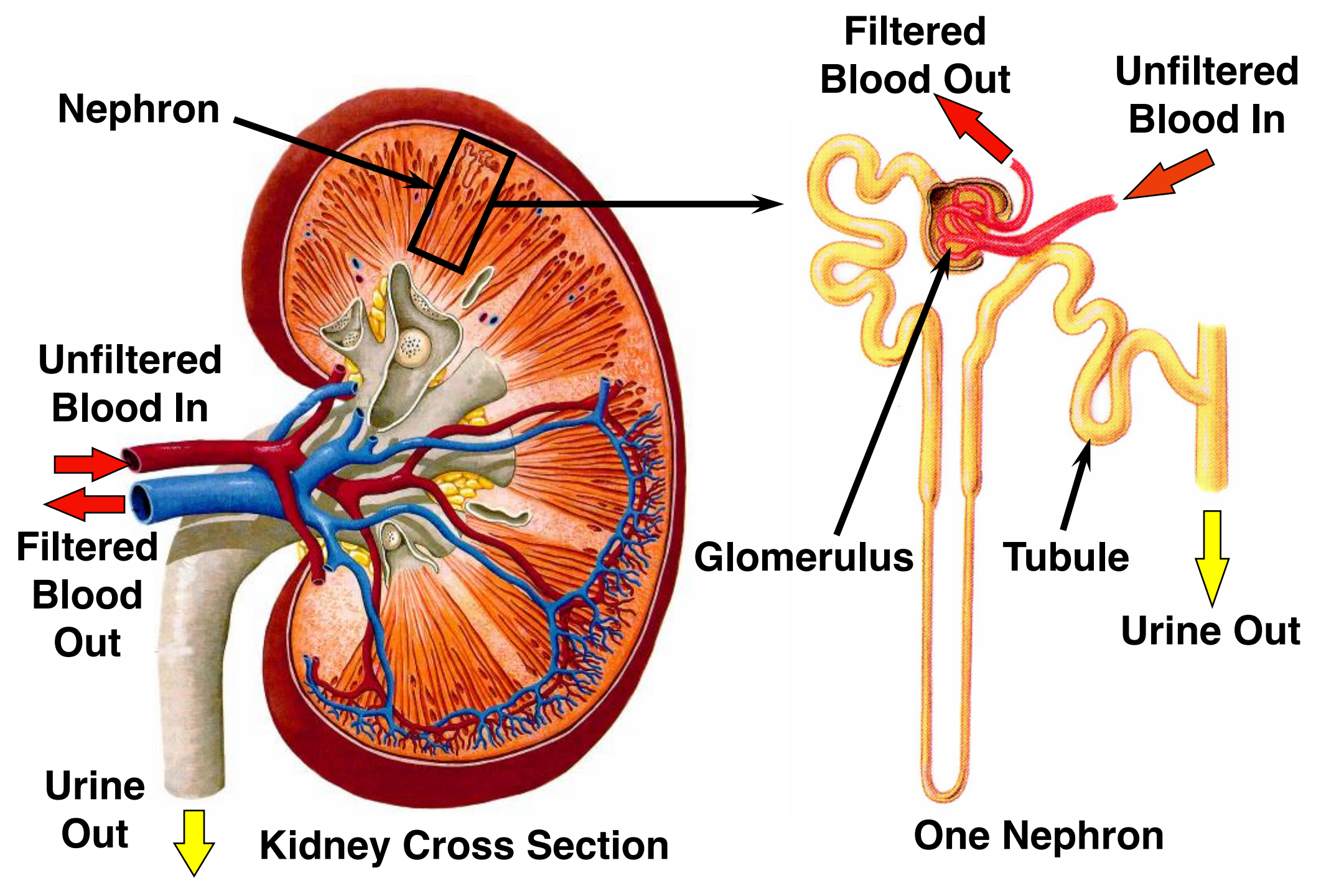
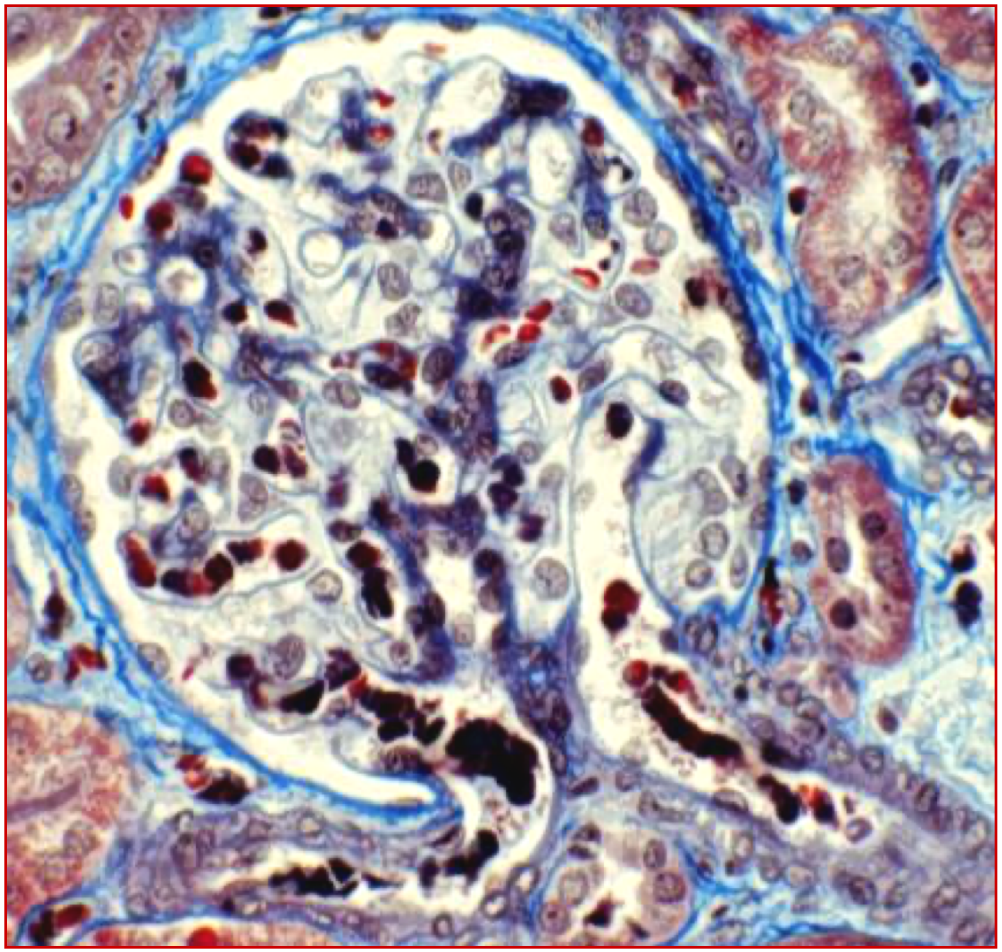
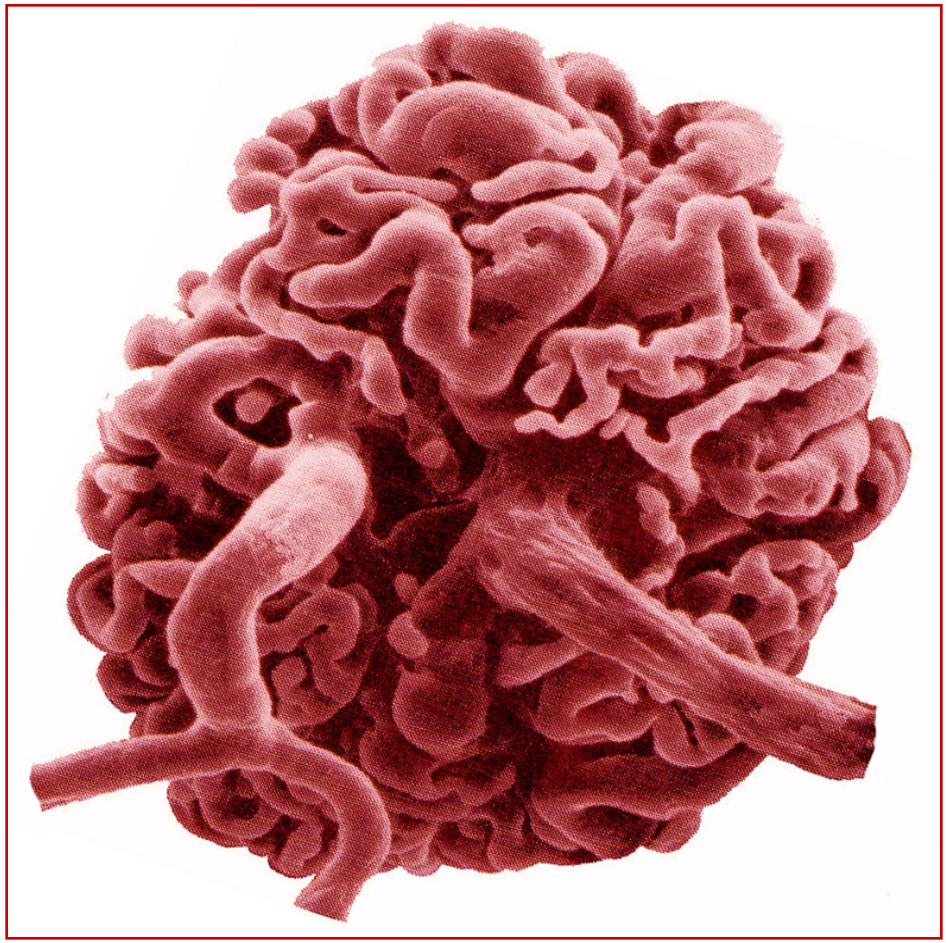
Νεφρωσικό Σύνδρομο

Σοφία Λιονάκη
Επίκουρη Καθηγήτρια Νεφρολογίας
Π.Γ.Ν ΑΤΤΙΚΟΝ, ΕΚΠΑ


Nephron
Unfiltered Blood In
Filtered Blood Out
Urine Out
Kidney Cross Section
Filtered Blood Out
Unfiltered Blood In
Glomerulus
Tubule
Urine Out
One Nephron

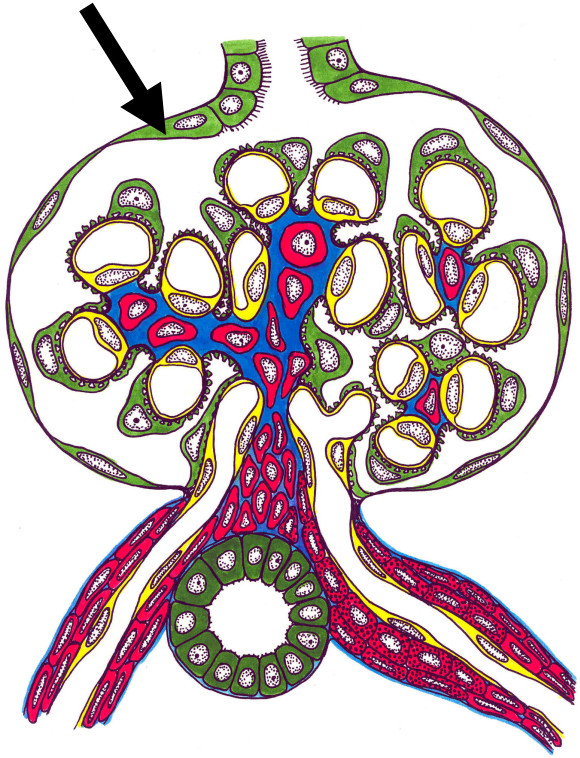
Φυσιολογικό σπείραμα



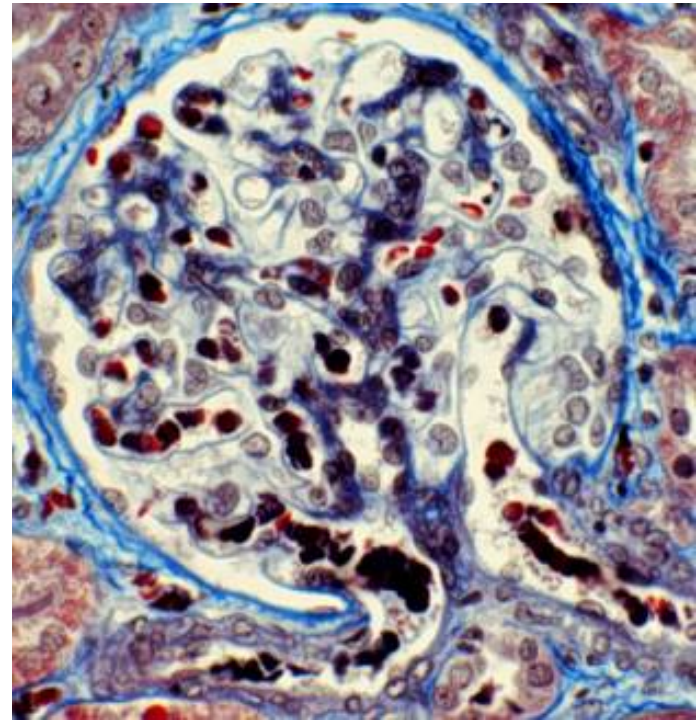


The Glomerulus

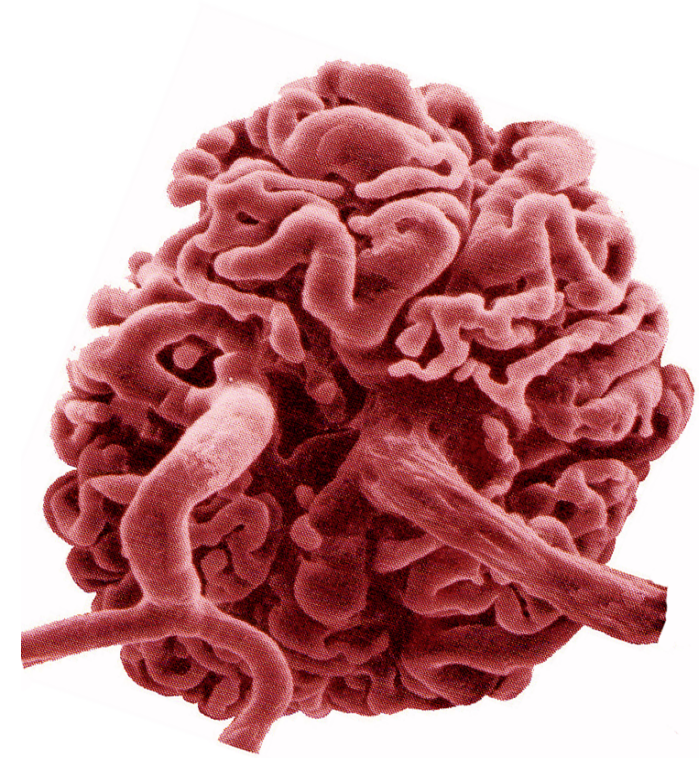
Bowman's capsule



Efferent arteriole



Afferent arteriole

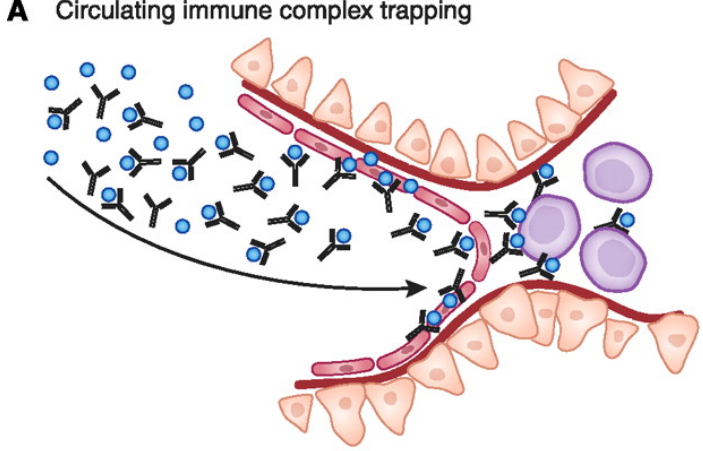


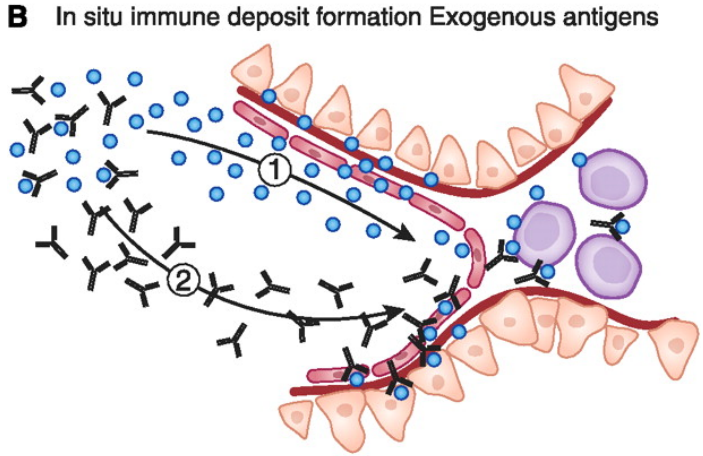
Efferent arteriole

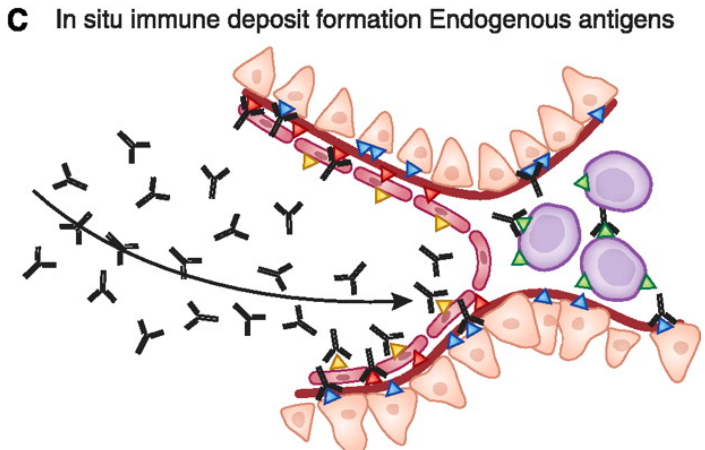
Afferent arteriole

Σπειραματικές παθήσεις

- Σπειραματοπάθειες
  - Διαταραχή του σπειραματικού φραγμού
- Σπειραματονεφρίτιδες
  - Φλεγμονή







<u>Μηχανισμοί σχηματισμού ανοσοεναποθέσεων στα σπειράματα:</u>

1. Παγίδευση κυκλοφορούντων ανοσοσυμπλεγμάτων.

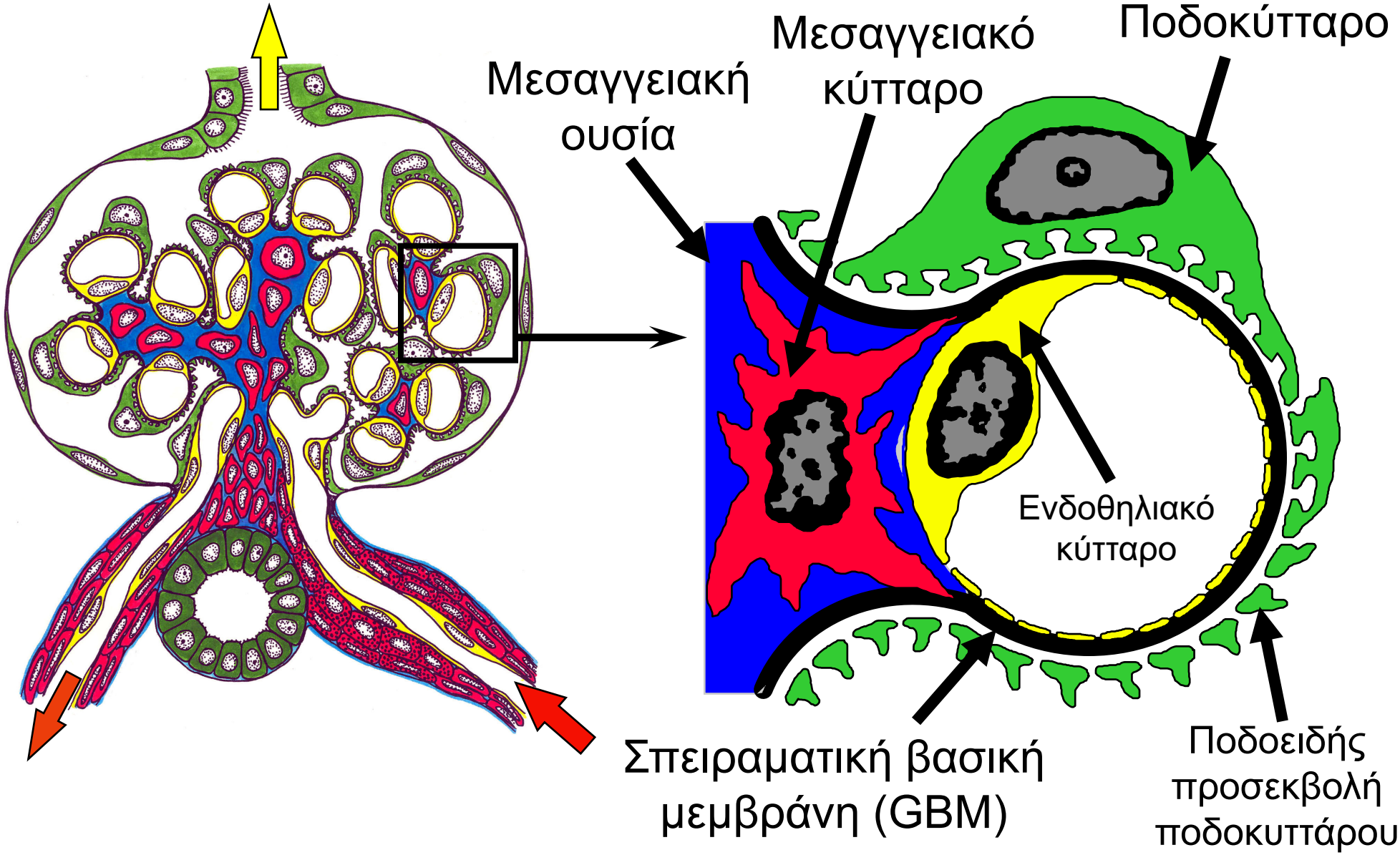
1. In situ σχηματισμός ανοσοσυμπλεγμάτων.

1. In situ σχηματισμός ανοσοσυμπλεγμάτων με σύνδεση αυτοαντισωμάτων σε φυσικά στοιχεία του σπειράματος

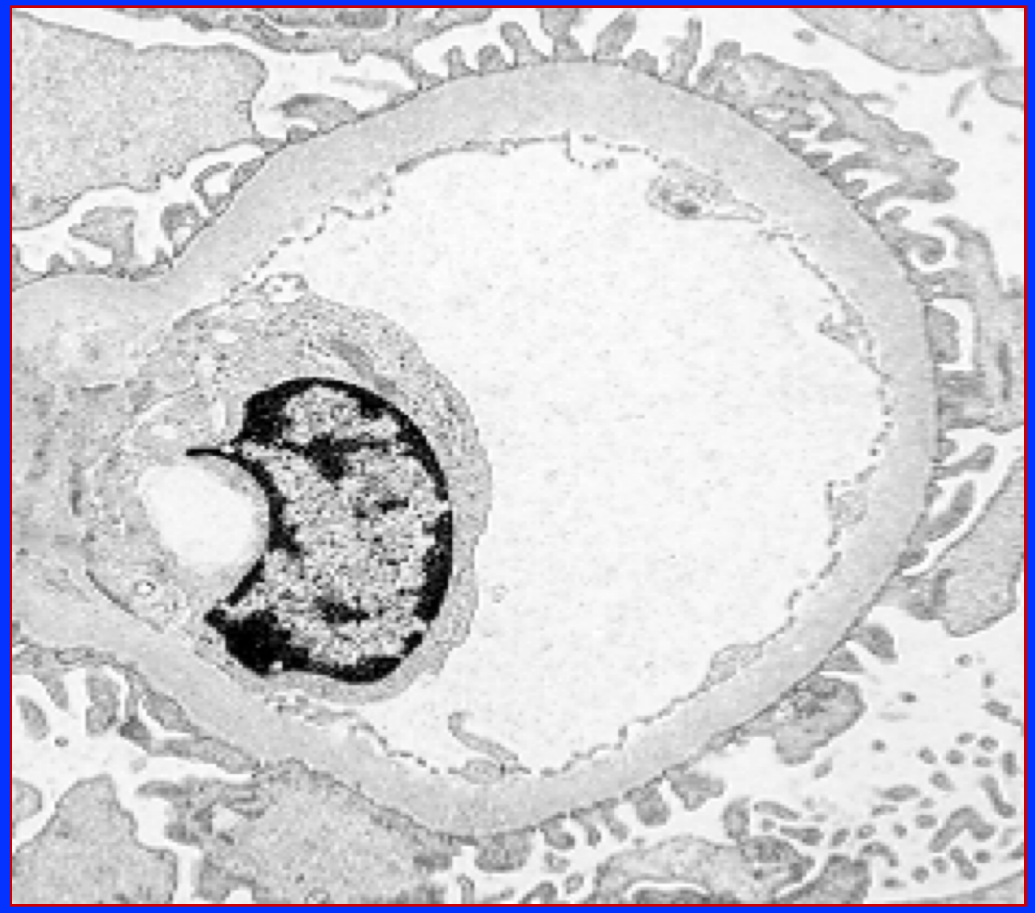
Couser W G JASN 2012;23:381-399

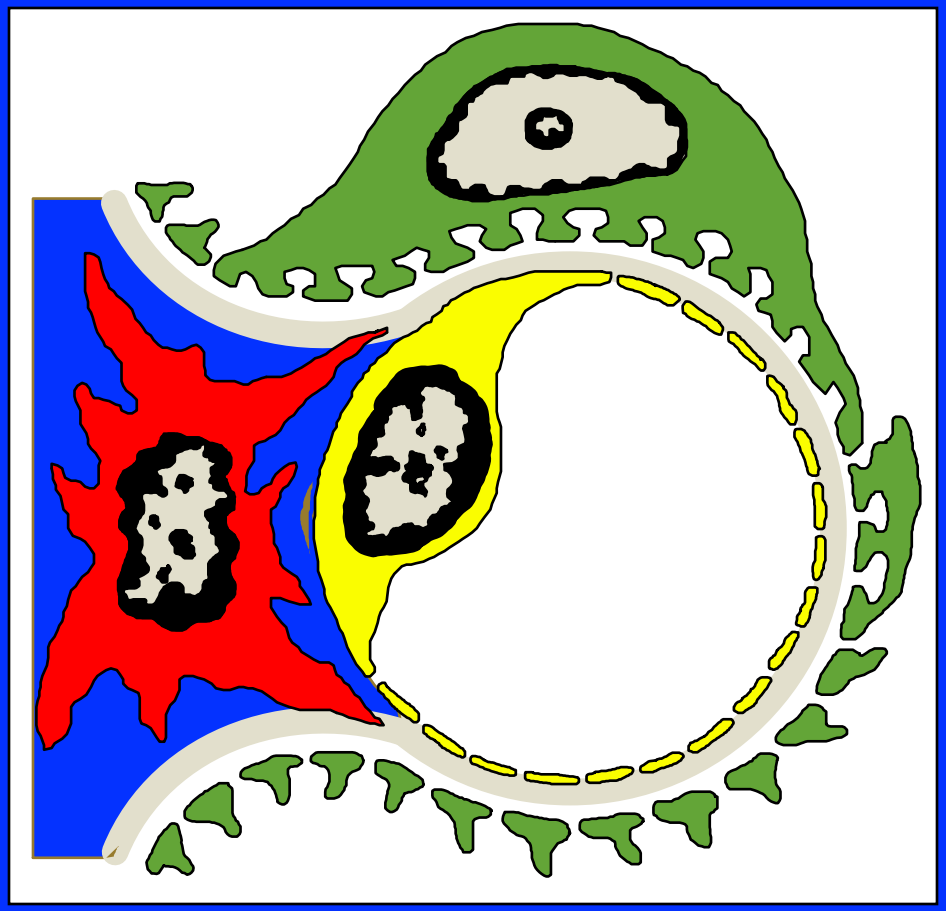
J.C. Jennette

Glomerular Capillary



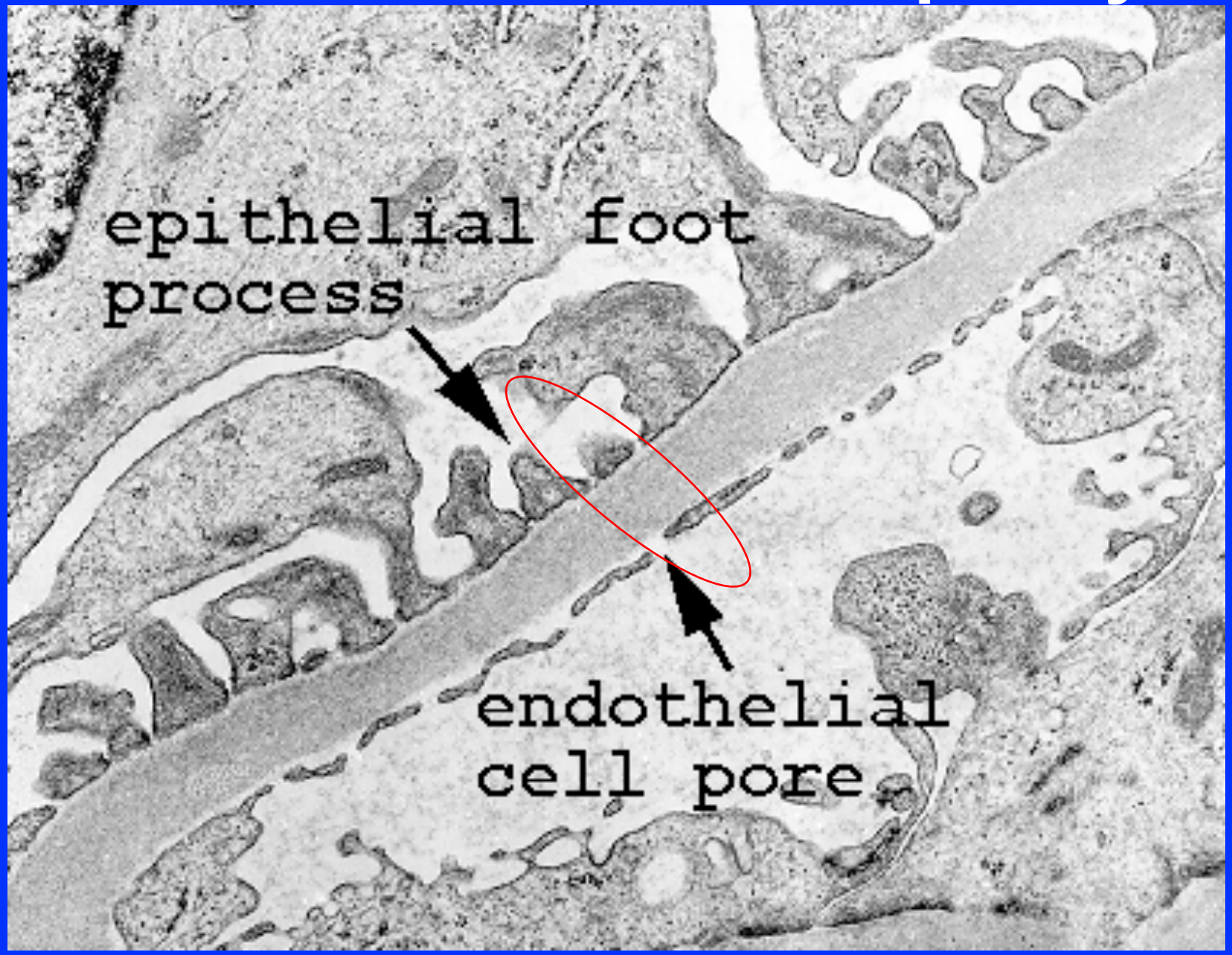
Φυσιολογικό σπειραματικό τριχοειδές





J.C. Jennette

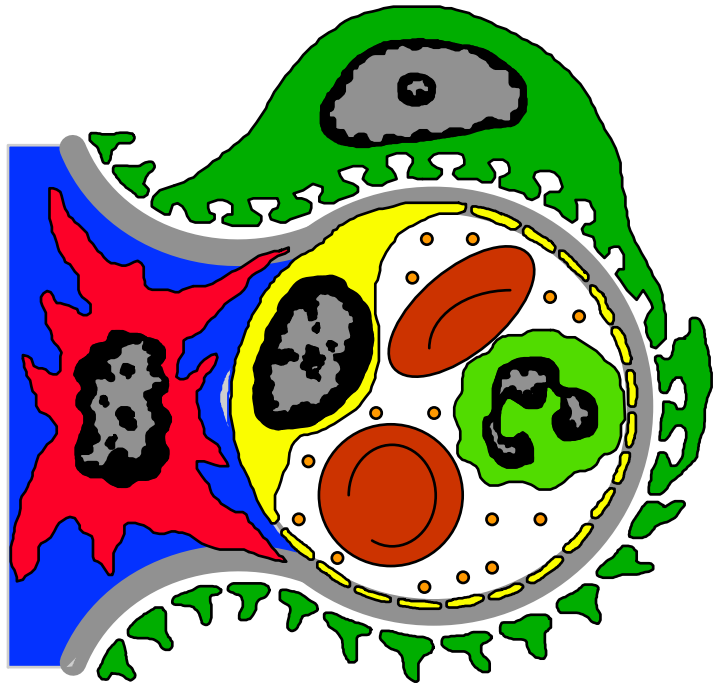
Normal Glomerular Capillary



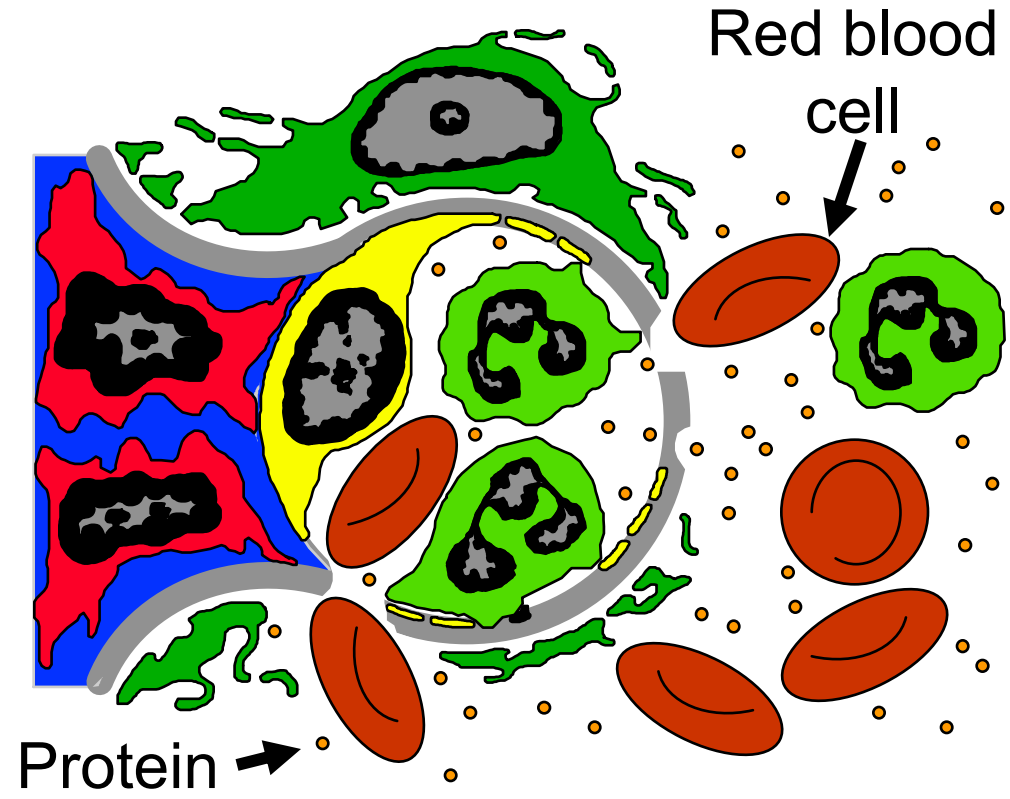
Κλινική εικόνα Σπειραματικών Παθήσεων

- Ασυμπτωματική αιματουρία/ή/και πρωτεϊνουρία
- Νεφρωσικό σύνδρομο
- Οξύ (σπειραματο) νεφριτιδικό σύνδρομο
- Ταχέως εξελισσόμενη σπειραματονεφρίτιδα
- Χρόνια σπειραματονεφρίτιδα

Πρωτεινουρία και αιματουρία



Το φυσιολογικό σπειραματικό τριχοειδές συγκρατεί τα ερυθρά αιμοσφαίρια, τα λευκά αιμοσφαίρια και τις πρωτείνες και αφήνει μόνο υδαρή στοιχεία να περάσουν στο ούρο.



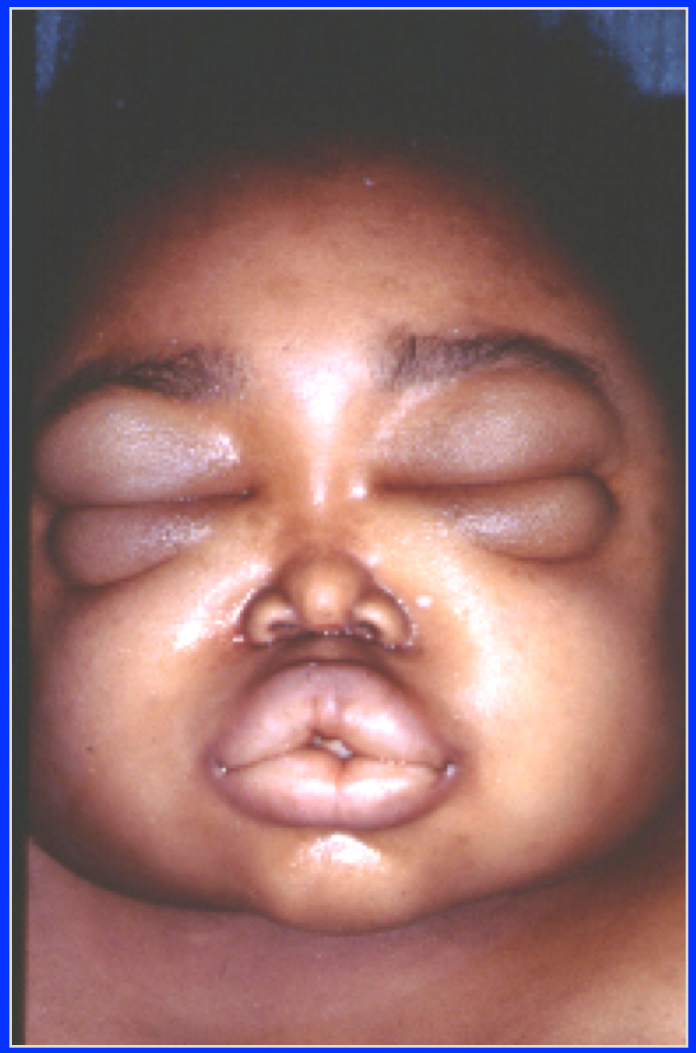
Το σπειραματικό τριχοειδές που έχει βλάβη αφήνει να διαφύγουν πρωτεϊνες (πρωτεϊνουρία) και ερυθρά αιμοσφαίρια στοιχεία (αιματουρία) να περάσουν στα ούρα.

J.C. Jennette

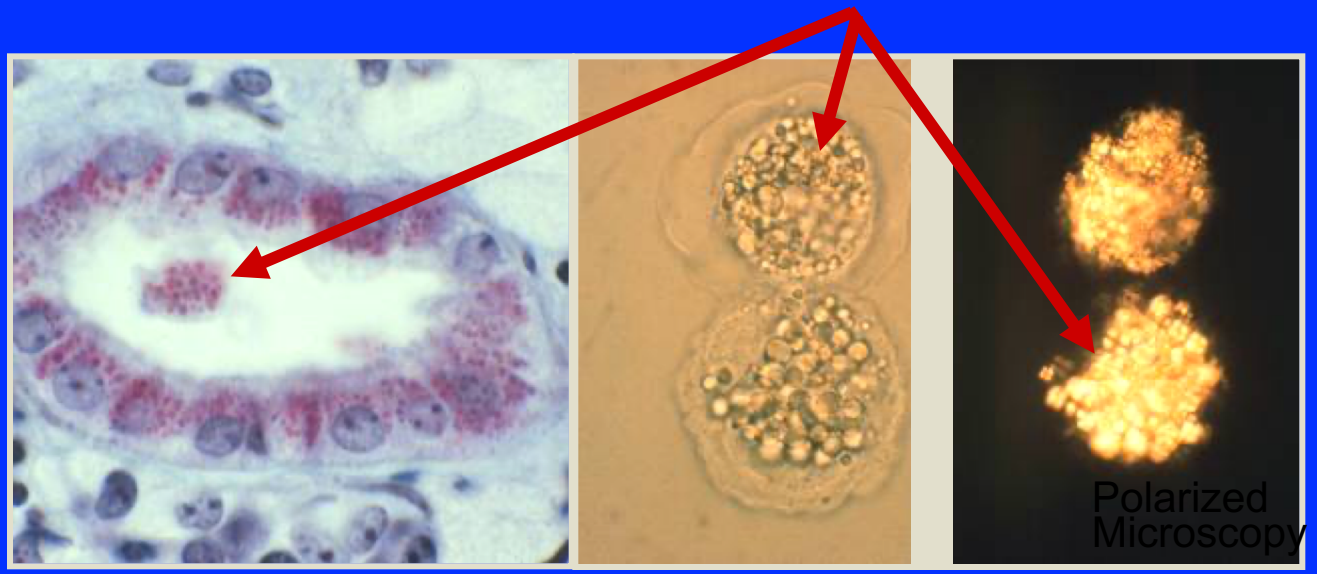
Νεφρωσικό versus Νεφριτιδικό Σύνδρομο

	Νεφρωσικό	Νεφριτιδικό
Πρωτεϊνουρία	++ έως +++	+ έως ++
Οίδημα	+ έως +++	0 έως ++
Υπαλβουμιναιμία	+ έως +++	0 έως +
Αιματουρία	0 έως ++	++ έως +++
Αζωθαιμία	0 έως ++	0 έως +++
Υπέρταση	0 έως +	0 έως +++

Νεφρωσικό σύνδρομο



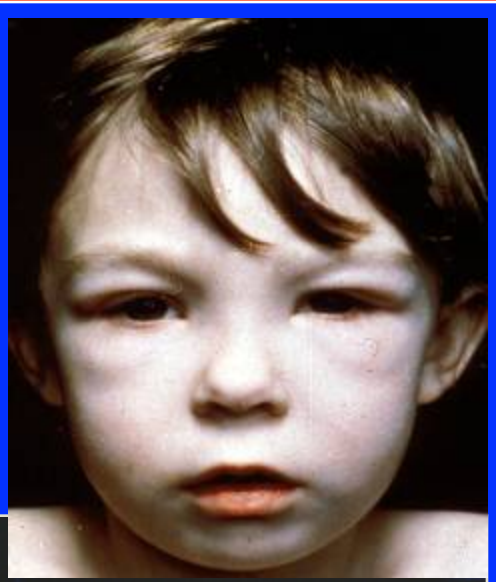
Οίδημα
Πρωτεϊνουρία (>3.5 g/24hrs)
Υπαλβουμιναιμία
Υπερλιπιδαιμία
Λιπιδουρία (συχνά με λιπώδη ωοειδή σωμάτια)

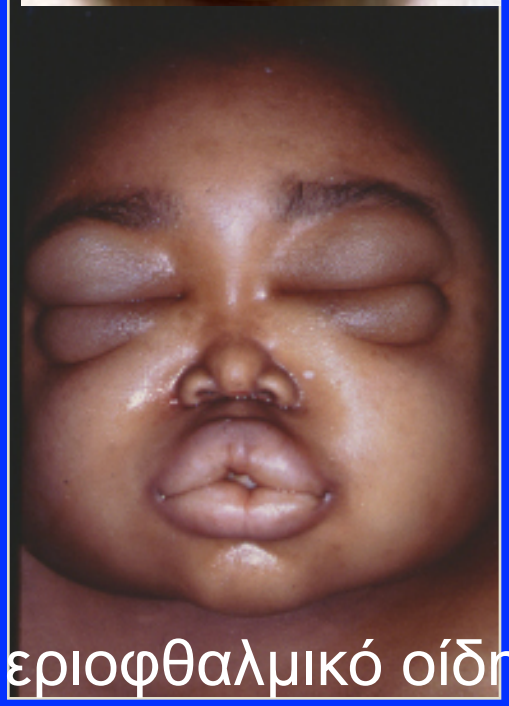


Biopsy

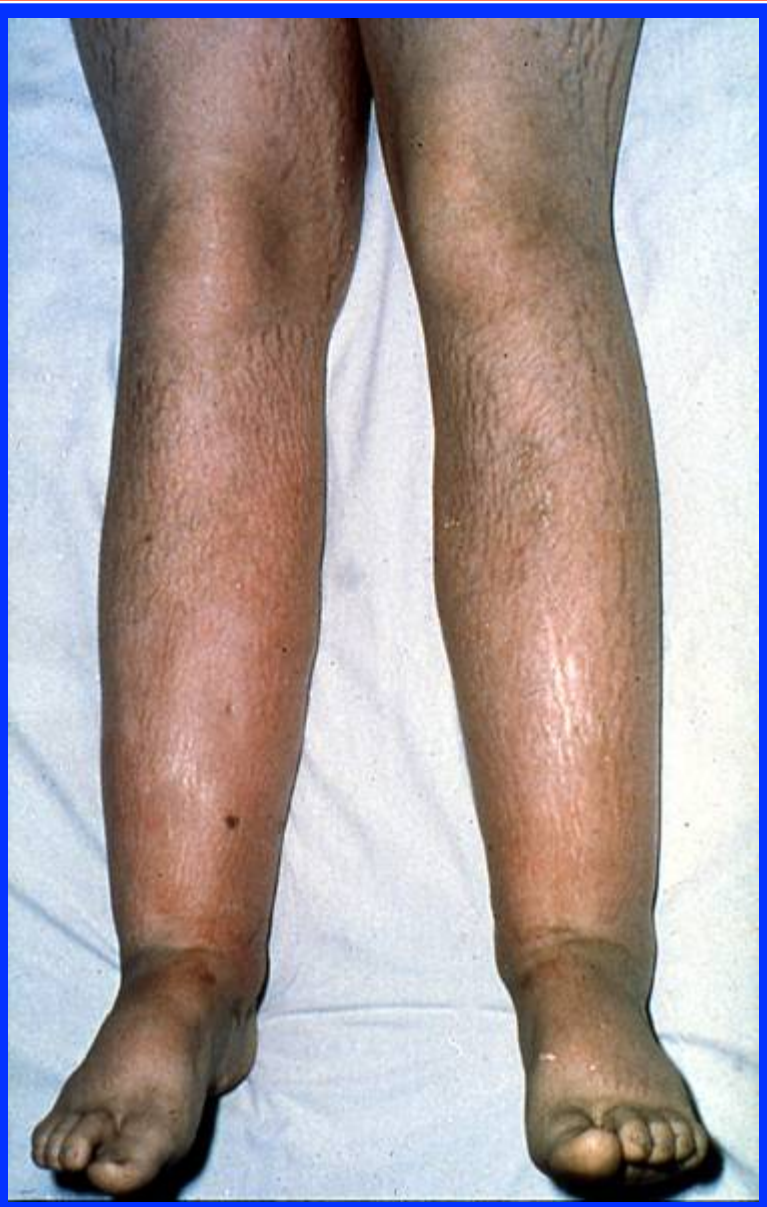
Urine

Νεφρωσικό σύνδρομο

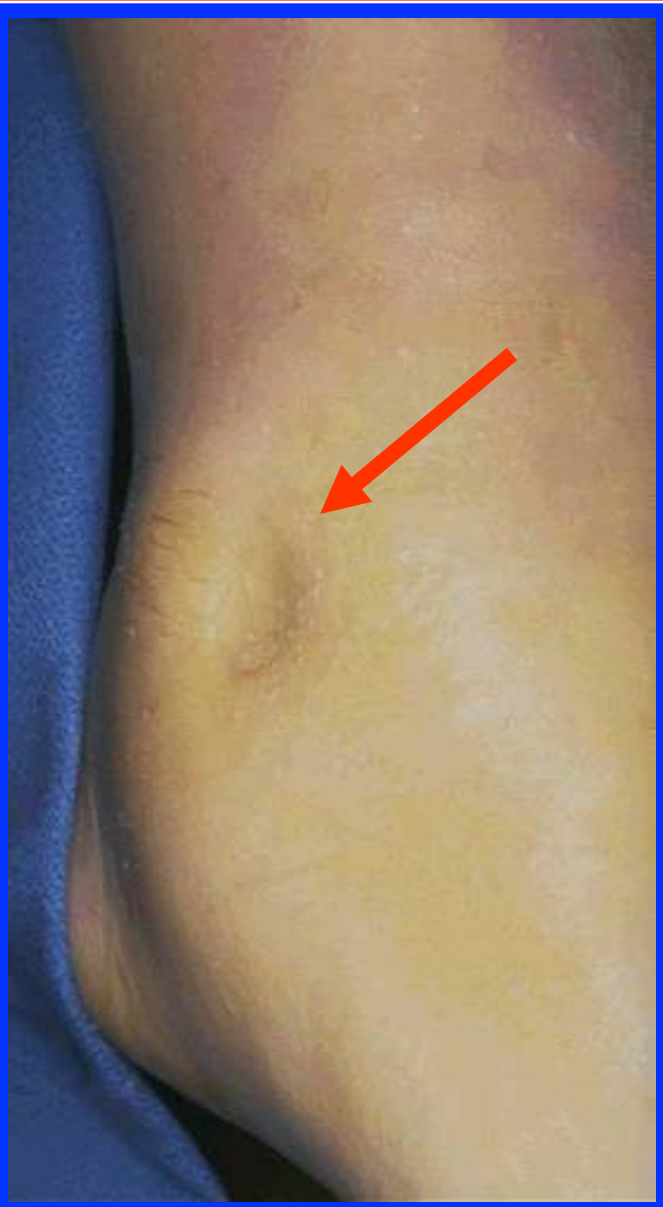




Περιοφθαλμικό οίδημα



Οίδημα κάτω άκρων



Οίδημα με εντύπωμα

Normal Protein Excretion

- Only low molecular weight proteins + small amount of albumin are filtered (< 1500 mg/day).
- Almost completely reabsorbed by proximal tubular epithelial cells.
- Normal protein excretion: 40-80 mg/day (<150)
  - 2/3 of protein excretion is Tamm-Horsfall protein (mucoprotein secreted by tubular cells)

Types of Proteinuria

- Transient:
  - occurs under certain physiologic situations in the absence of kidney disease.
- Orthostatic:
  - Increased protein excretion in the upright position.
  - usually < 500 mg/day.
- Fixed:
  - Denotes a glomerular disease.

Measurement of Proteinuria

- 24 hour Urine Collection:
  - verify that the collection is complete. Normal creatinine excretion is
    - 20-25 mg/kg/day for males
    - 15-20 mg/kg/day for females
- Spot Urine Protein/Creatinine ratio:
  - correlates well with daily protein excretion.
  - Normal is <0.2

Nephrotic Syndrome

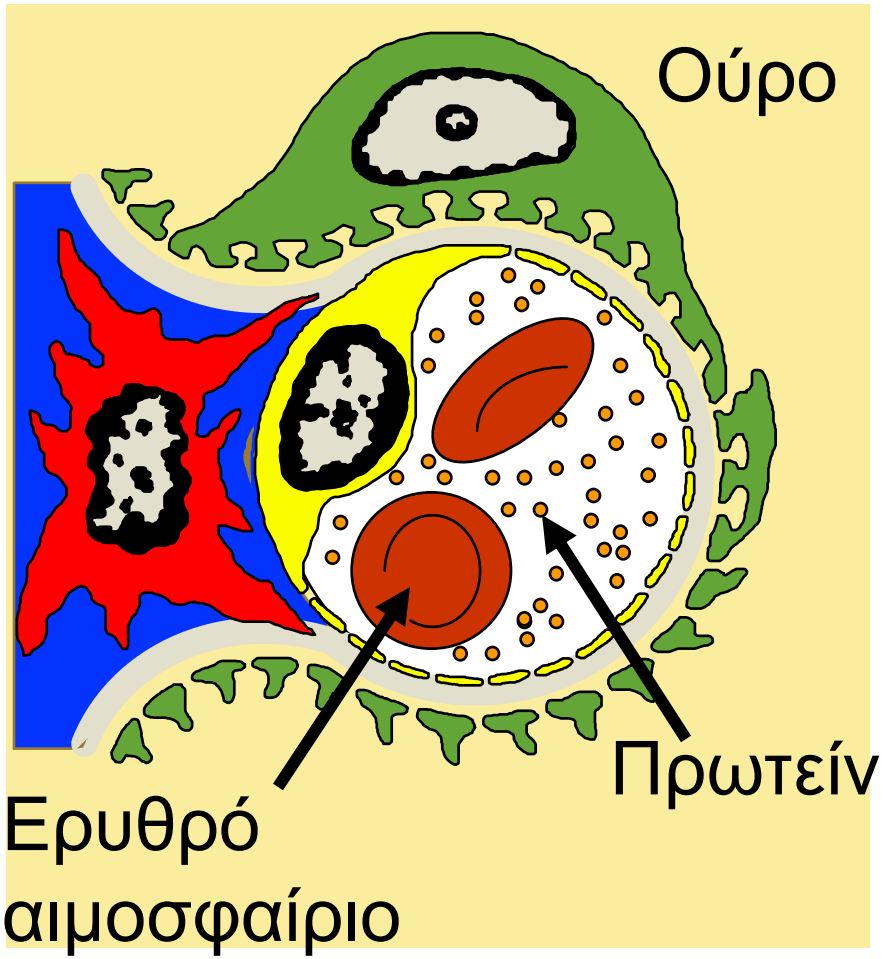
- Proteinuria:
  - >3.5 g/day/1.73 m2
- Hypoproteinemia
- Edema
- Hyperlipidemia and lipiduria

Nephrotic Syndrome: Most Common Causes

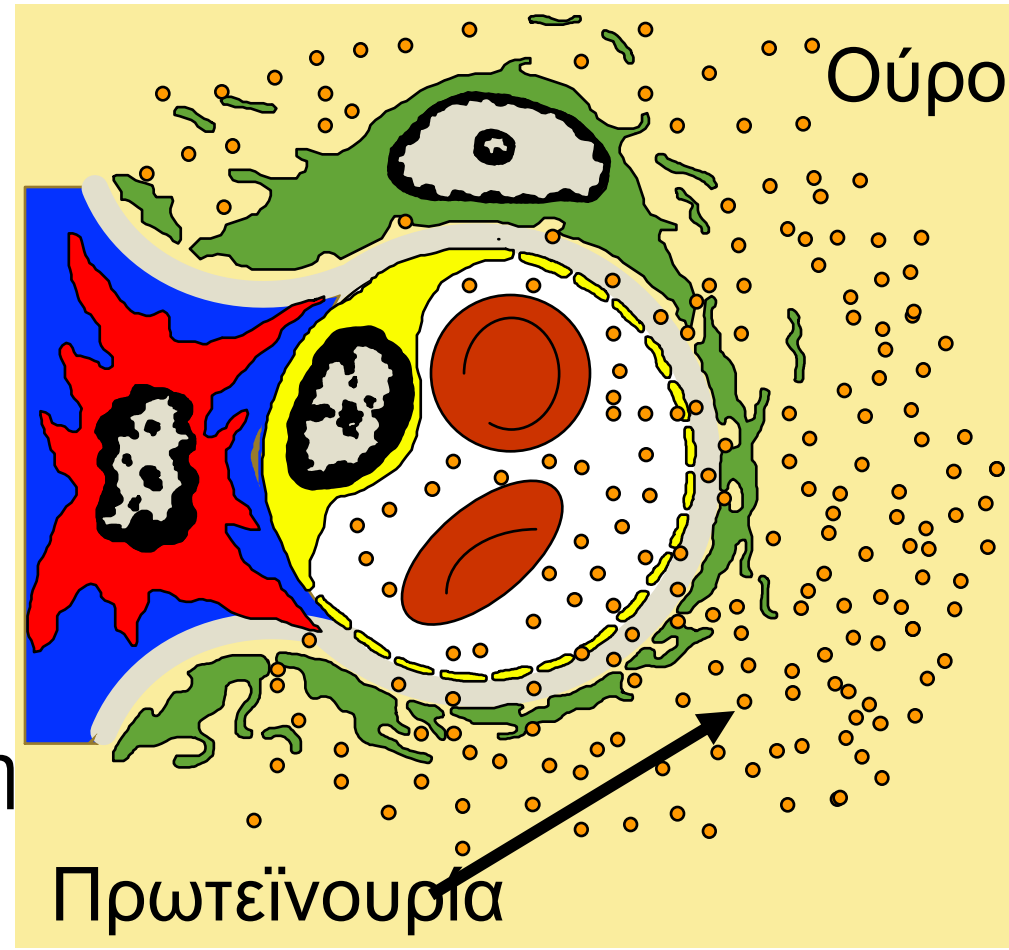
- **"Primary"**
  - Minimal Change Disease
  - Focal Segmental Glomerulosclerosis (FSGS)
  - Membranous Nephropathy
- **"Secondary"**
  - Diabetic Nephropathy
  - FSGS
  - Membranous Nephropathy
  - Minimal Change Disease

Η πρωτεϊνουρία προκύπτει όταν υπάρχουν χάσματα στο σπειραματικό φραγμό που επιτρέπουν τη διαφυγή μορίων πρωτείνης στα ούρα.

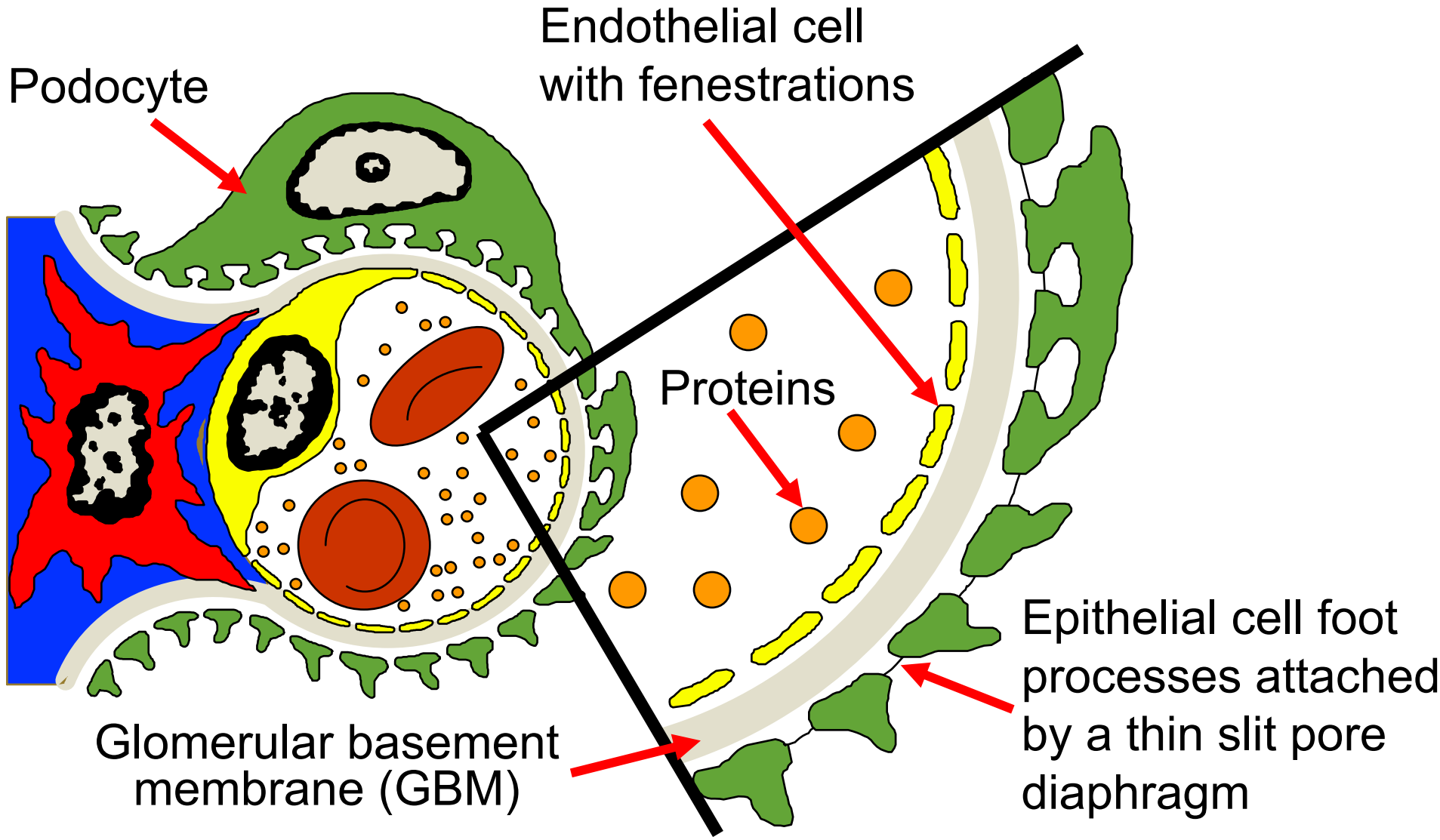
Normal glomerular capillary

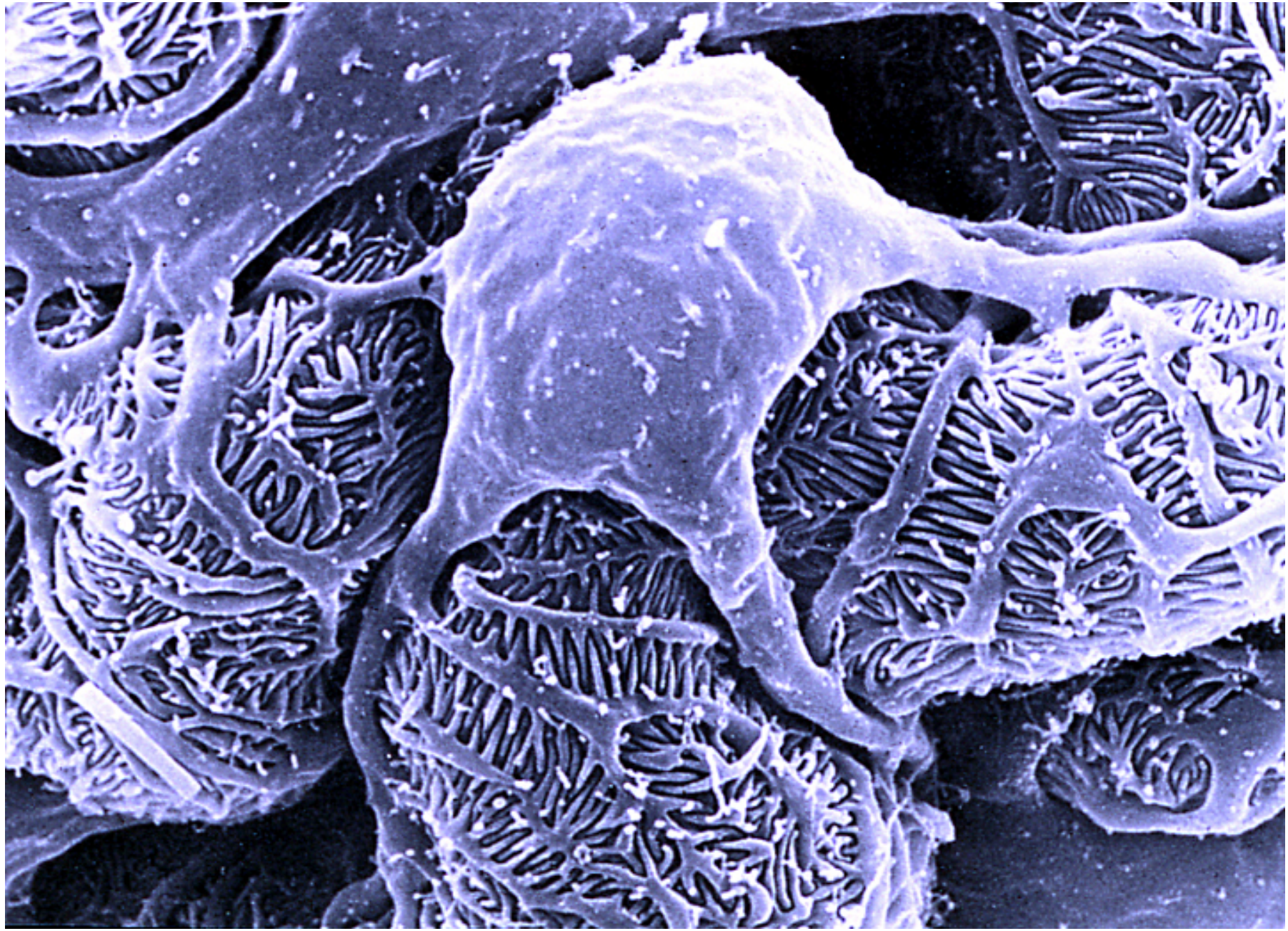


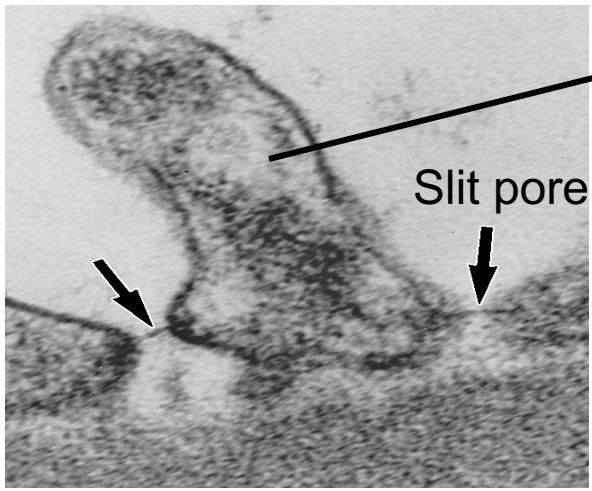
Capillary with proteinuria

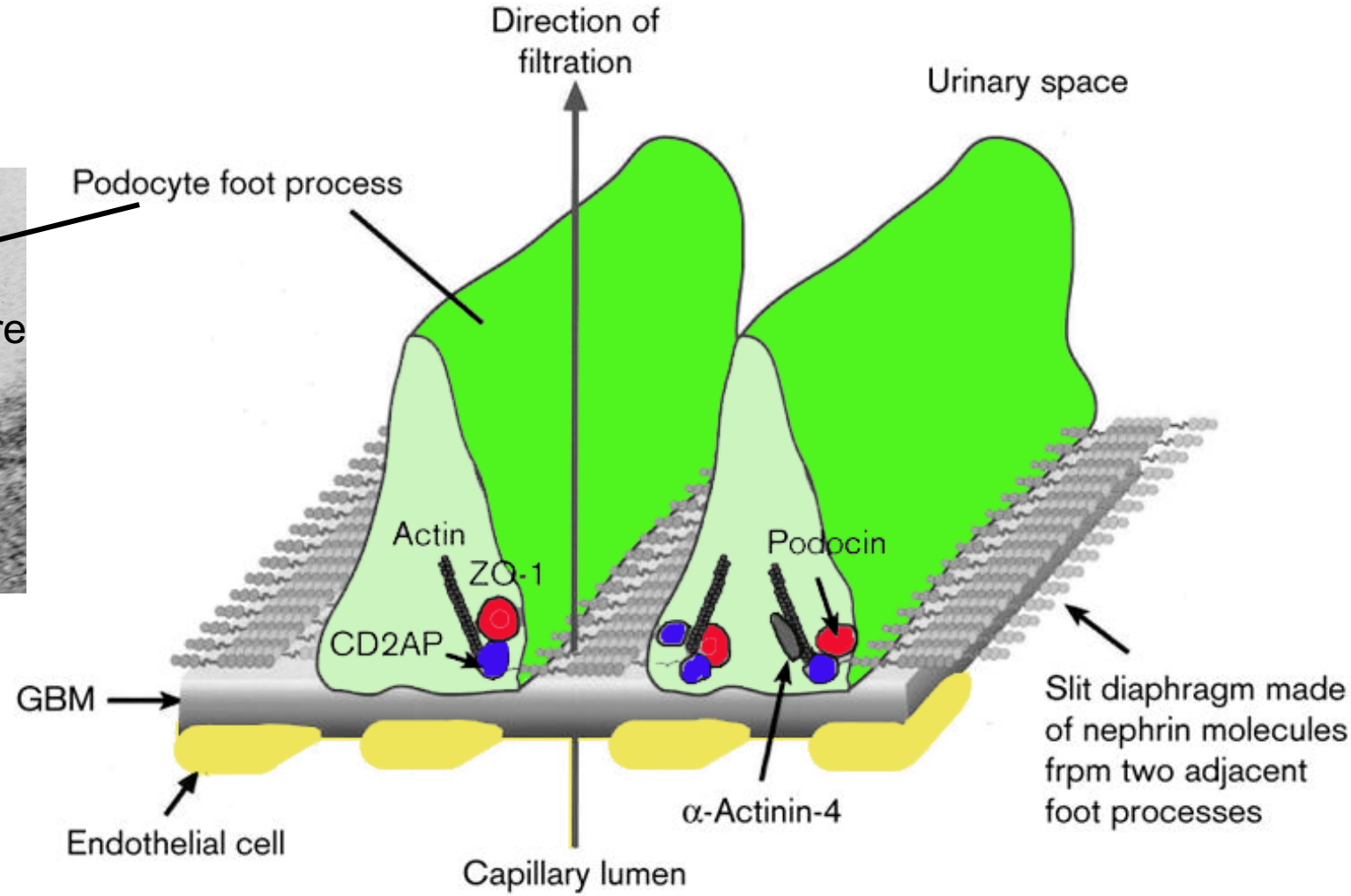


Ο σπειραματικός φραγμός είναι αυτός που συγκρατεί την πρωτεΐνη και τα κύτταρα του αίματος στο τριχοειδές και δε διαφεύγουν στα ούρα. Ο φραγμός αυτός περιλαμβάνει το ενδοθηλιακό κύτταρο, τη βασική μεμβράνη και το επιθηλιακό κύτταρο (ποδοκύτταρο). Το ποδοκύτταρο είναι πιθανότατα το πιο σημαντικό.






Slit pore


Direction of filtration
Urinary space
Podocyte foot process
Actin
ZO-1
CD2AP
Podocin
GBM
Slit diaphragm made of nephrin molecules frpm two adjacent foot processes
α-Actinin-4
Endothelial cell
Capillary lumen

Nephrotic syndrome

- The nephrotic sediment: Heavy proteinuria & Lipiduria
- The term "nephrotic syndrome" refers to a distinct constellation of clinical and laboratory features of kidney disease.
- Heavy proteinuria (protein excretion greater > 3.5 g/24 hours)
- Hypoalbuminemia (<than 3.5 g/dL)
- Peripheral edema
- Hyperlipidemia
- Thrombotic disease

Isolated heavy proteinuria

- Suggestive of a glomerulopathy
- Same etiologies as the nephrotic syndrome
- Not necessarily associated with the multiple clinical and management problems characteristic of the nephrotic syndrome.
- More likely to be due to secondary focal segmental glomerulosclerosis (FSGS) (due, for example, to diabetes)

Etiology of nephrotic syndrome

- **Children:** Minimal change disease is the predominant cause.
- **Adults**: 30% have a systemic disease (diabetes mellitus, amyloidosis, or systemic lupus erythematosus)
- The remaining cases are usually due to primary kidney disorders such as minimal change disease, focal segmental glomerulosclerosis (FSGS), and membranous nephropathy

Most common causes of nephrotic syndrome:

Patients between 15 and 65 years of age:

- Membranous nephropathy (24%)
- Minimal change disease (16%)
- Lupus (14%)
- FSGS (12%)
- Membranoproliferative glomerulonephritis (7%)
- Amyloidosis (6%)
- IgA nephropathy (6%)
- Adult individuals (> 65 years): increased prevalence of amyloidosis (17%) and decreased prevalence of lupus (1%).

Mechanisms of glomerular injury

- Circulating factors in minimal change disease (MCD) and primary focal segmental glomerulosclerosis (FSGS).
- Circulating immune factors in disorders such as membranoproliferative glomerulonephritis, poststreptococcal glomerulonephritis, and lupus nephritis.
- Mutations in podocyte or slit diaphragm proteins (eg, CD2AP, podocin, and nephrin) in inherited forms of congenital, infantile, or glucocorticoid-resistant nephrotic syndrome.

Pathophysiology of proteinuria

- Protein loss due to glomerular proteinuria
- Podocyte: Major target of injury in diseases that cause idiopathic nephrotic syndrome in adults and children
- Podocyte foot process effacement
- Slit diaphragm disruption
- Relative or absolute depletion of podocytes

Hereditary podocyte injury

- ✓ Mutations of podocyte proteins that are important in the maintenance of the slit diaphragm such as nephrin and podocin
- ✓ Mutations in proteins that affect the integrity of the podocyte cytoskeleton such as alpha-actinin-4.

Pathogenesis of proteinuria

- Autoantibodies to podocyte antigens or circulating factors that affect the podocyte.
- The engagement or activation of these podocyte proteins alters the arrangement of the slit diaphragm or podocyte cytoskeleton.

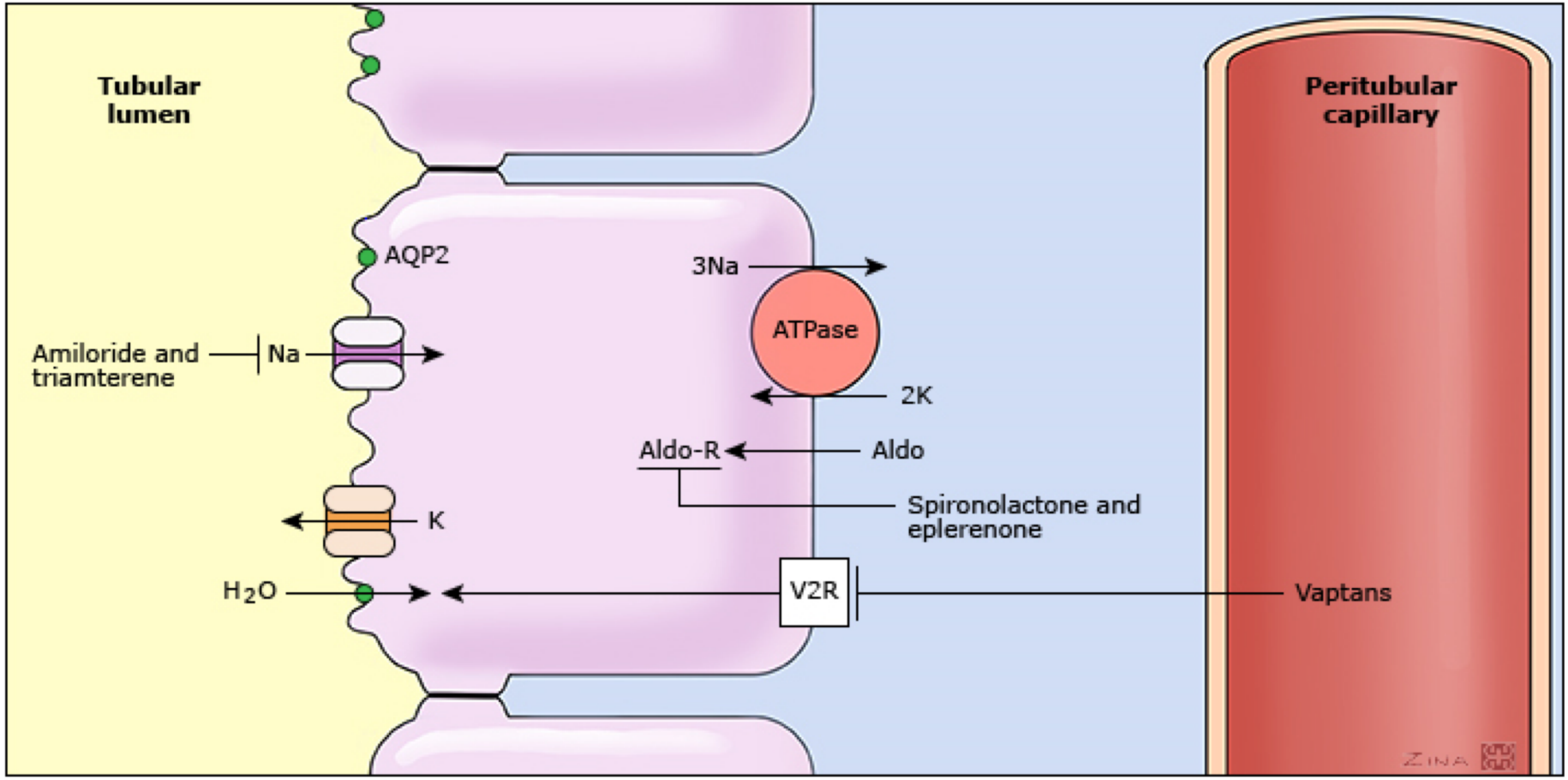
Hypoalbuminemia

- Most of albumin loss is due to urinary excretion.
- Hepatic albumin synthesis does increase in response to the albumin loss.
- This effect is mediated by an increase in hepatic albumin gene expression stimulated in part by the low oncotic pressure.
- The low oncotic pressure has a second clinically important effect: it increases hepatic lipoprotein synthesis.
- It remains unclear why, in a patient excreting 4-6 g of protein per day, the liver is usually unable to sufficiently increase albumin synthesis to normalize the plasma albumin concentration.

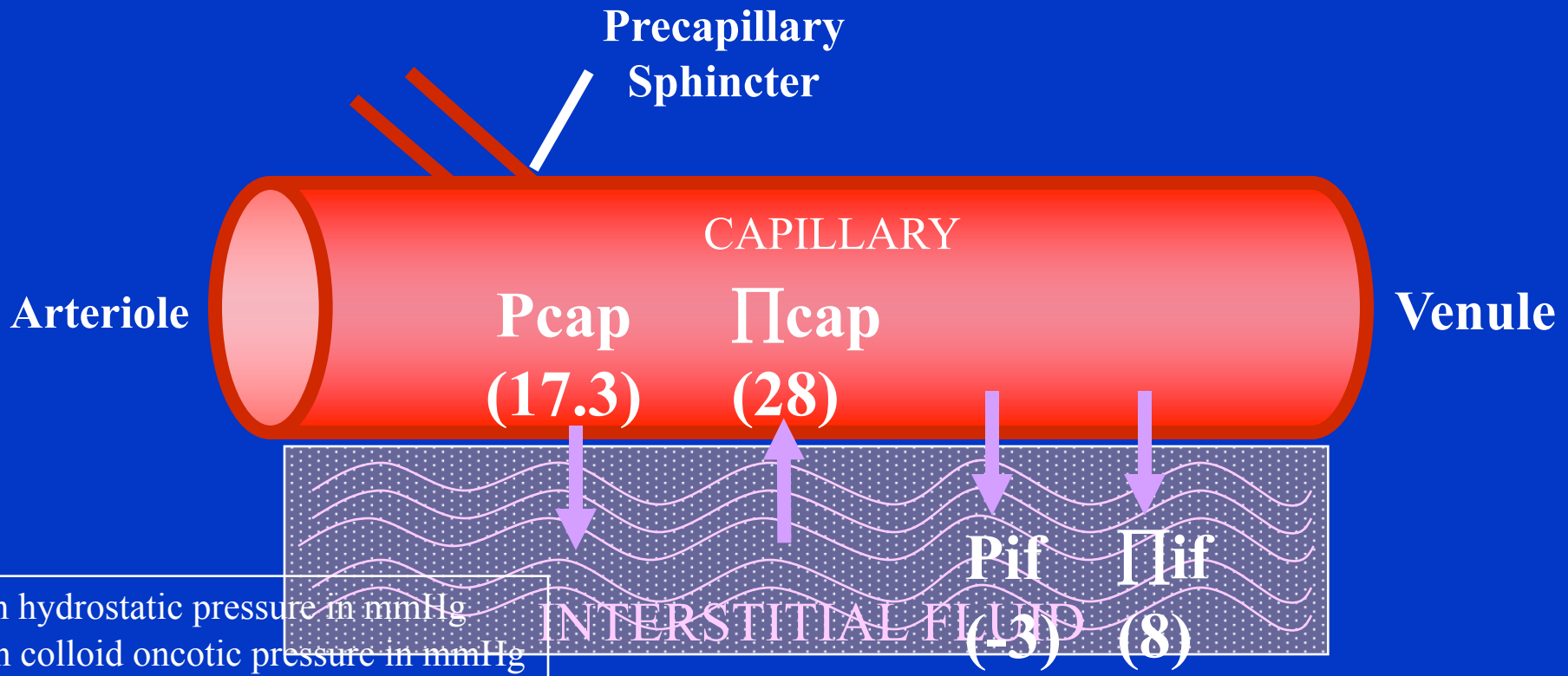
Edema

- 2 mechanisms
- Marked hypoalbuminemia leads to egress of fluid into the interstitial space by producing a decrease in plasma oncotic pressure.
- Parallel fall in the interstitial protein concentration and little change in the transcapillary oncotic pressure gradient.
- Edema appears to be the consequence of primary renal sodium retention in the collecting tubules mediated through the epithelial sodium channel and the basolateral Na-K-ATPase.

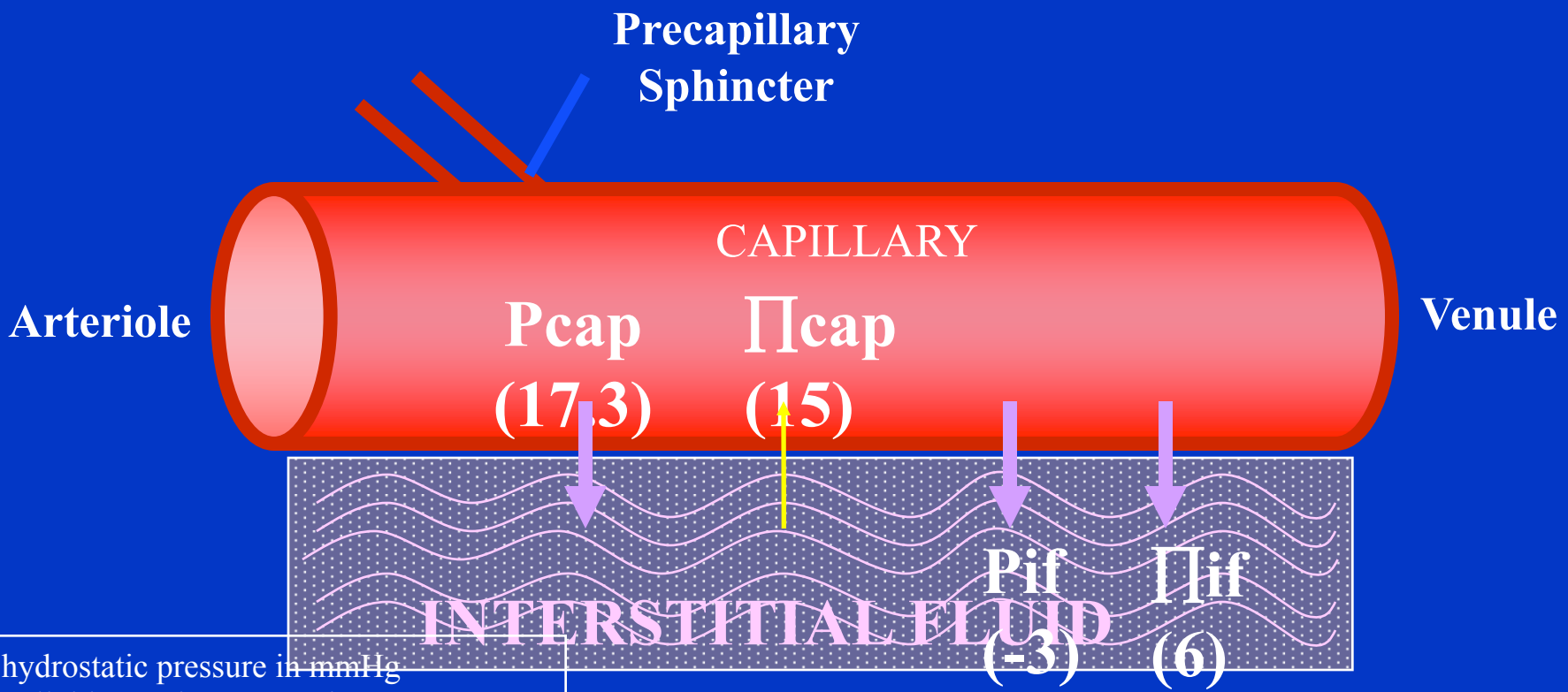
Ion transport in collecting tubule principal cells



Hemodynamic Factors Controlling Fluid Movement Across the Capillary Wall

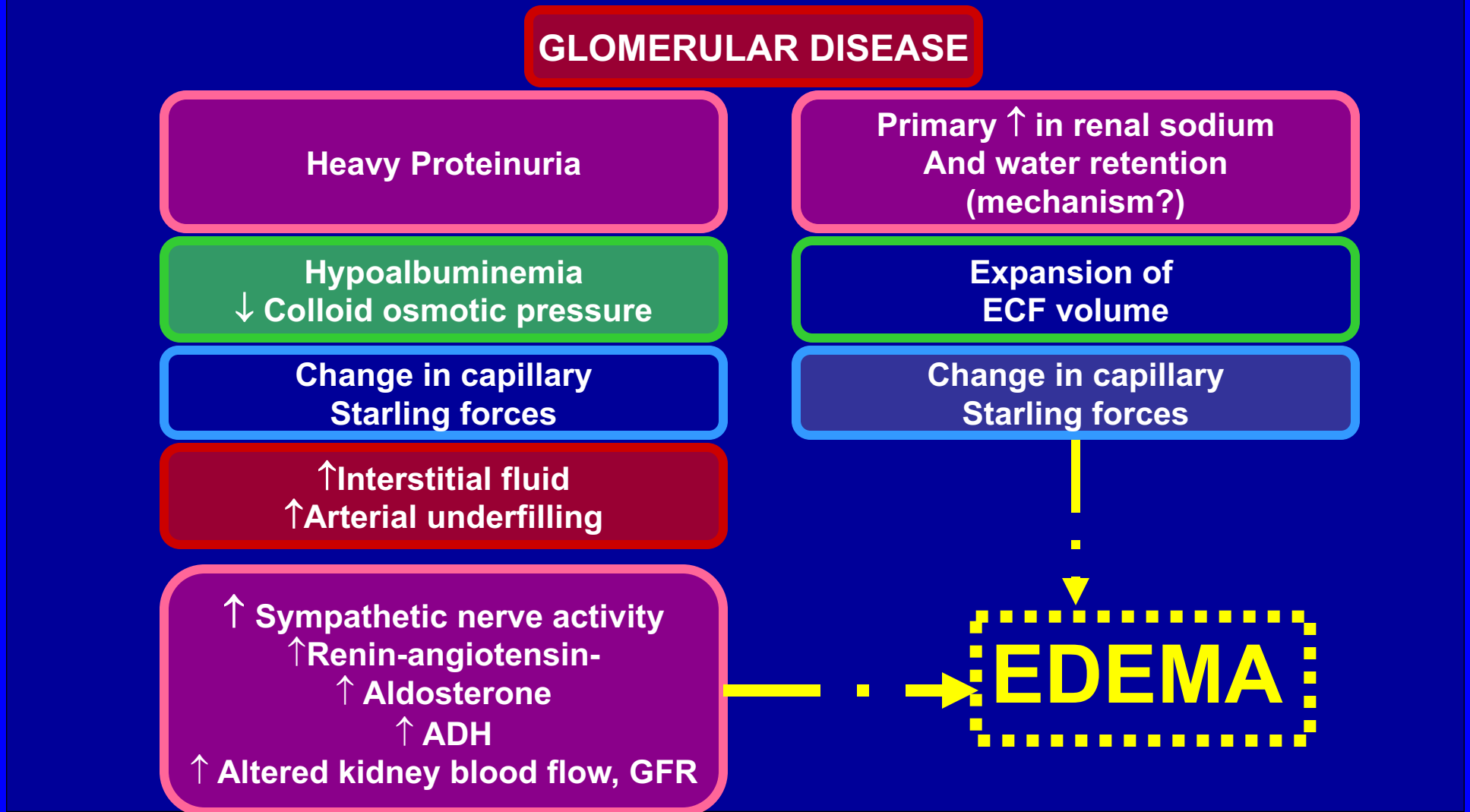


Edema Formation Caused by Decreased Capillary Oncotic Pressure



P = mean hydrostatic pressure in mmHg
Π= mean colloid oncotic pressure in mmHg
If = interstitial fluid
Cap = capillary

Mechanisms of Sodium and Water Retention in the Nephrotic Syndrome



Hyperlipidemia and lipiduria

- Hypercholesterolemia and hypertriglyceridemia.
- ↓ Plasma oncotic pressure appears to stimulate hepatic lipoprotein synthesis resulting in hypercholesterolemia.
- Diminished clearance may also play a role in the development of hypercholesterolemia.
- Impaired metabolism is primarily responsible for nephrotic hypertriglyceridemia.

Complications of nephrotic syndrome

- Protein malnutrition
- Hypovolemia
- Acute kidney injury
- Thromboembolism
- Infection

Hypercoagulability in nephrotic syndrome

- Increased incidence (10-40 % of patients) of arterial and venous thrombosis
- Deep vein, renal vein thrombosis, pulmonary emboli.
- Renal vein thrombosis is found disproportionately in patients with membranous nephropathy, particularly those excreting >10 g of protein per day.
- It can present acutely or, much more commonly, in an indolent manner.
- Acute presentation: flank pain, gross hematuria, and a decline in kidney function.
- Most patients are asymptomatic, and the diagnosis of renal vein thrombosis is suspected only when pulmonary thromboembolism develops.

Risk factors for thromboembolism

- Histologic diagnosis
- In a cohort of 1313 patients with idiopathic glomerular disease due to membranous nephropathy, focal segmental glomerulosclerosis, or immunoglobulin A (IgA) nephropathy
- The incidence of venous thromboembolic events was much higher in

✓ Membranous nephropathy 7.9 %

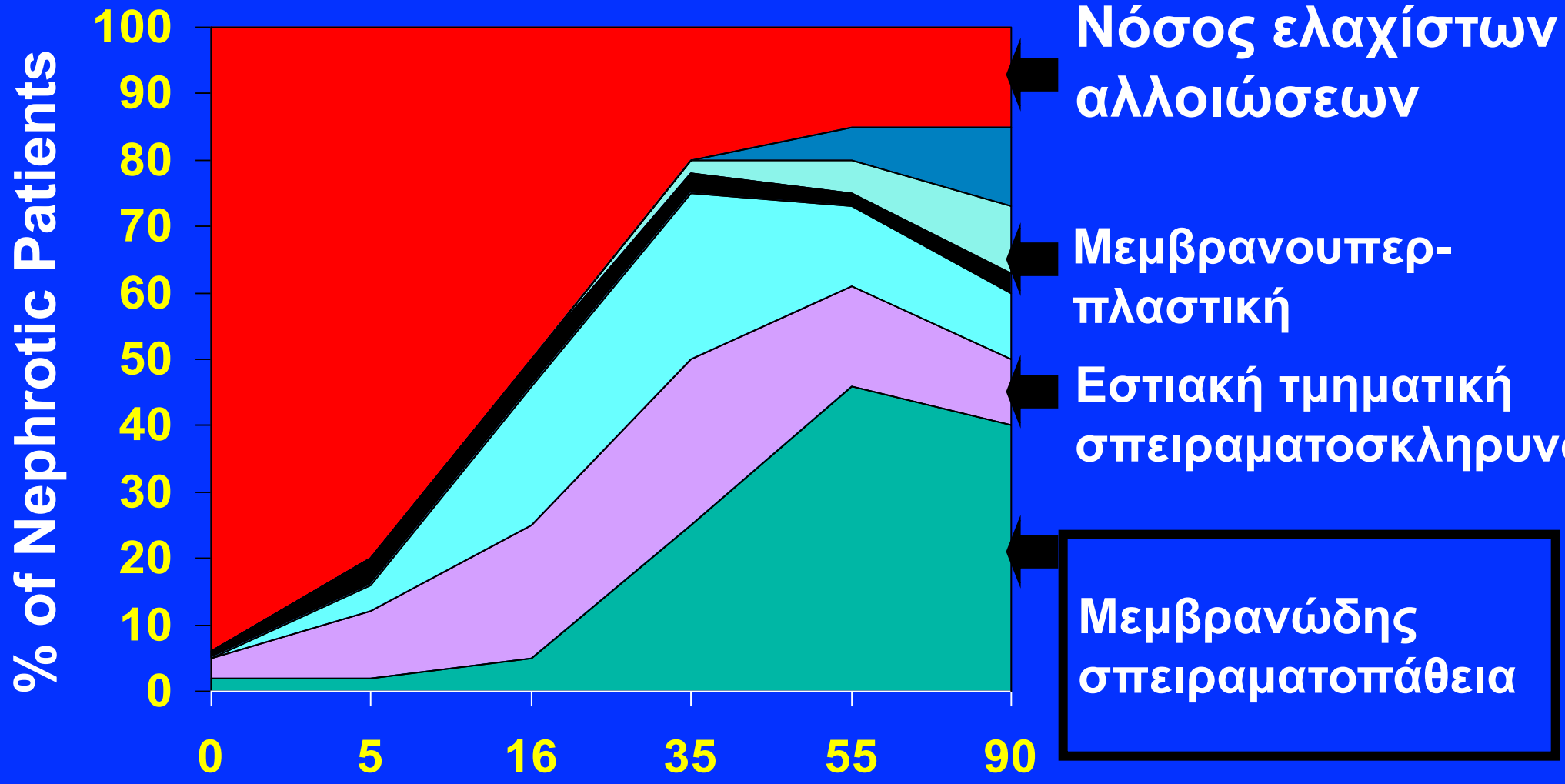
✓ Focal segmental glomerulosclerosis 3.0 %

✓ IgA nephropathy 0.4 %

Risk factors for thromboembolism

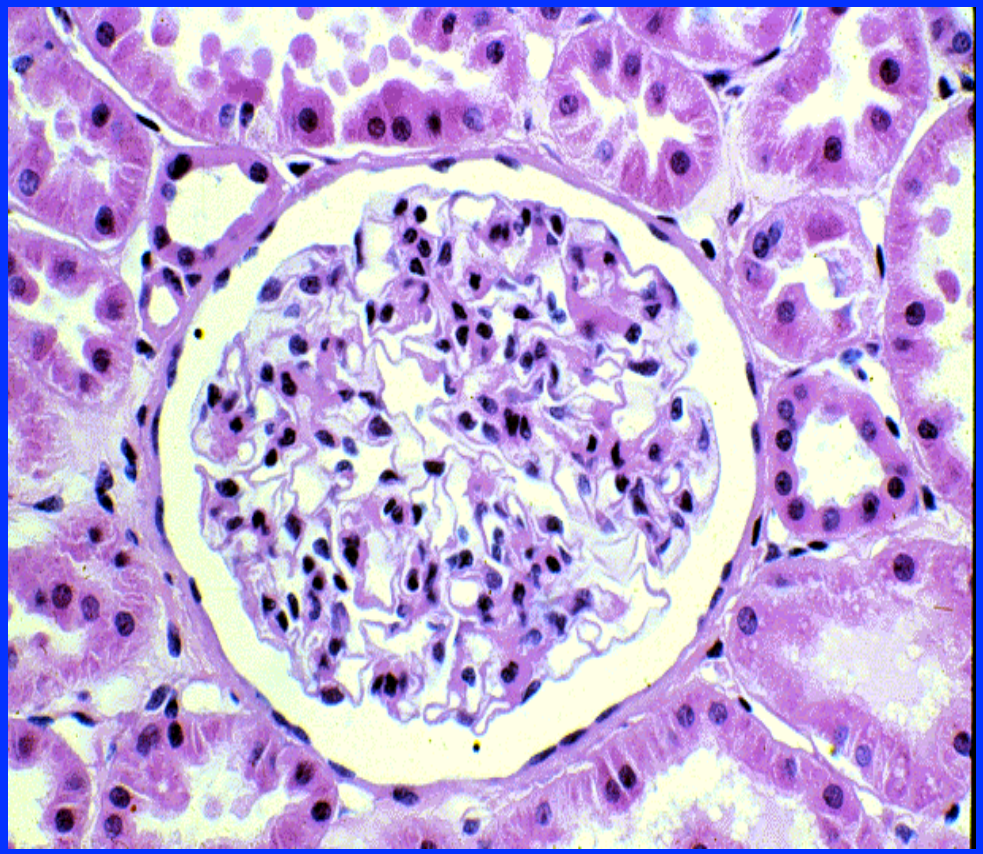
- **Serum albumin concentration at the time of diagnosis** (not the degree of proteinuria).
- A **serum albumin concentration ≤2.8 g/dL** (9.4 % vs 3.2 %, adjusted RR 2.5)
- ↑ risk 2-fold for every 1 g/dL (10 g/L) reduction in serum albumin below this threshold.

Συχνότητα αιτίων νεφρωσικού συνδρόμου κατά ηλικία (κατά προσέγγιση)

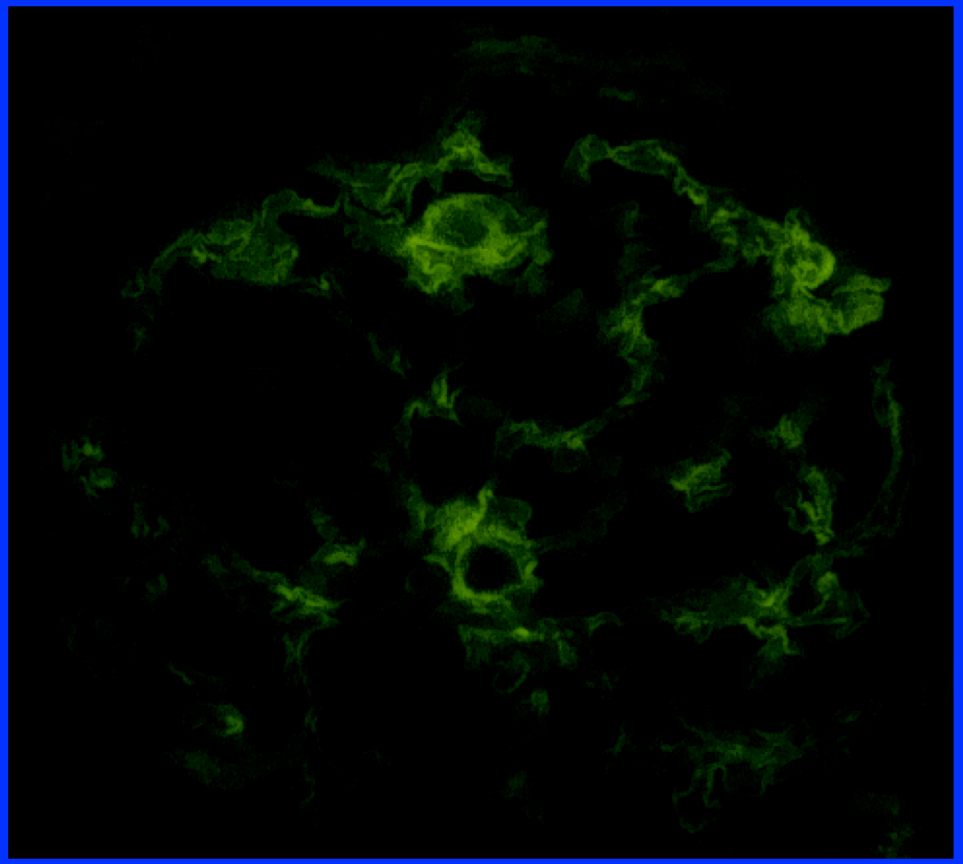


Νόσος ελαχίστων αλλοιώσεων

Φωτονικό μικροσκόπιο

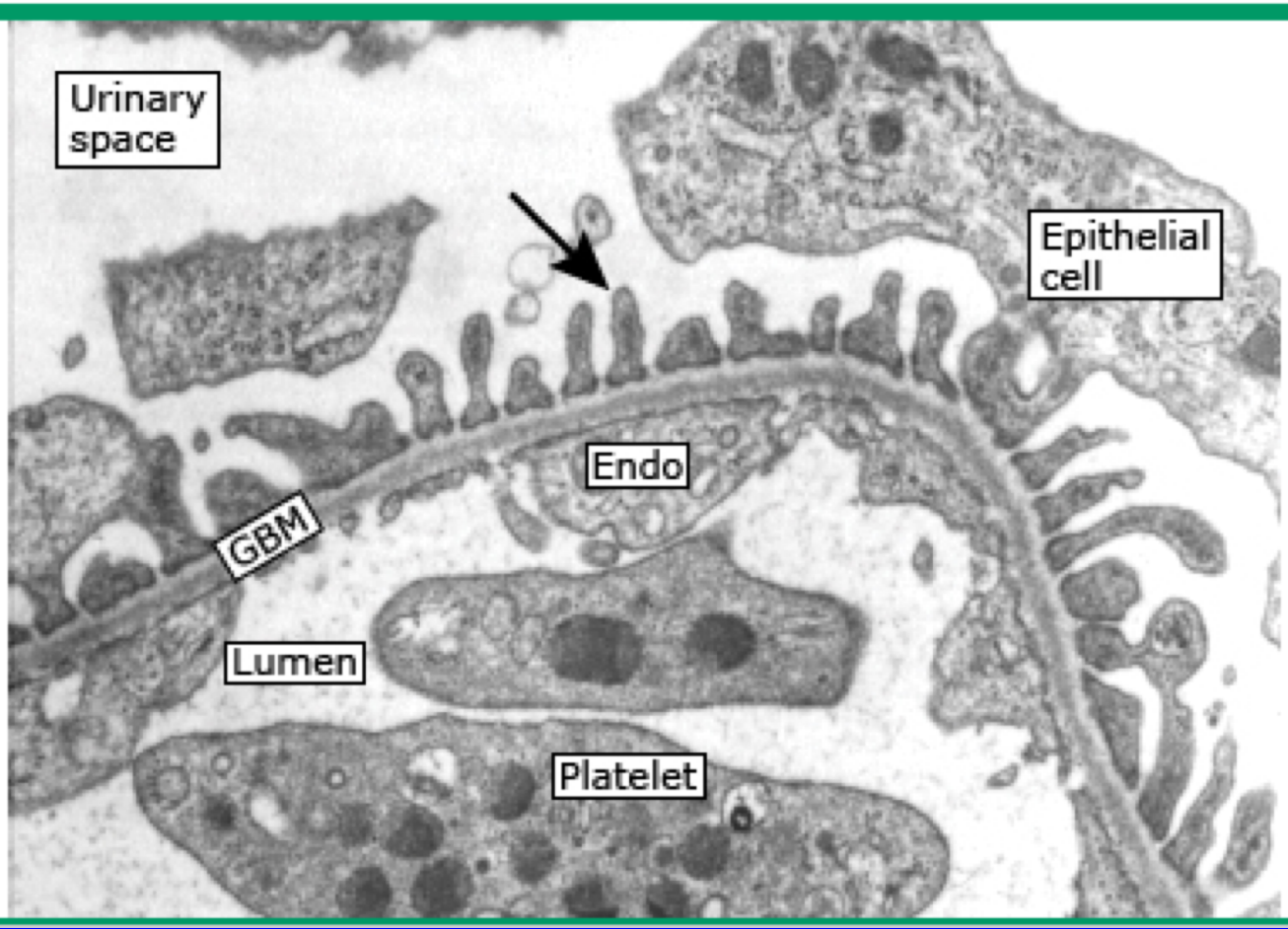


Ανοσοφθορισμός

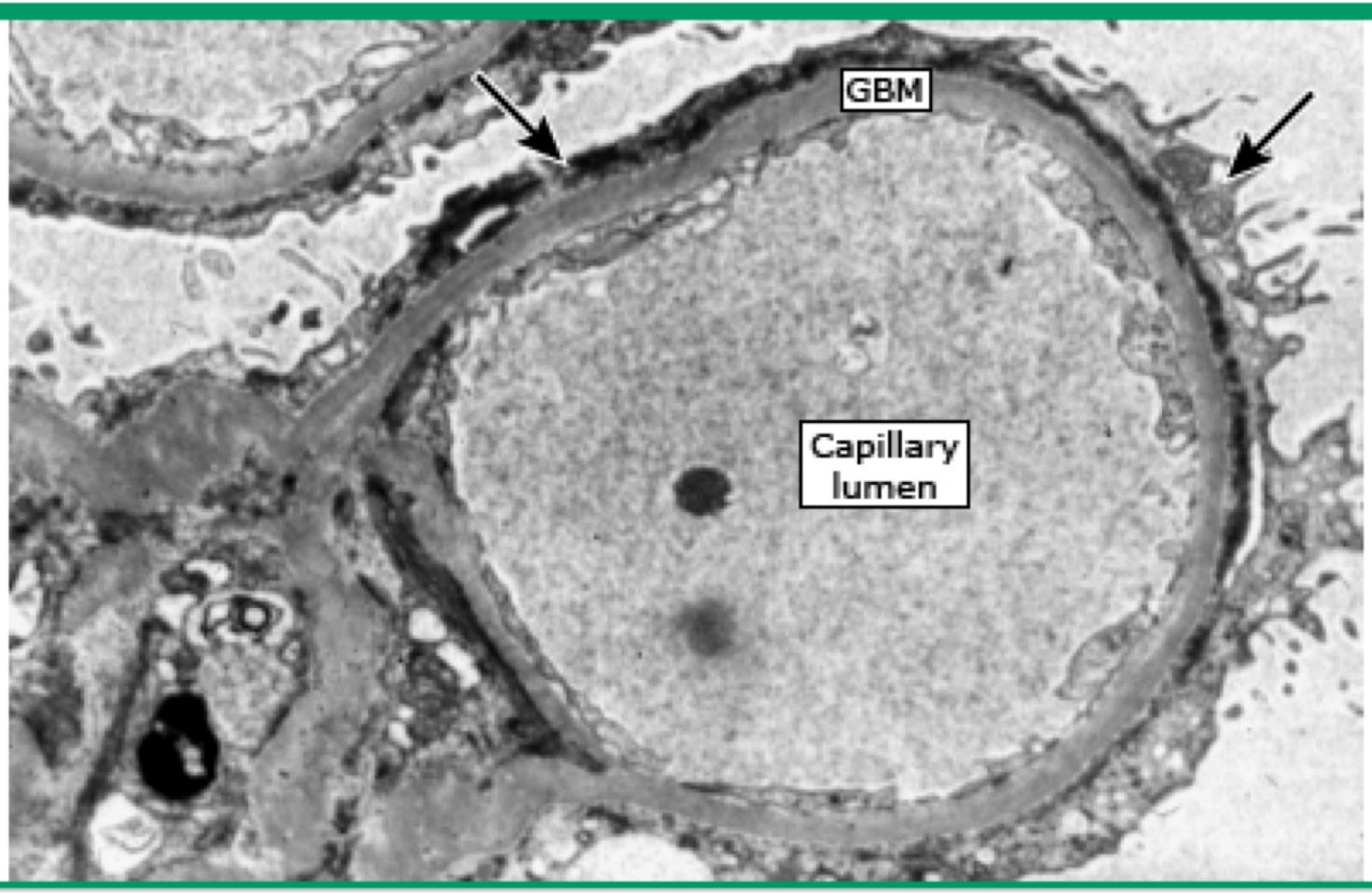


Ελάχιστες ή καθόλου βλάβες στο φωτονικό μικροσκόπιο και τον ανοσοφθορισμό.

Electron micrograph of a normal glomerulus

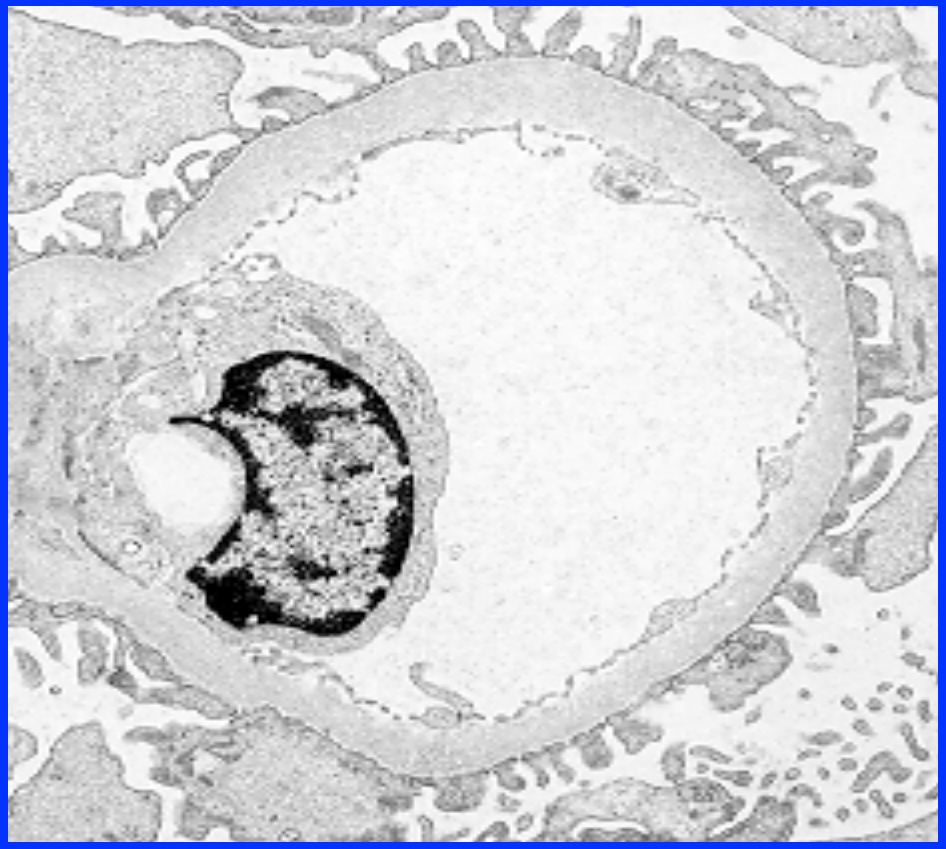


Electron microscopy in minimal change disease

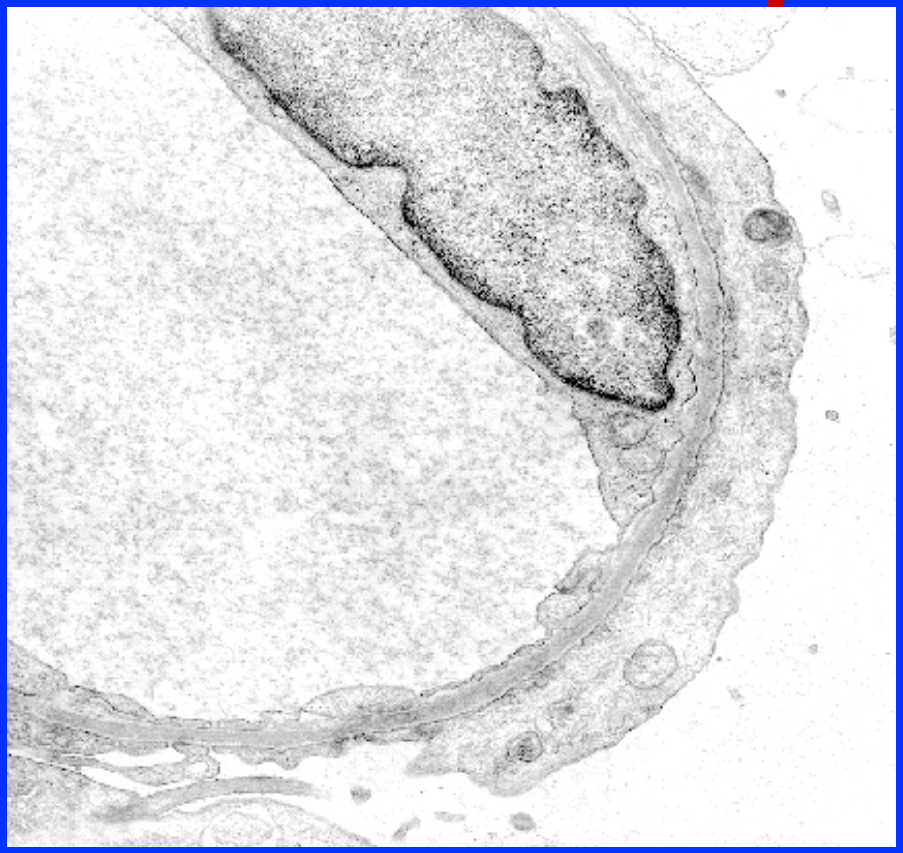


Νόσος ελαχίστων αλλοιώσεων
Ηλεκτρονικό μικροσκόπιο

Φυσιολογικό



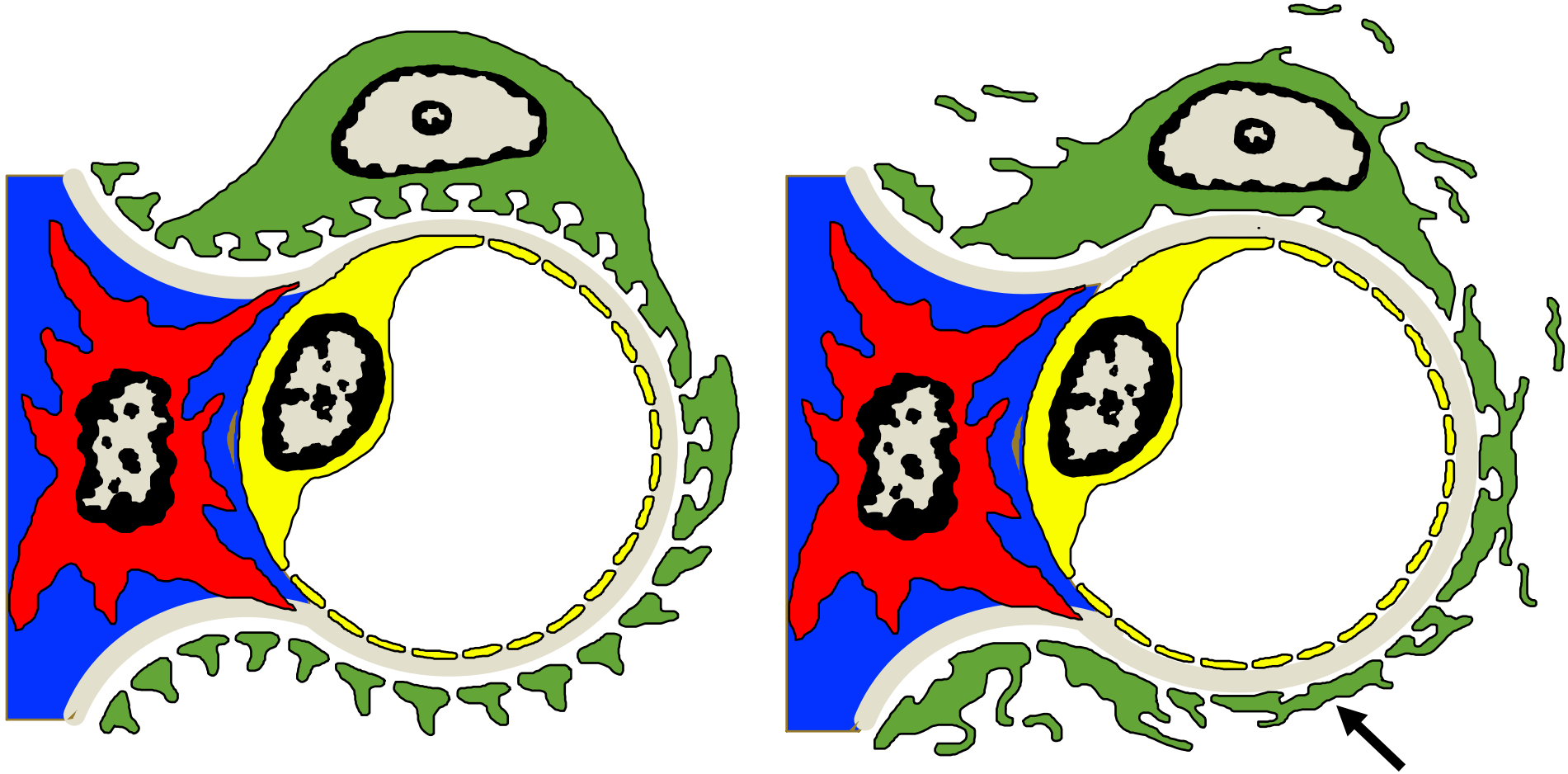
Σύντηξη προδοειδών προσεκβολών



Ιστοπαθολογία: Διάχυτη σύντηξη των ποδοειδών προσεκβολών των ποδοκυττάρων

Φυσιολογικό τριχοειδές

Νόσος ελαχίστων αλλοιώσεων



Σύντηξη των ποδοειδών προσεκβολών

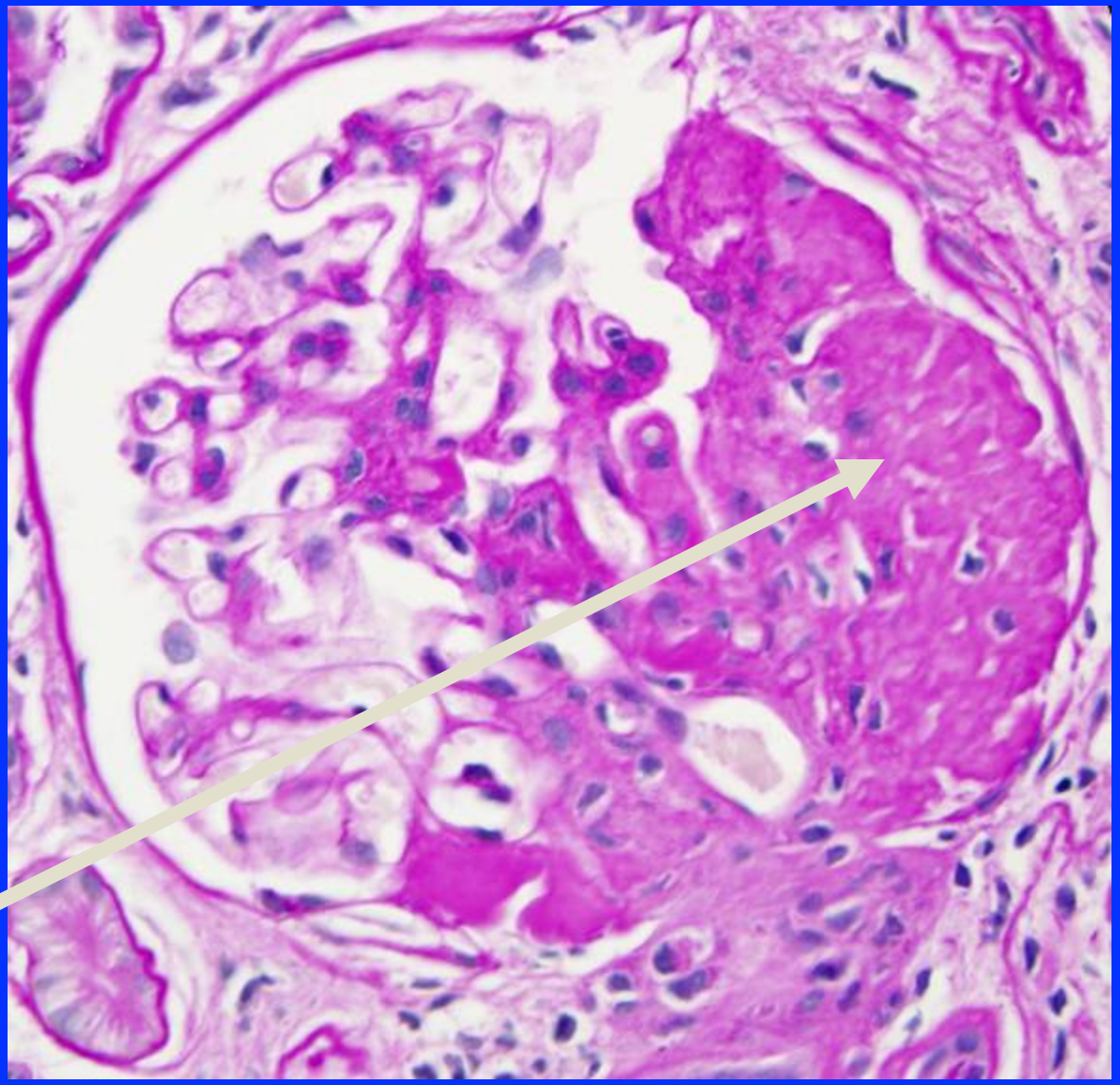
Εστιακή Τμηματική Σπειραματοσκλήρυνση

- Η πιο συχνή αιτία νεφρωσικού συνδρόμου σε African-Americans
- Πρωτοπαθής (ιδιοπαθής) σπειραματική πάθηση ή
- Δευτεροπαθής (π.χ παχυσαρκία, HIV λοίμωξη, και κληρονομικές γενετικές διαταραχές).
- Ιστοπαθολογικά και κλινικά χαρακτηρίζεται από ετερογένεια

Εστιακή Τμηματική Σπειραματοσκλήρυνση

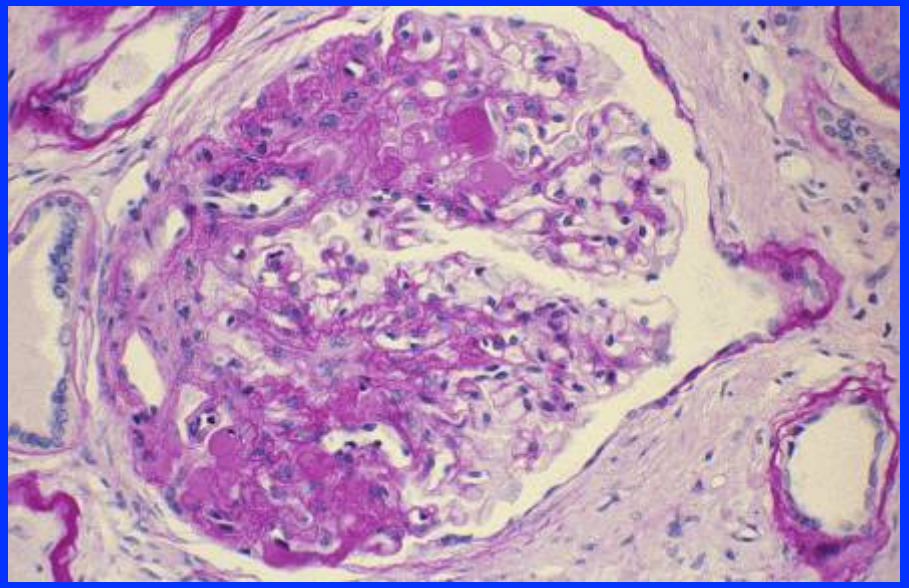
Early phase histology:

- Lesion in some but not all glomeruli (**focal**) and
- In some but not all portions of the glomerular tuft (**segmental**) .
- The lesions often included deposition of increased extracellular matrix material **(sclerosis).**



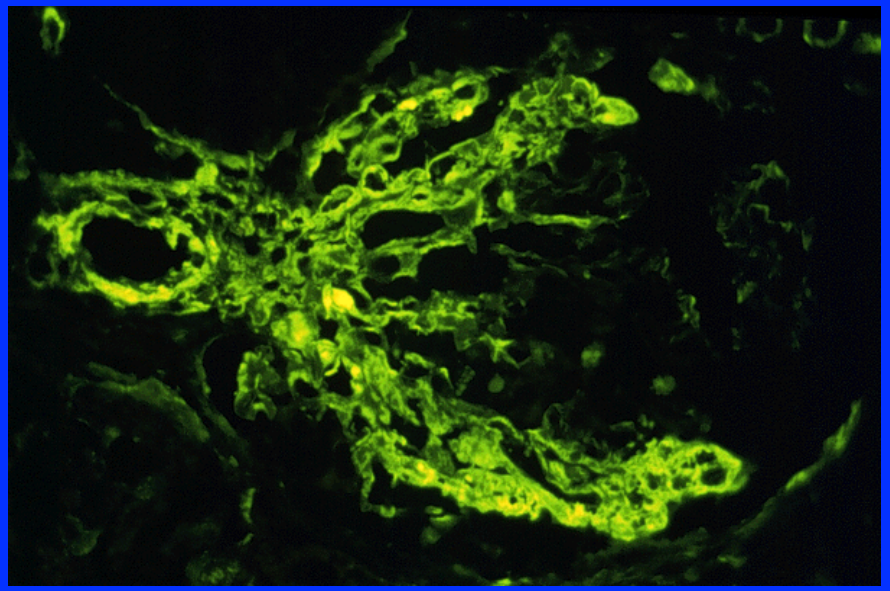
Εστιακή Τμηματική Σπειραματοσκλήρυνση (ΕΤΣΚ)

Φωτονικό μικροσκόπιο (PAS)



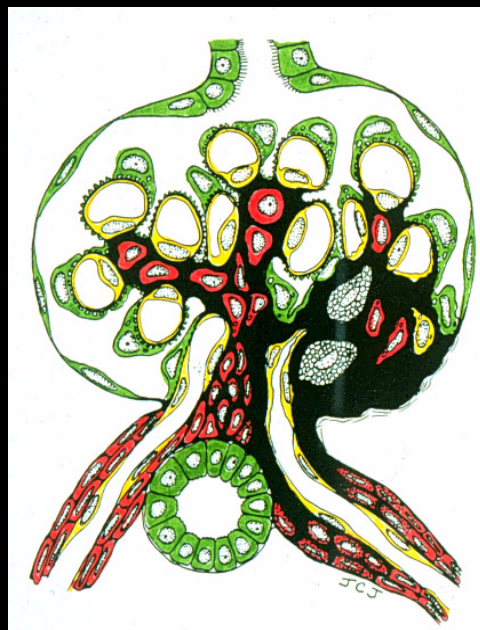
Τμηματική σκλήρυνση

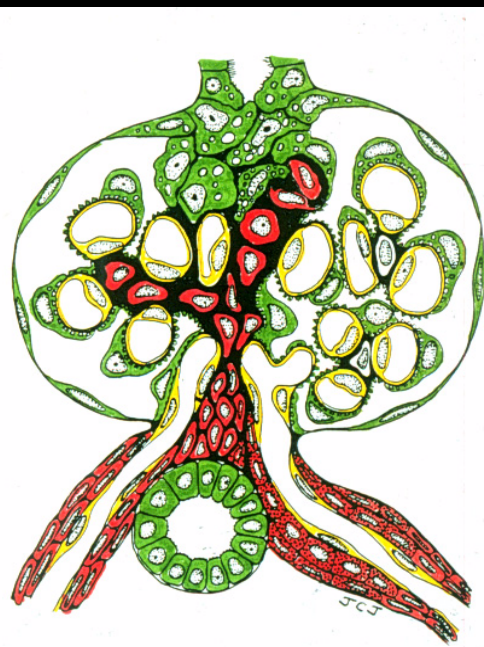
Ανοσοφθορισμός (C3)

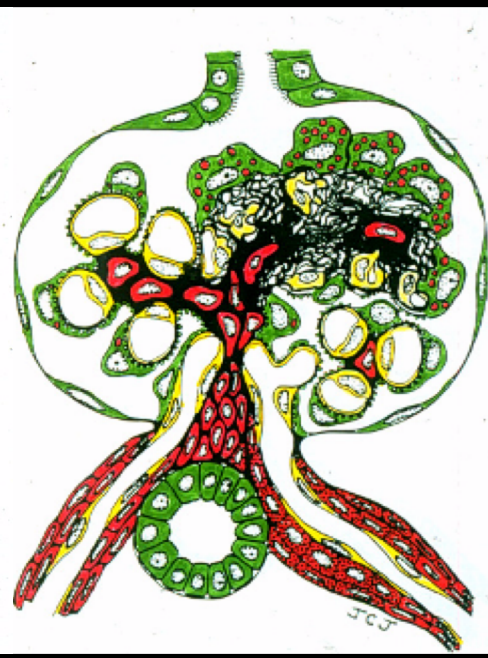


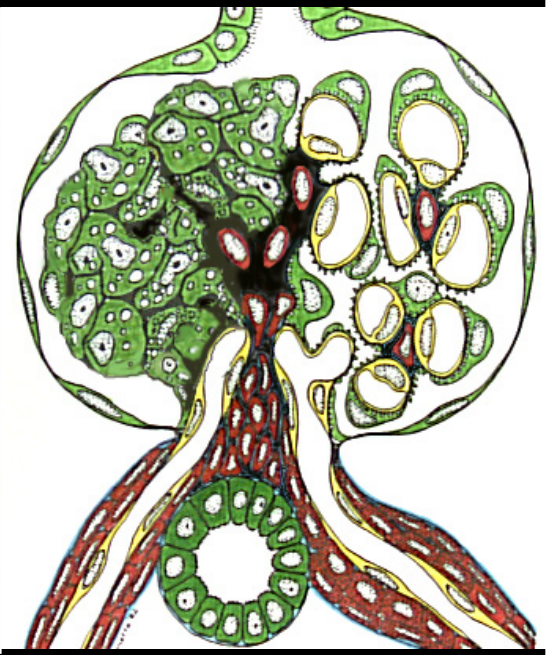
Παγίδευση IgM and C3 στις περιοχές της σκλήρυνσης

Ιστολογικοί Υπότυποι ΕΤΣΚ

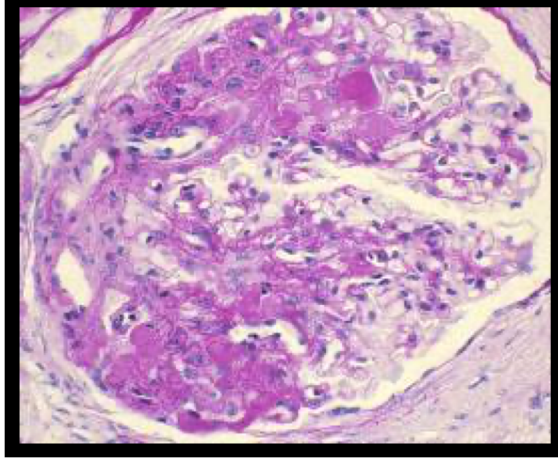


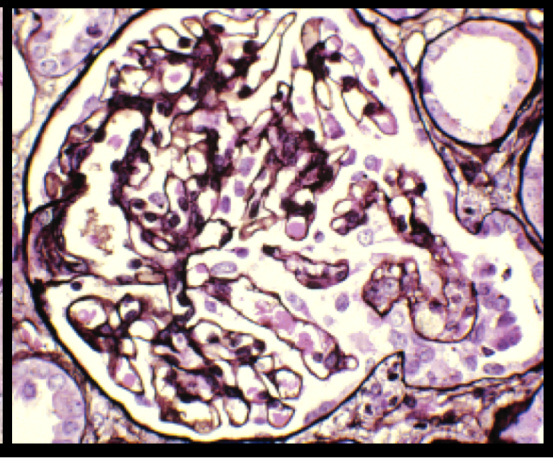


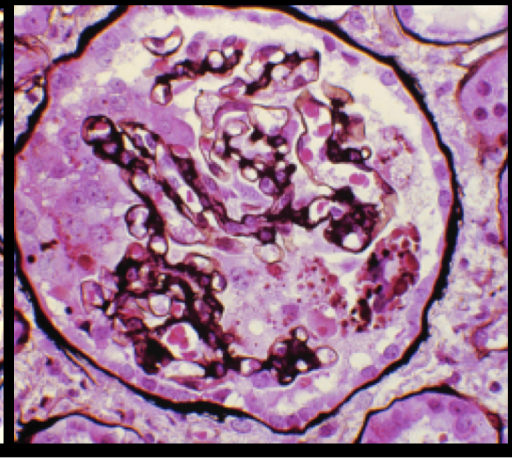


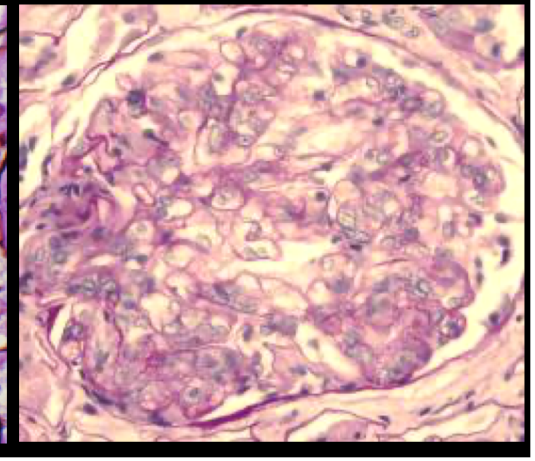


Perihilar | **Tip Lesion** | **Collapsing** | **Cellular**









- **PRIMARY (IDIOPATHIC) FSGS**
- **SECONDARY FSGS**
  - **VIRUS-ASSOCIATED**
    - HIV-1 (“HIV-associated nephropathy”)
    - Parvovirus B-19
  - **FAMILIAL FSGS**
    - Mutations in α-actinin 4 gene
    - Mutations in NPHS2 gene for podocin
    - Mutations in TRPC6 gene for a cation channel
  - **DRUG TOXICITY**
    - Heroin (“Heroin nephropathy”)
    - Pamidronate
    - Interferon-α
  - **MEDIATED BY ADAPTIVE STRUCTURAL RESPONSES**
    - Reduced renal mass
    - Obesity
    - Cyanotic congenital heart disease
    - Sickle cell anemia

FSGS: Diagnostic concerns in FSGS:

- Sampling error (FSGS vs. minimal change disease)
- Distinguishing primary and secondary FSGS
- Identifying FSGS with collapsing glomerulopathy

- ➢ Primary may respond to immunosuppressive agents (glucocorticoids)
- ➢ Secondary disease is best treated with modalities aimed at lowering the intraglomerular pressure, such as angiotensin-converting enzyme inhibitors.

FSGS: Primary vs. secondary

2 major features distinguish it from primary FSGS:

- Tendency toward **collapse** and **sclerosis** of the entire glomerular tuft, rather than segmental injury
- Severe tubular injury with proliferative microcyst formation and tubular degeneration.
- These patients often have rapidly progressive kidney failure.

FSGS : Primary vs. secondary

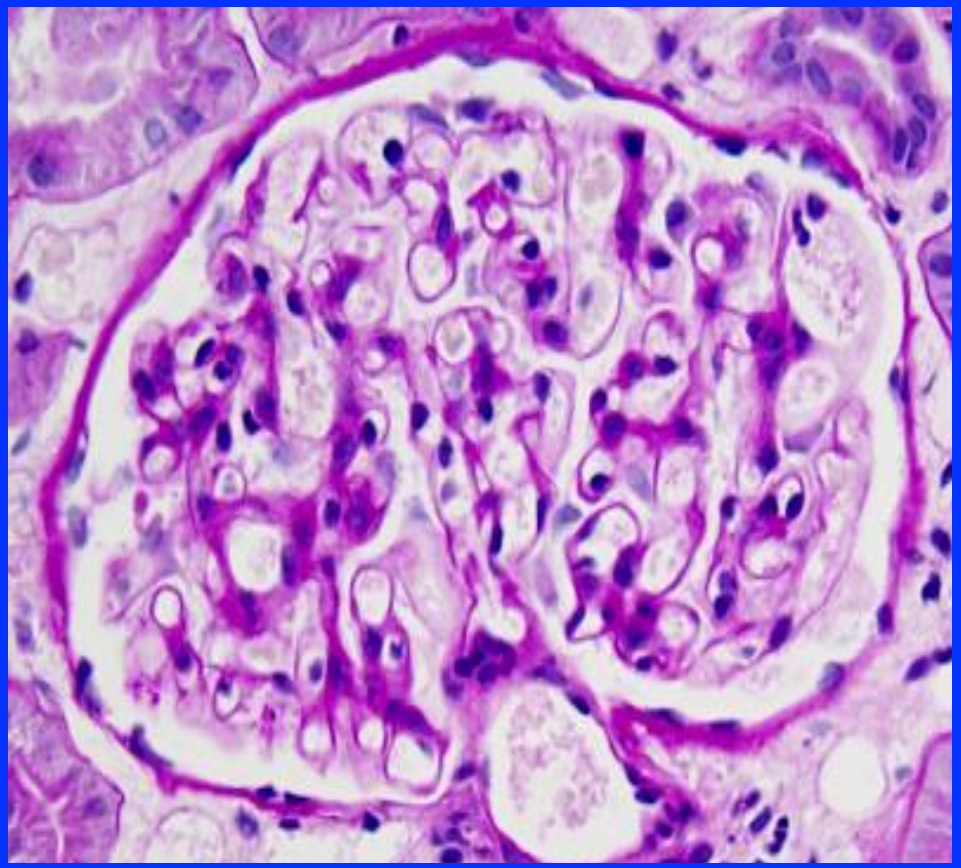
Primary: Acute onset of the nephrotic syndrome

Secondary:

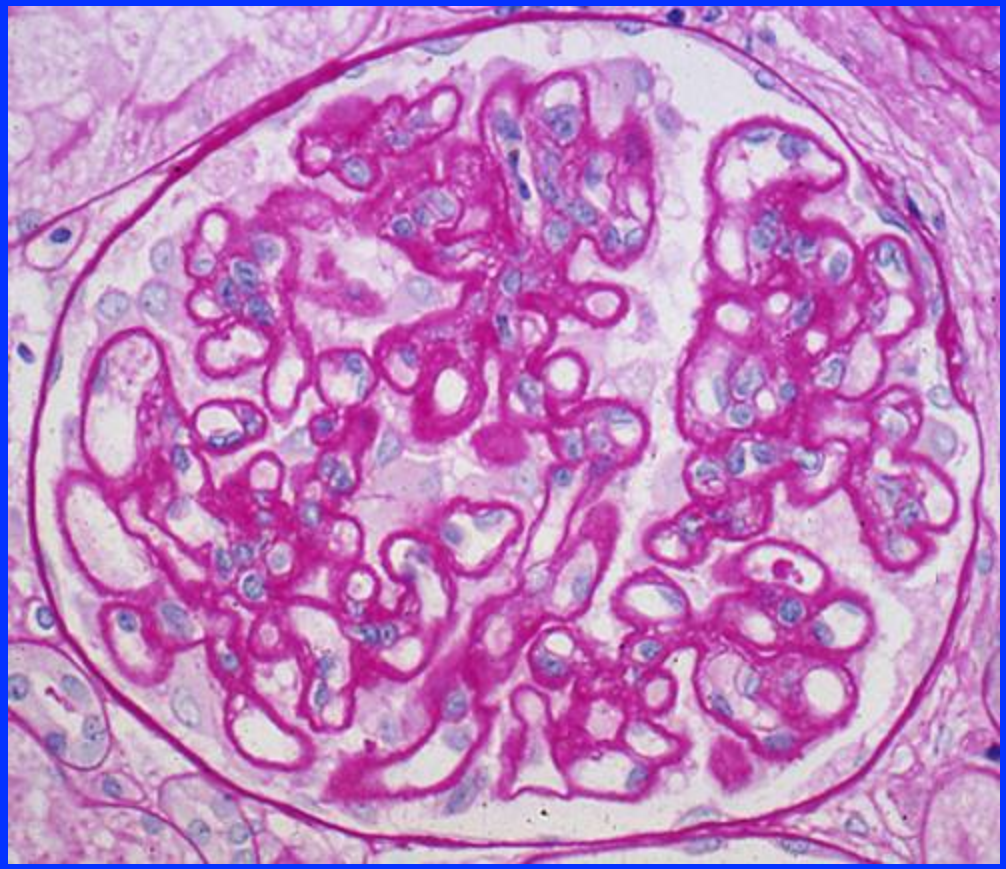
- ✓ Slowly increasing proteinuria and kidney function impairment over time are characteristic of the secondary disorders.
- ✓ Proteinuria in secondary FSGS is often non-nephrotic
- ✓ Even when protein excretion exceeds 3-4 g/day, both hypoalbuminemia and edema are unusual.

Μεμβρανώδης σπειραματοπάθεια

Πάχυνση του τοιχώματος των σπειραματικών τριχοειδών στο φωτονικό μικροσκόπιο χωρίς υπερκυτταρικότητα

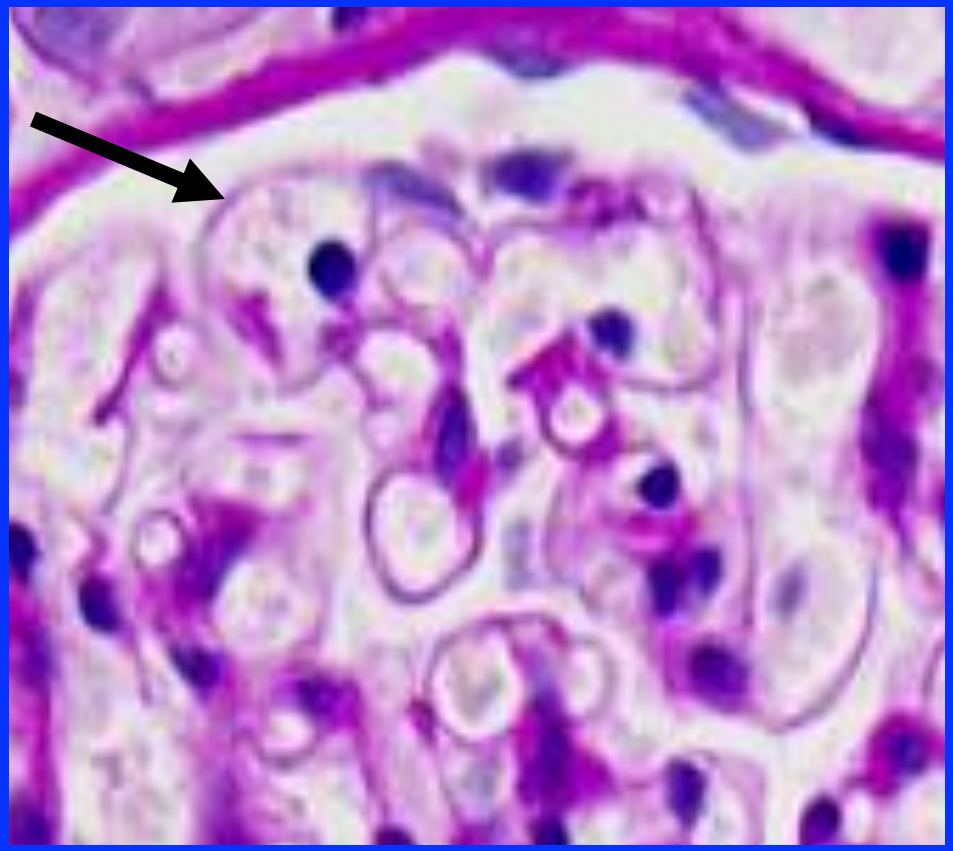


Φυσιολογικό

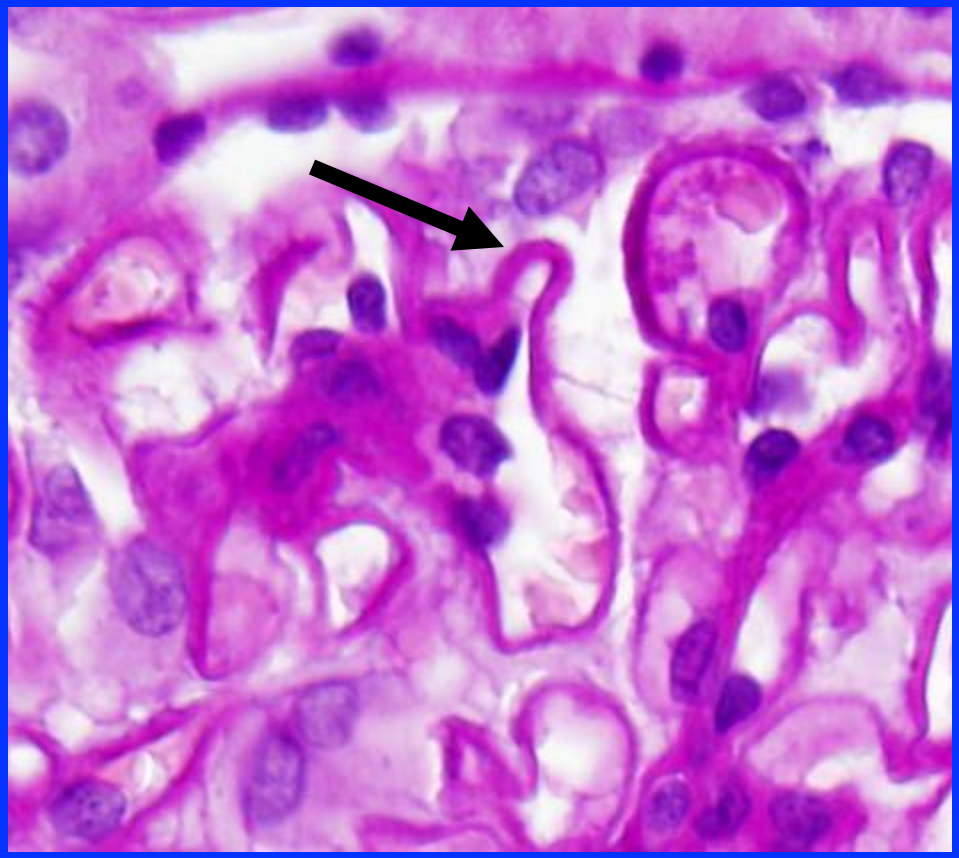


Μεμβρανώδης σπειραματοπάθεια

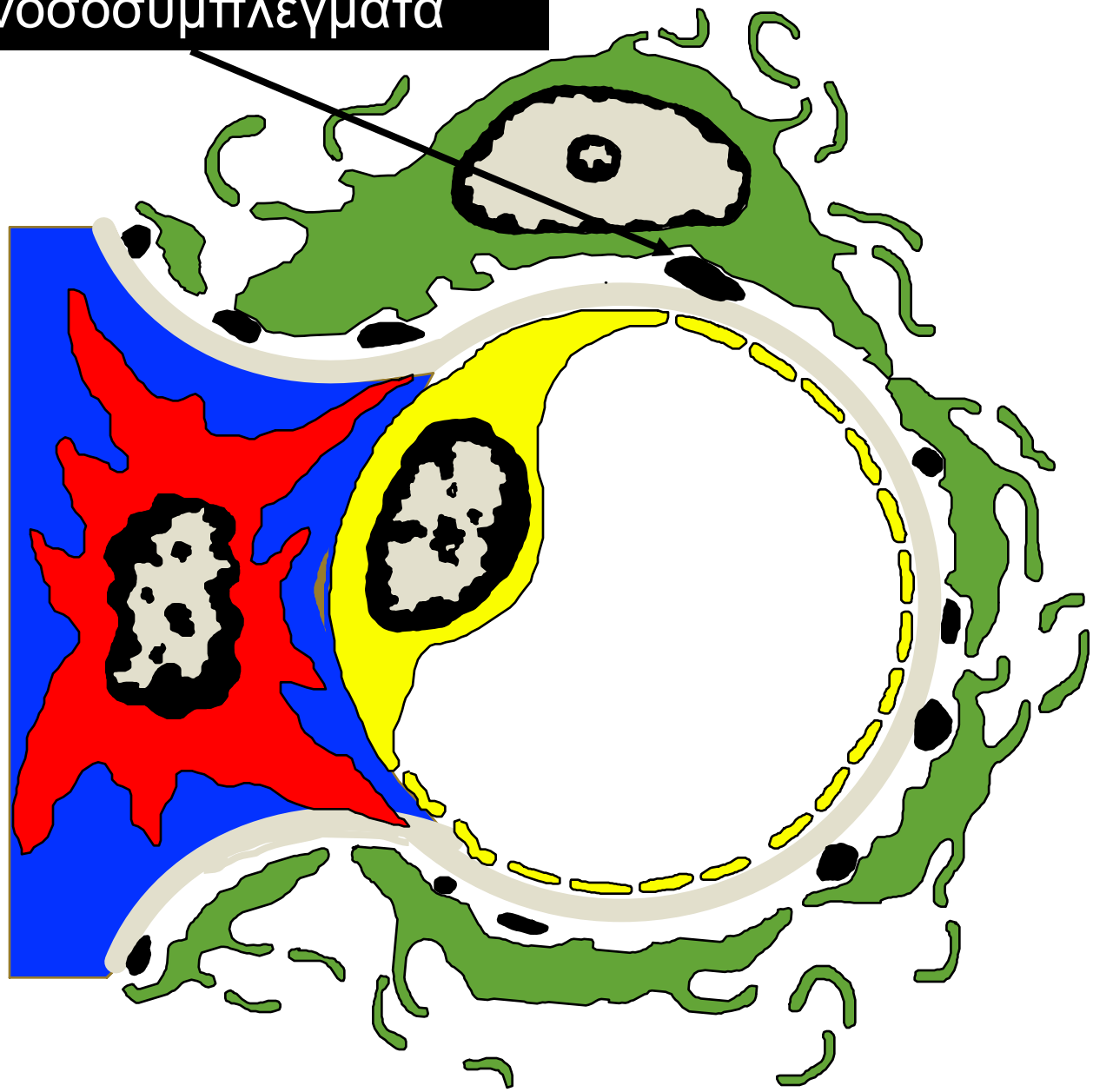
Φυσιολογικό πάχος τοιχώματος τριχοειδών



Μεμβρανώδης νεφροπάθεια με παχυσμένο τοίχωμα τριχοειδούς



Ανοσοσυμπλέγματα

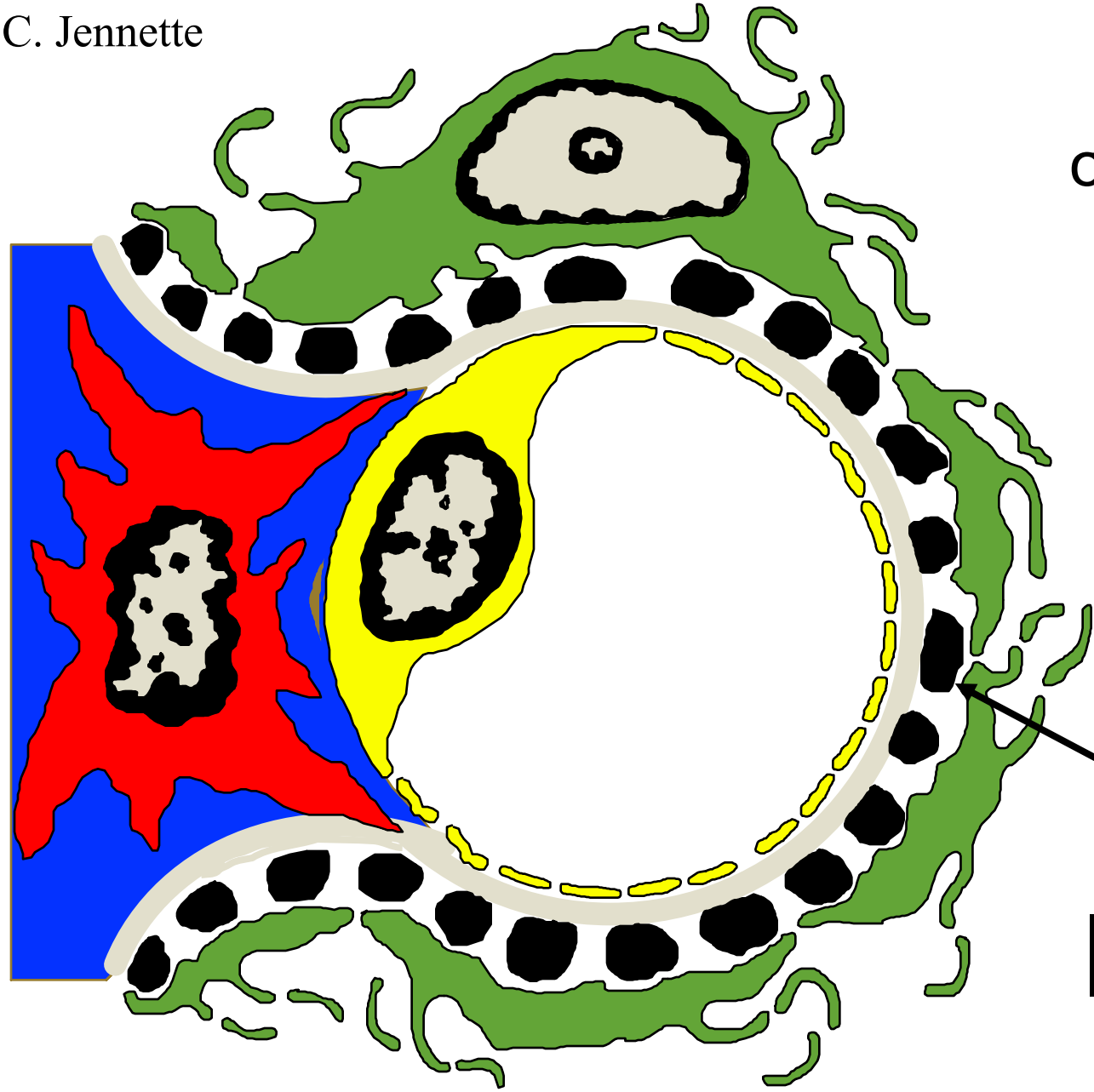


Η μεμβρανώδης νεφροπάθεια προκαλείται από την <u>άθροιση ανοσυμπλεγμάτων στον υποεπιθηλιακό χώρο</u> (=χώρος μεταξύ των ποδοκυττάρων και της σπειραματικής βασικής μεμβράνης)

J.C. Jennette

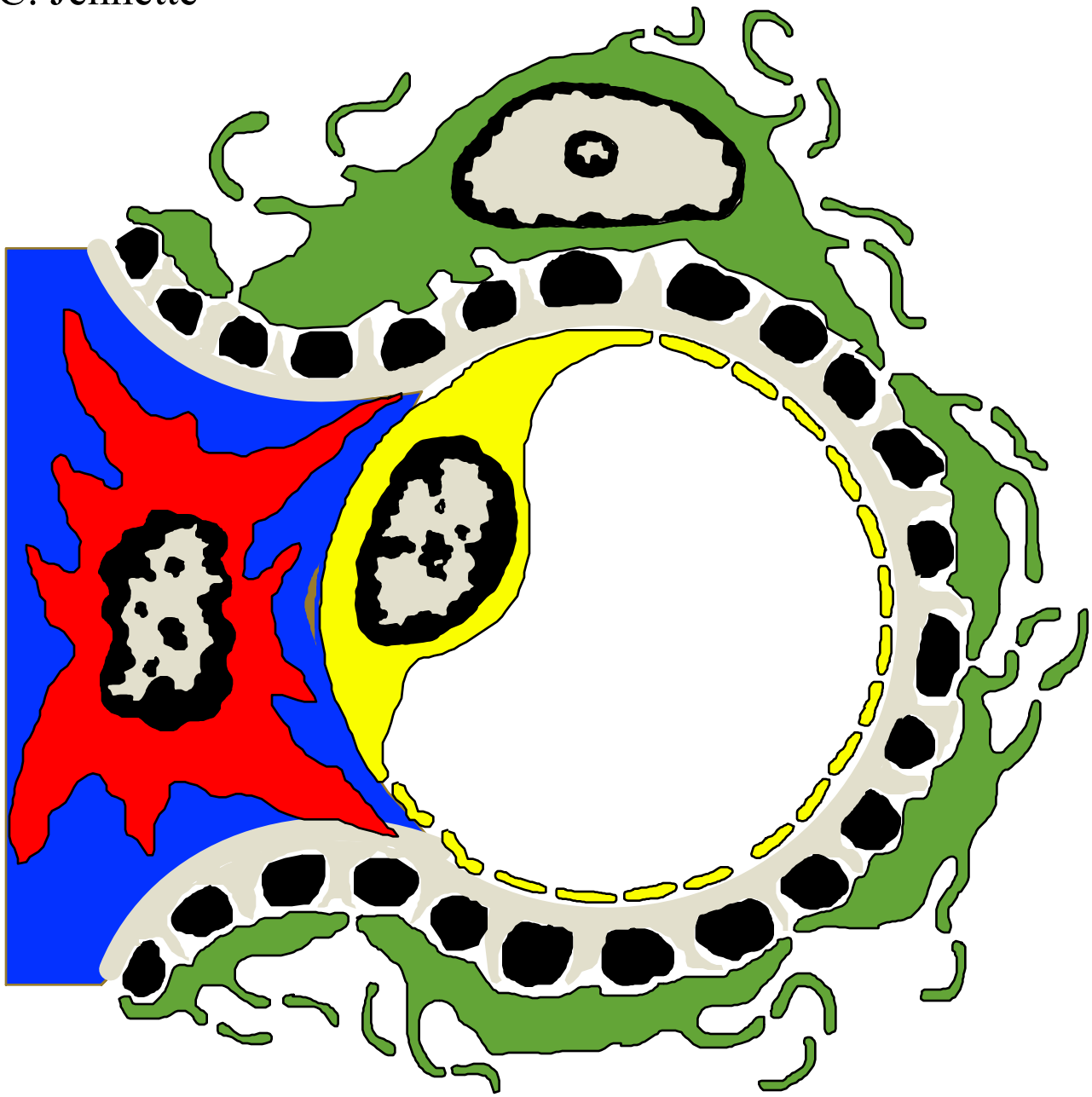
J.C. Jennette

Μεμβρανώδης σπειραματοπάθεια



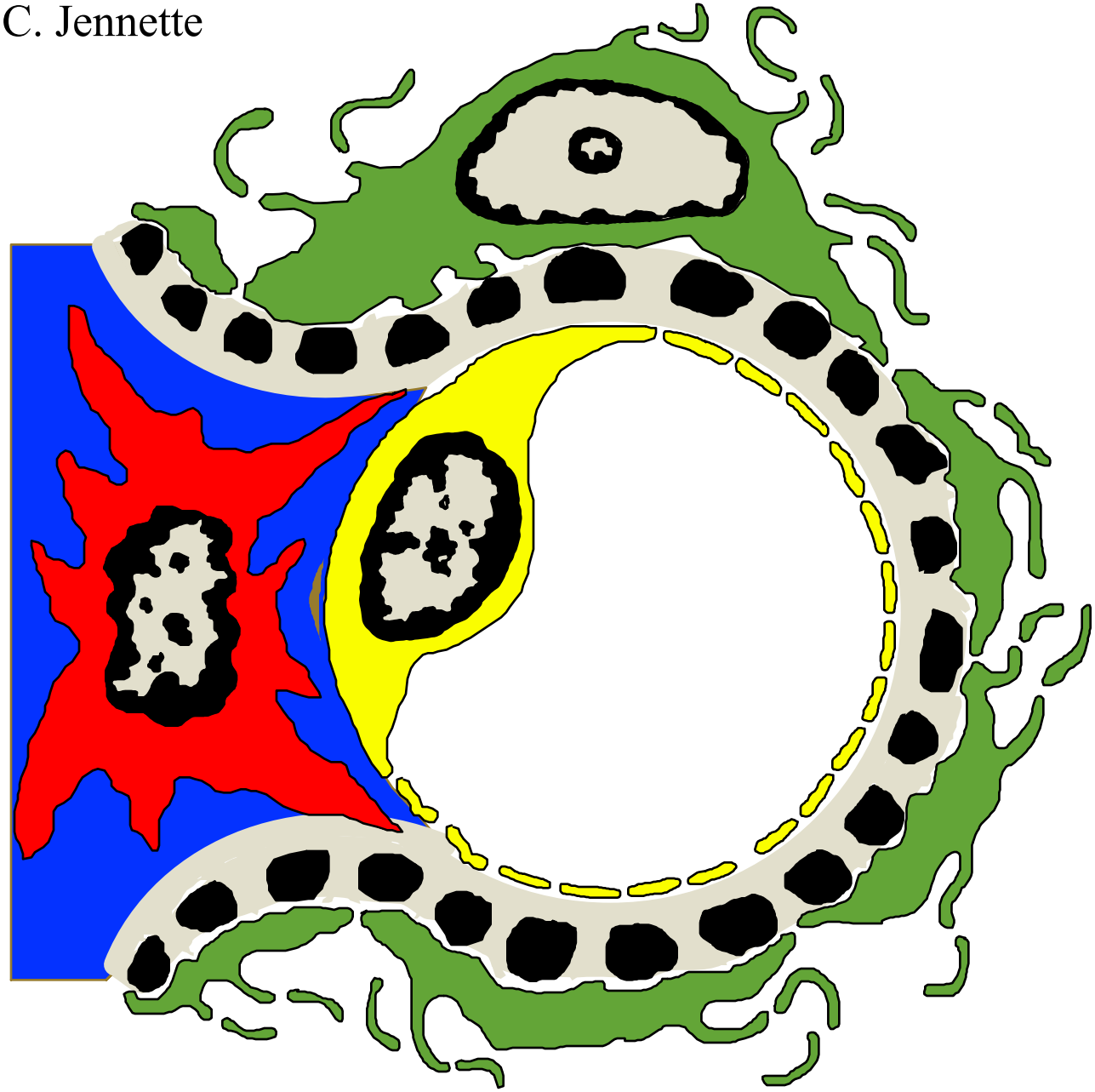
Ανοσοσυμπλέγματα

J.C. Jennette



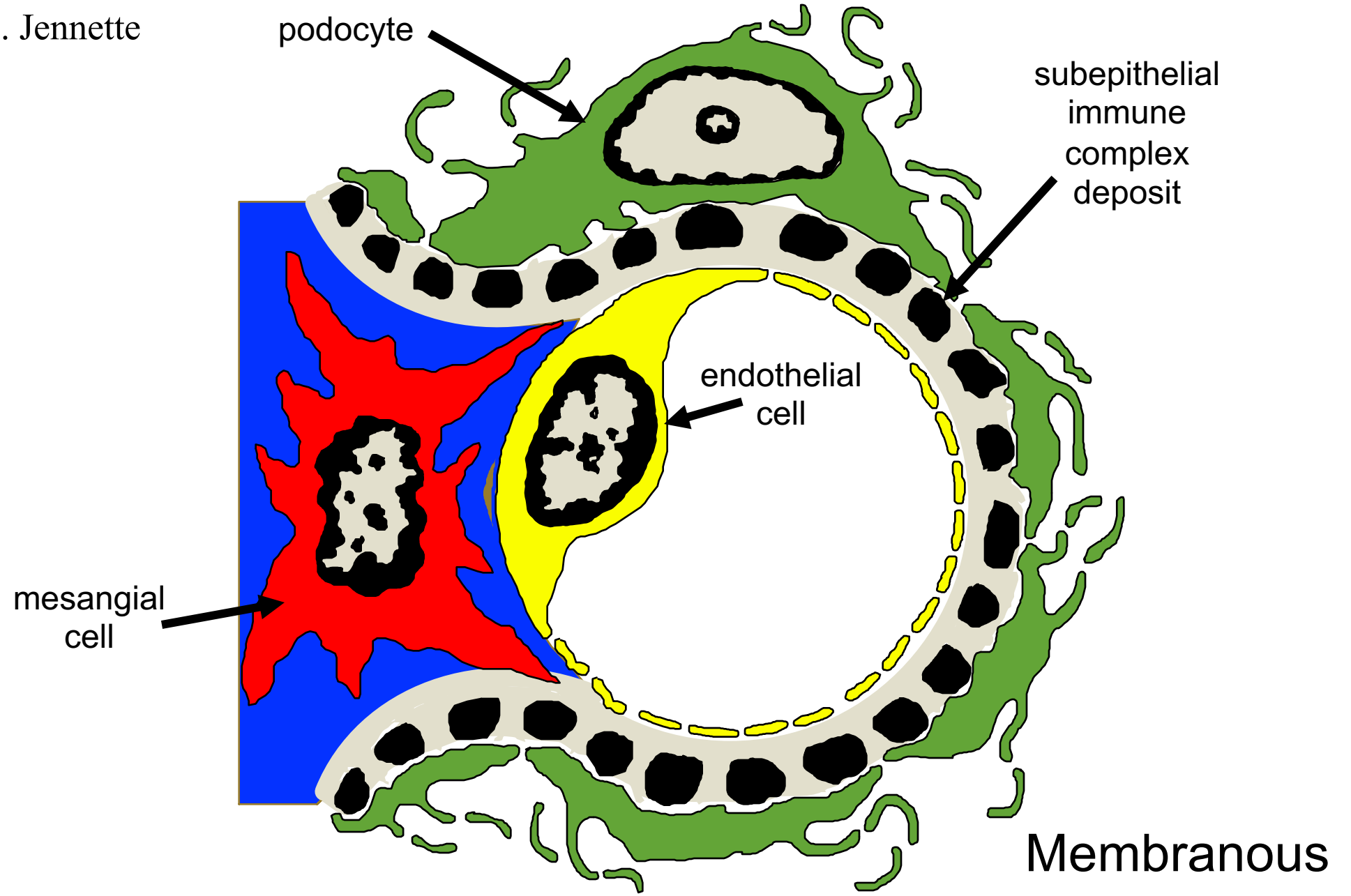
Membranous glomerulopathy

J.C. Jennette



Membranous glomerulopathy

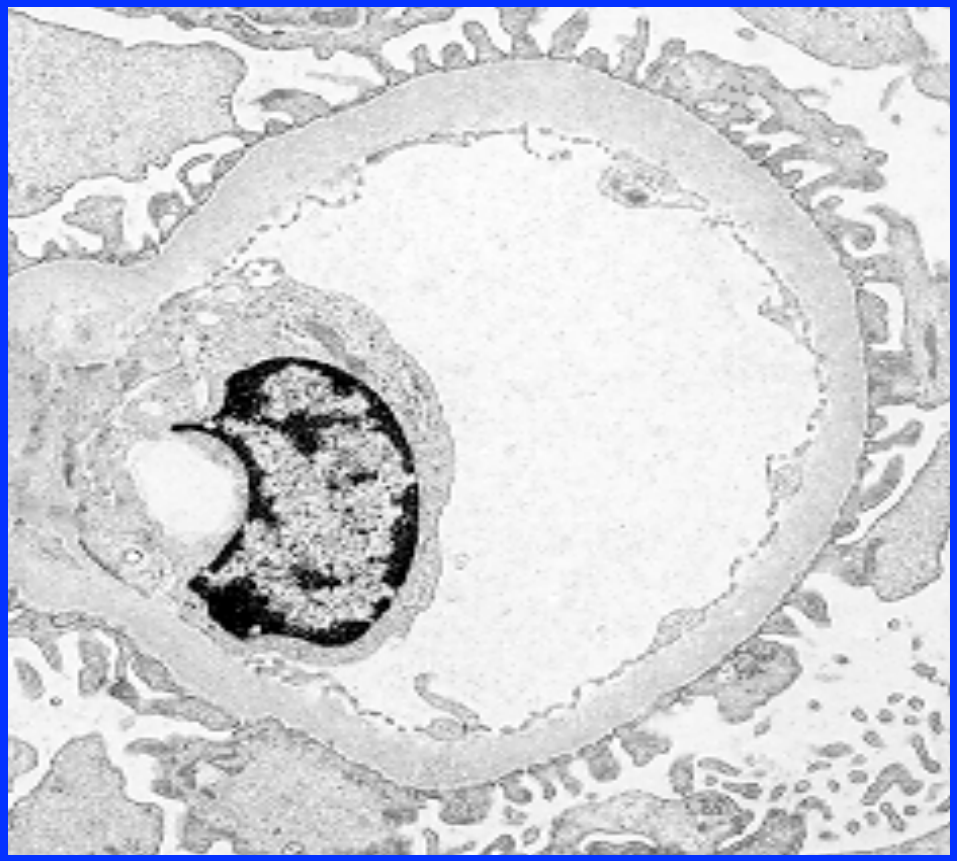
J.C. Jennette



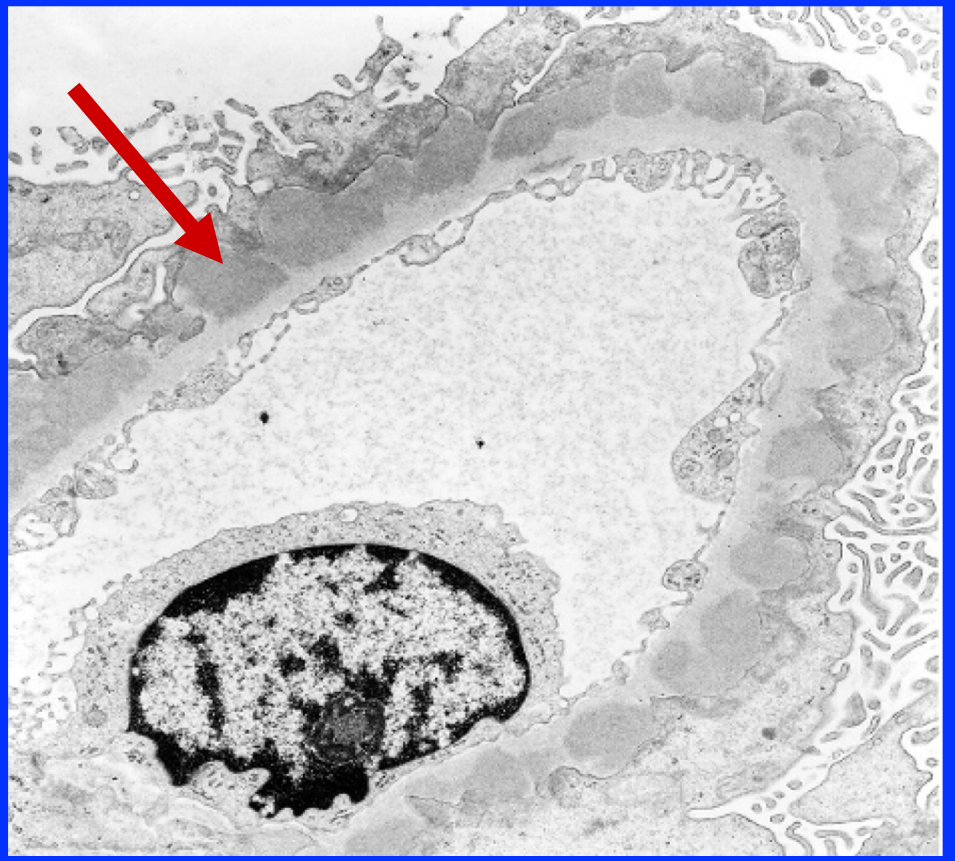
Membranous glomerulopathy

Μεμβρανώδης σπειραματοπάθεια-ΗΜ

Φυσιολογικό

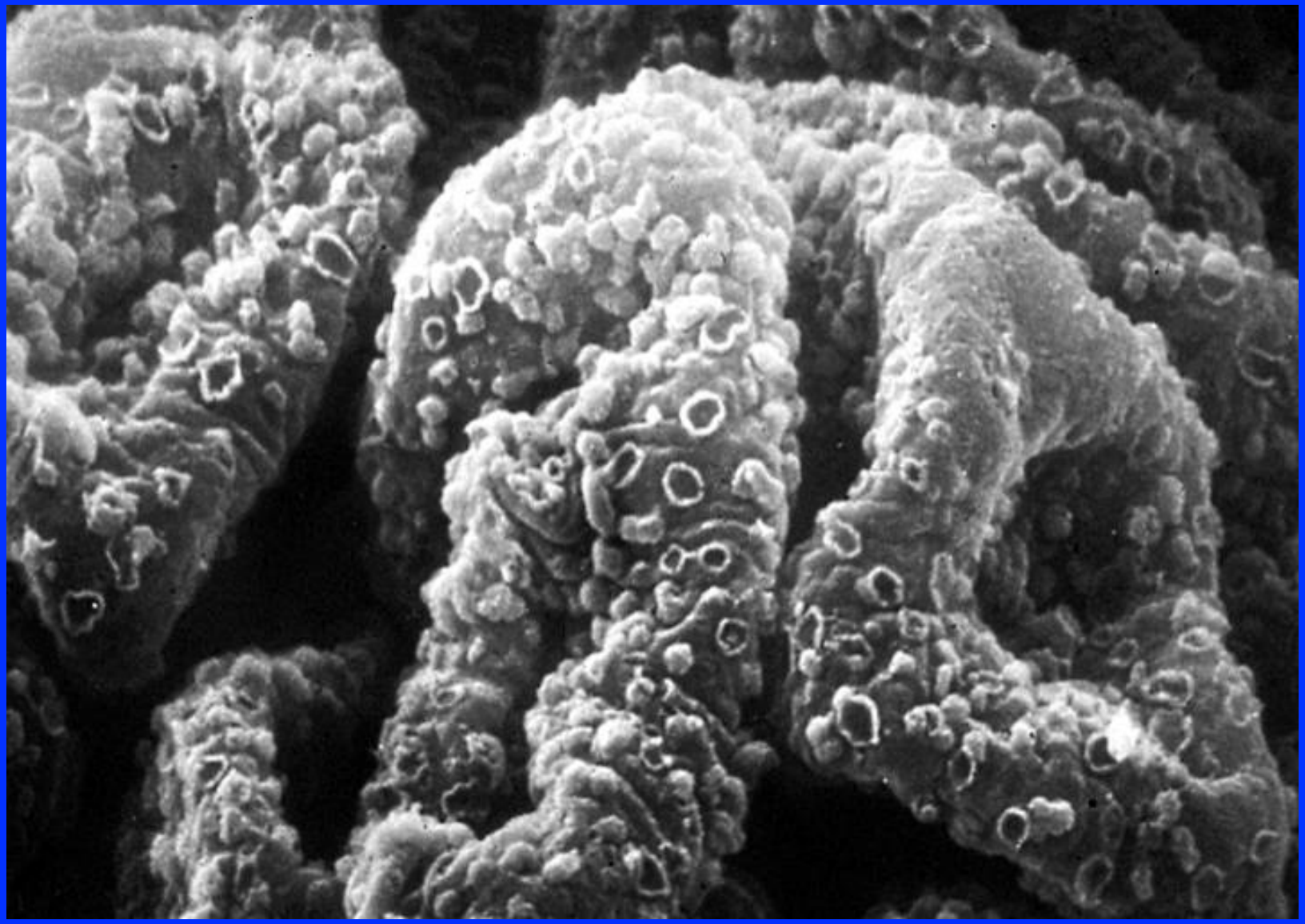


Μεμβρανώδης ΣΠ



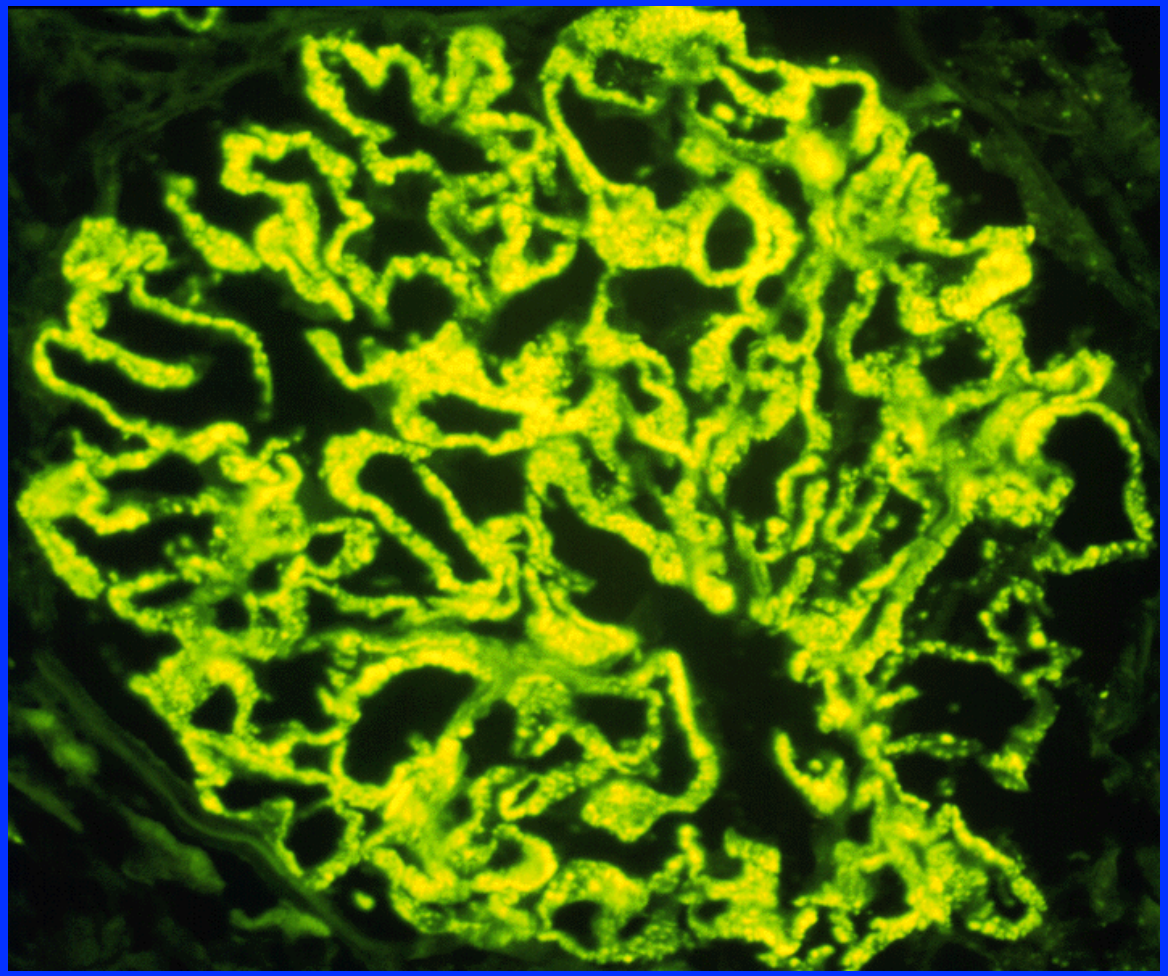
J.C. Jennette

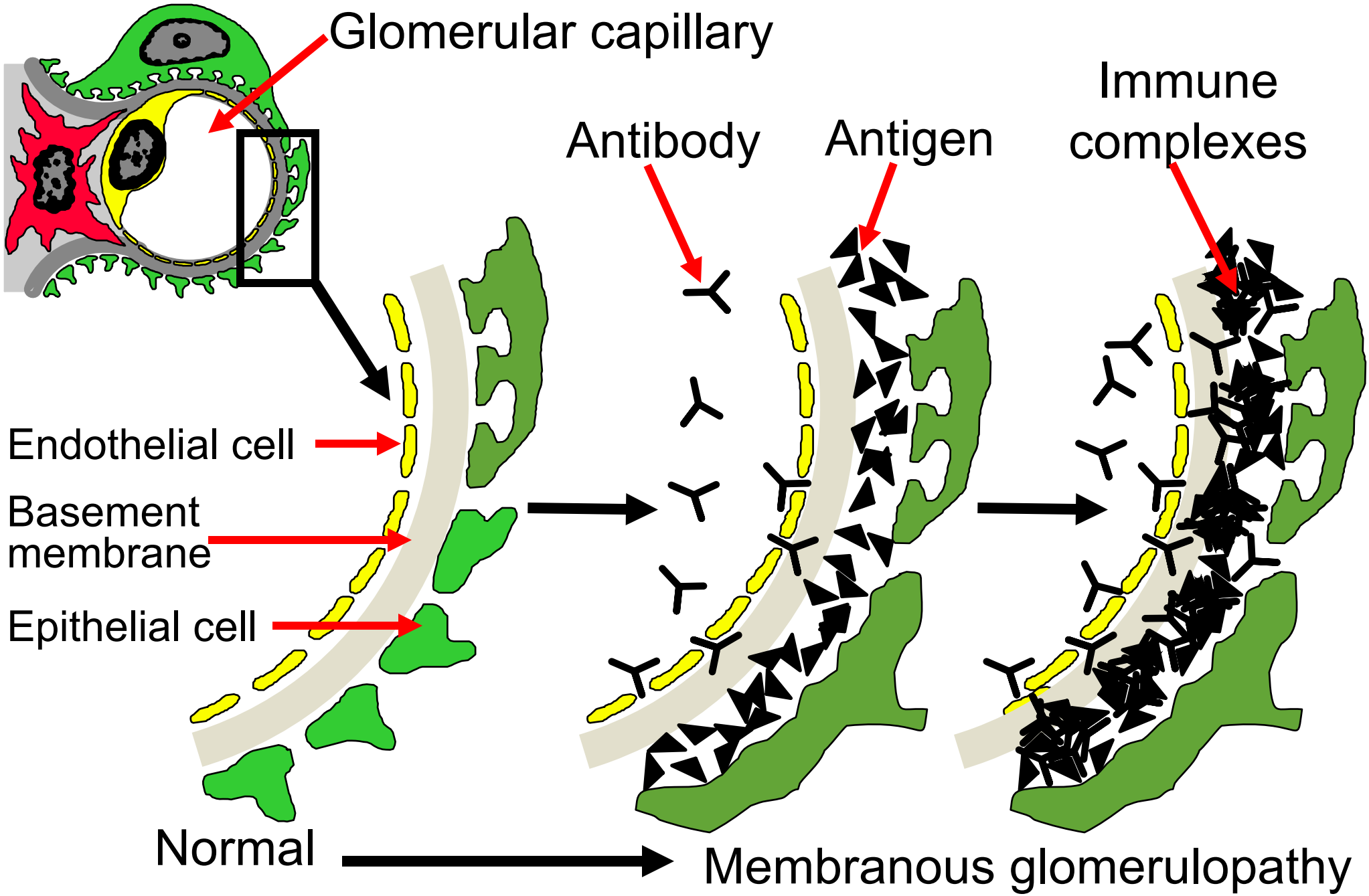
Ηλεκτρονικό Μικροσκόπιο: Ανοσοσυμπλέγματα στα τοιχώματα των σπειραματικών τριχοειδών



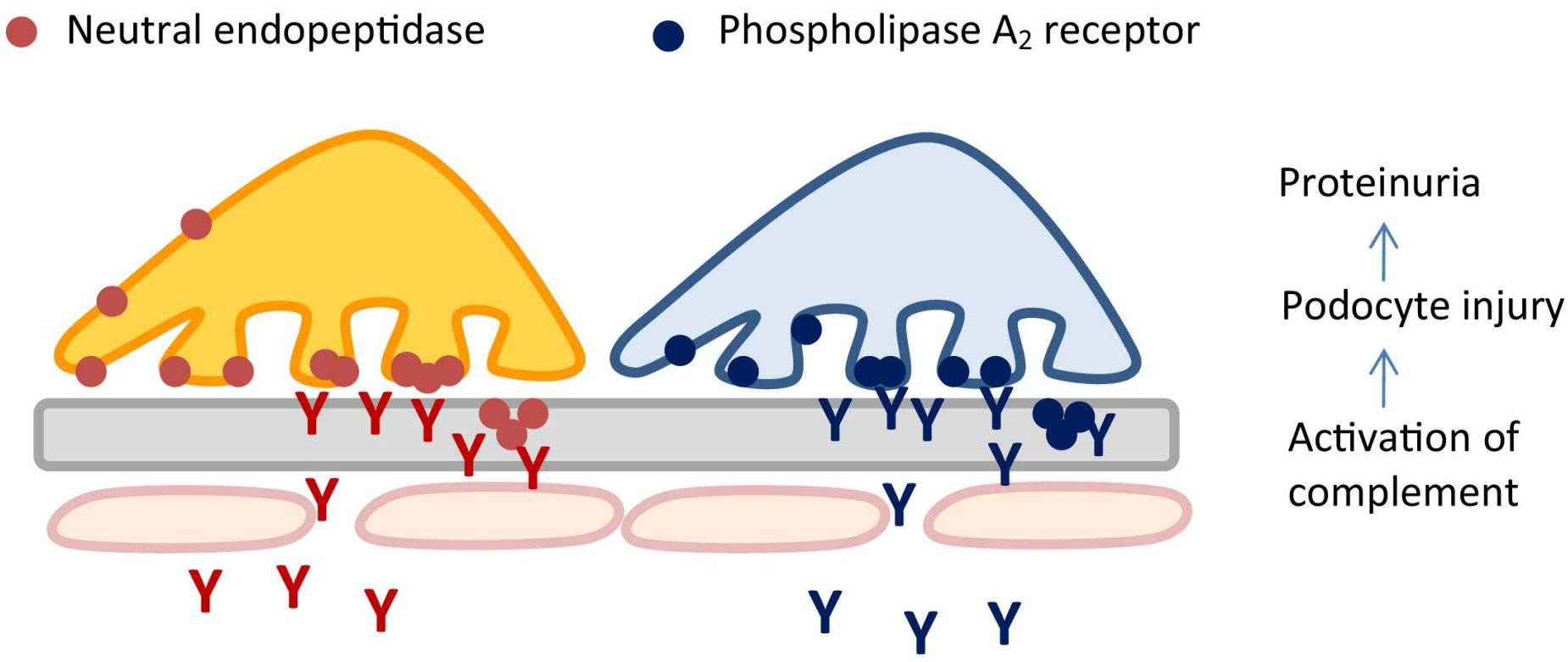
Μεμβρανώδης Σπειραματοπάθεια

Ανοσοφθορισμός- IgG ανοσοσφαιρίνη στα σπειραματικά τοιχώματα (κοκκιώδης)




Glomerular capillary
Antibody
Antigen
Immune complexes
Endothelial cell
Basement membrane
Epithelial cell
Normal
Membranous glomerulopathy

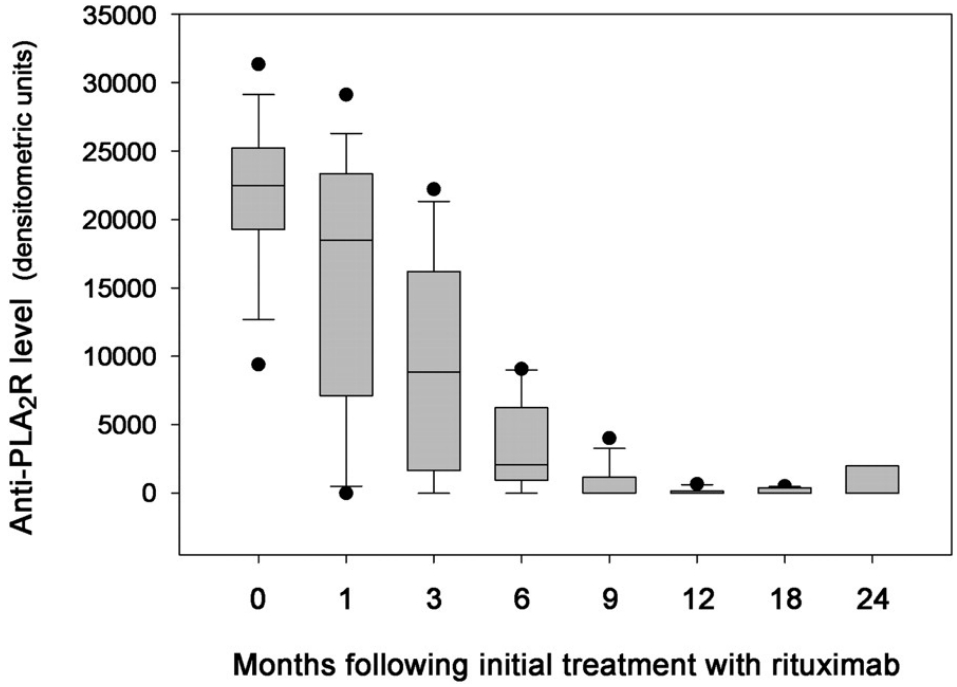
Anti-PLA_2R αντισώματα στην Ιδιοπαθή Μεμβρανώδη Νεφροπάθεια



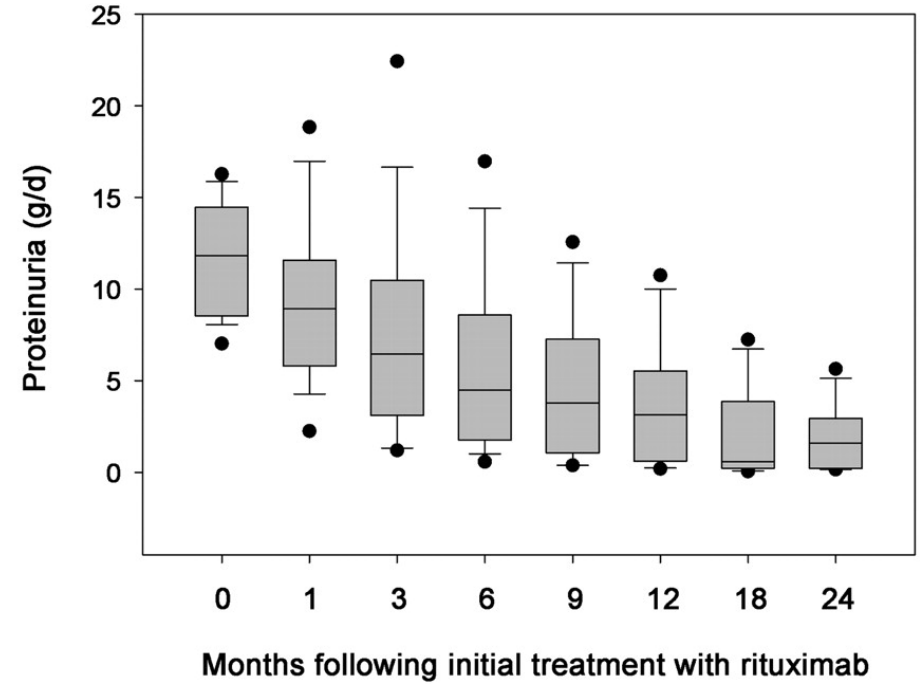
Beck LH Jr, NEJM, 2009

Η μείωση των Anti-PLA_2R αντισωμάτων είναι ταχύτερη από την μείωση της πρωτεινουρίας

Anti-PLA_2R



Proteinuria



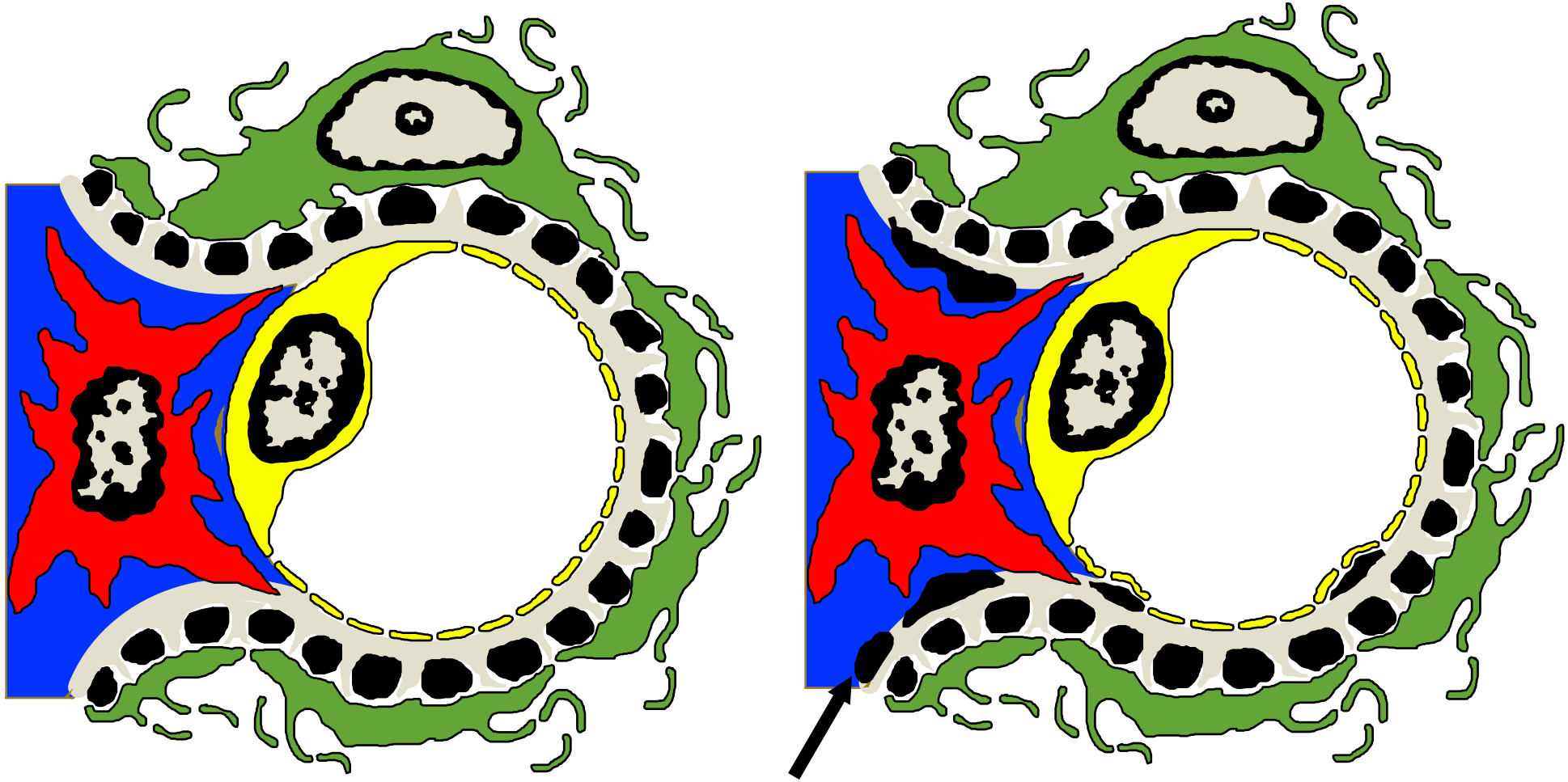
Beck L H et al. JASN 2011;22:1543-1550

Membranous Glomerulopathy

- **Ιδιοπαθής** (η πιο συχνή)
- **Δευτεροπαθής** :
  - Συστηματικός ερυθηματώδης λύκος
  - Ηπατίτιδα Β
  - Σύφιλη
  - Έκθεση σε φάρμακα/ μέταλλα
    - PENICILLAMIN, GOLD, MERCURIC CHLORIDE
  - Κακοήθειες

Idiopathic
Membranous
Glomerulopathy

Secondary
Membranous
Glomerulopathy



mesangial immune complex deposits

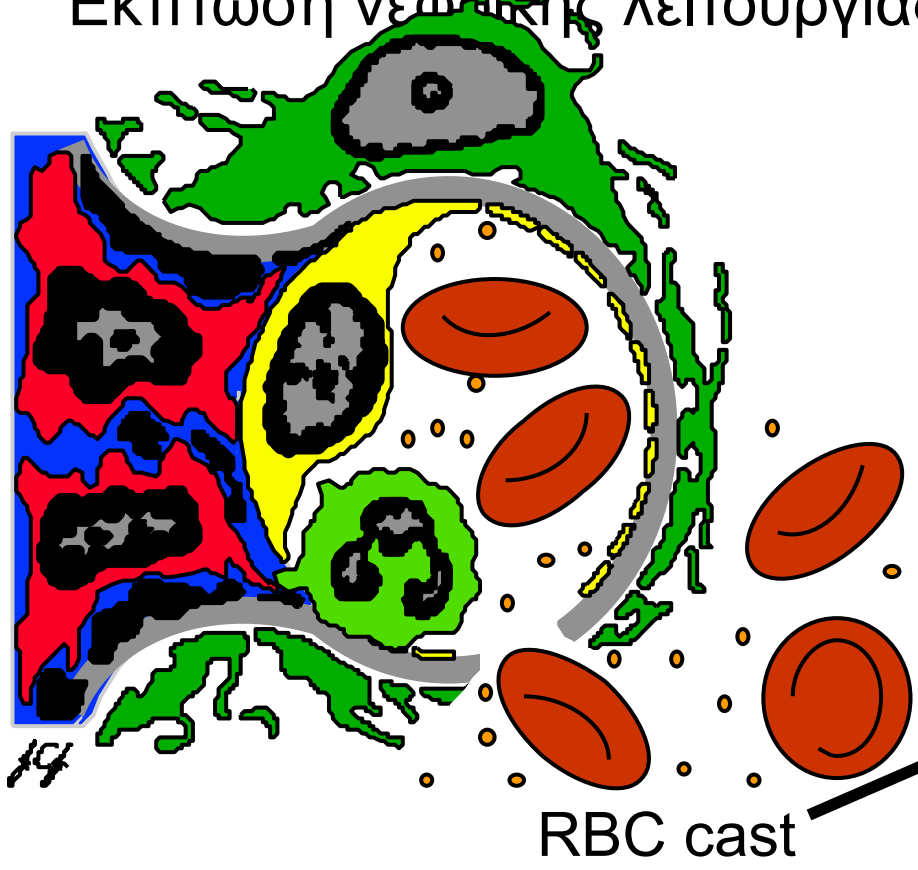
Σπειραματονεφρίτιδα (Νεφριτιδικό σύνδρομο)

Αιματουρία

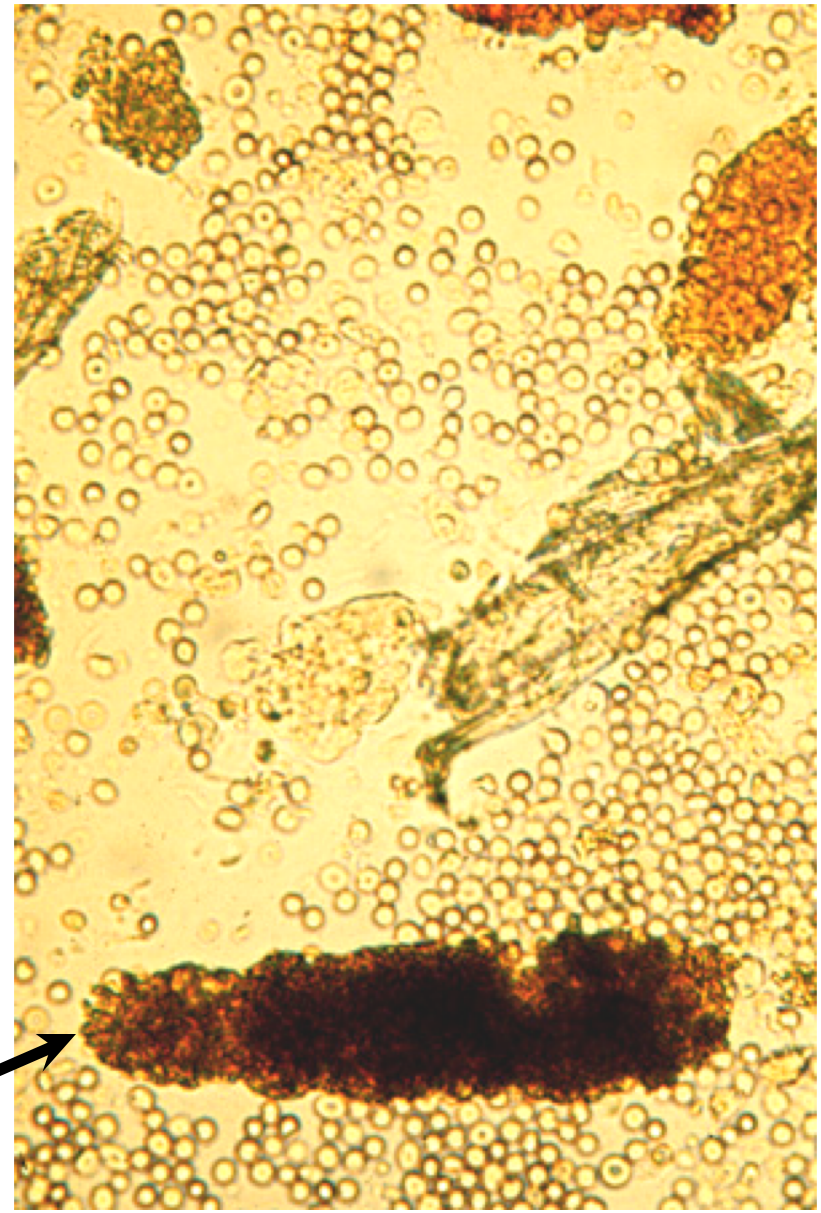
Πρωτεϊνουρία

Υπέρταση

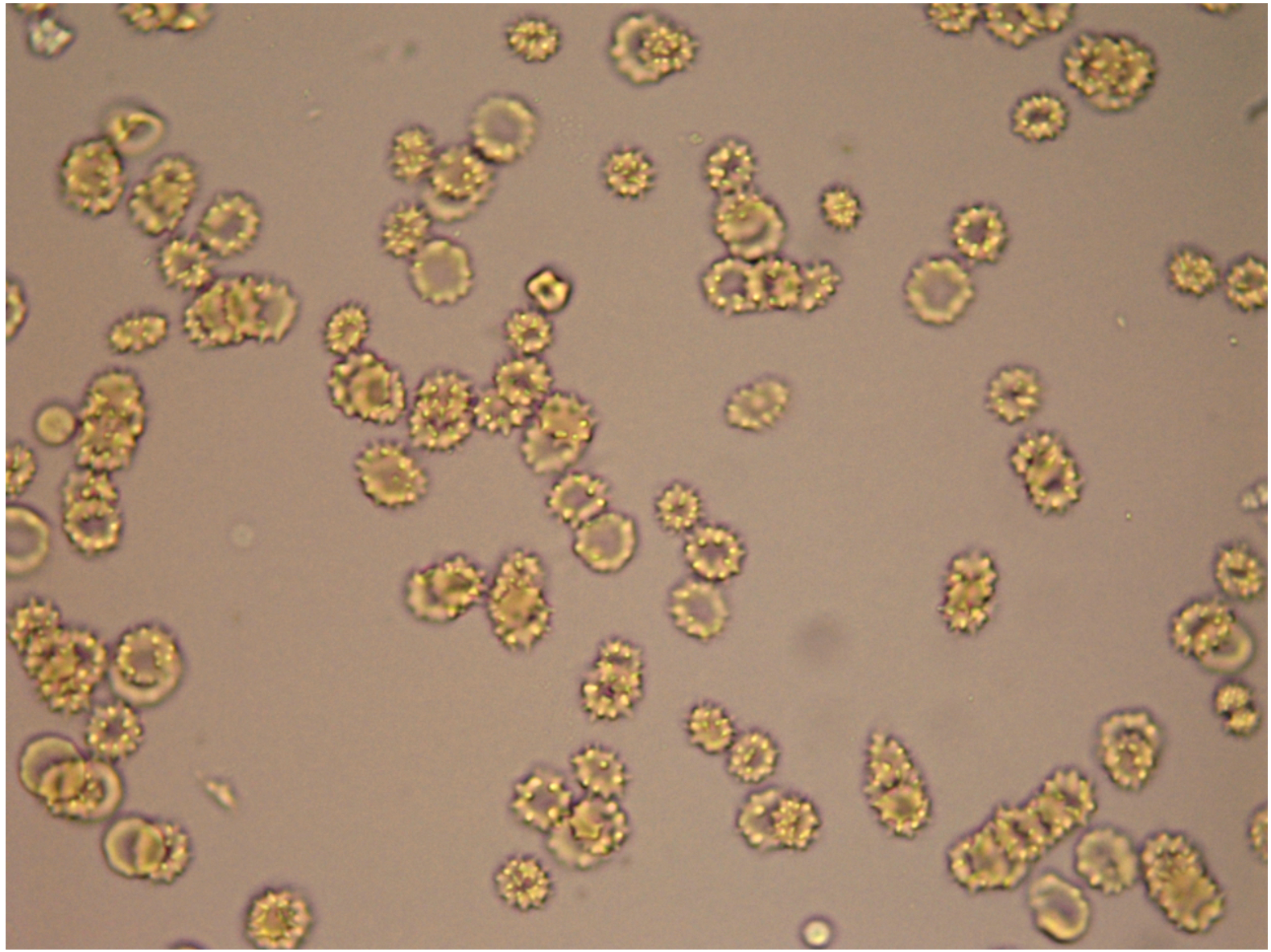
Έκπτωση νεφρικής λειτουργίας



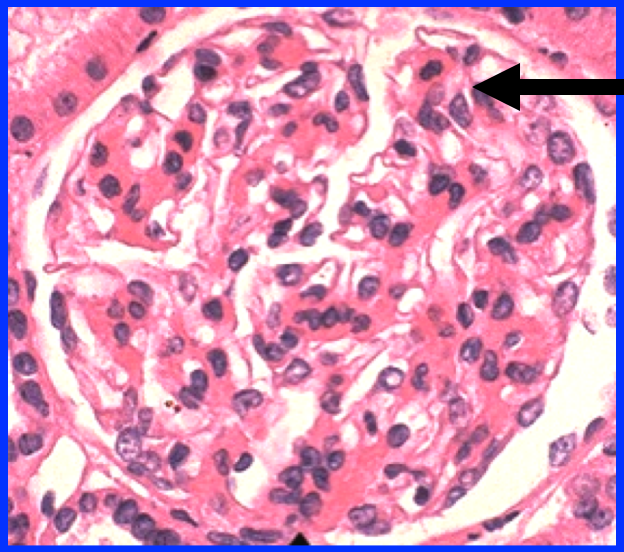
Σπειραματική αιματουρία



Δύσμορφα RBCs-Ακανθοκύτταρα

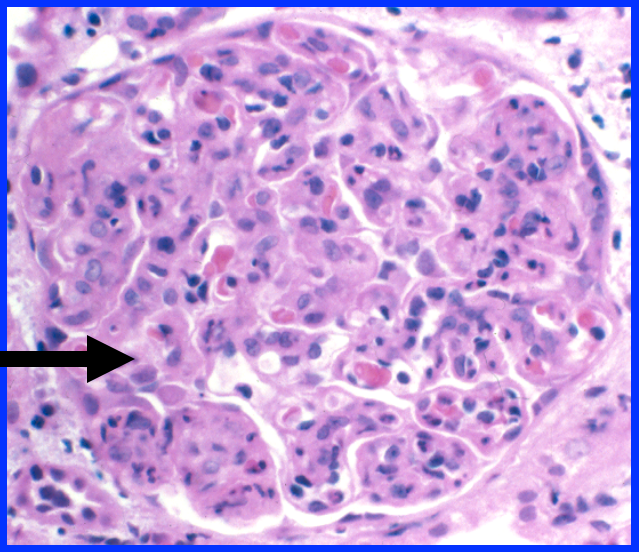


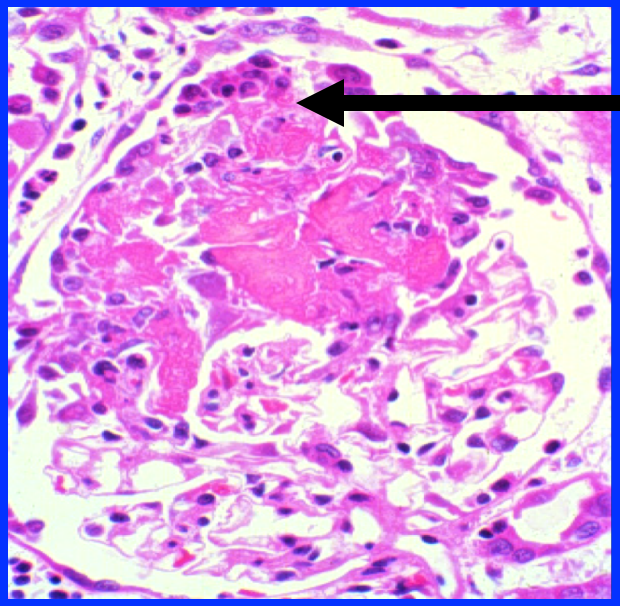
Glomerulonephritis



Mesangioproliferative GN
(mesangial hypercellularity)

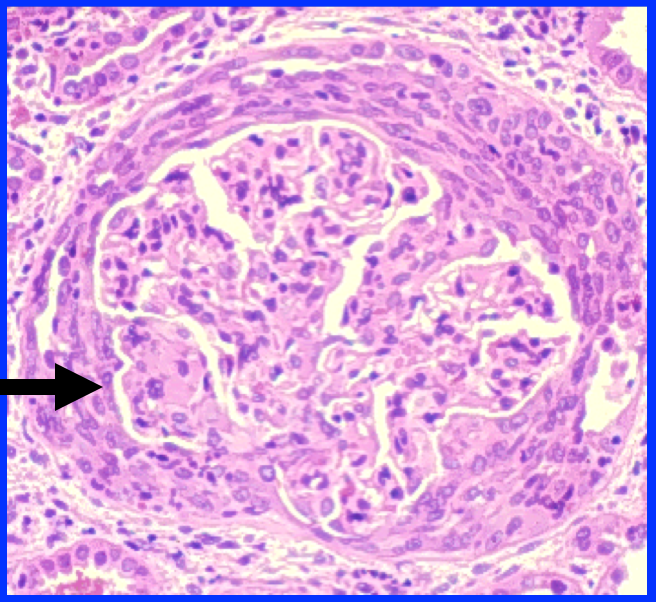
Proliferative GN
(endocapillary hypercellularity)



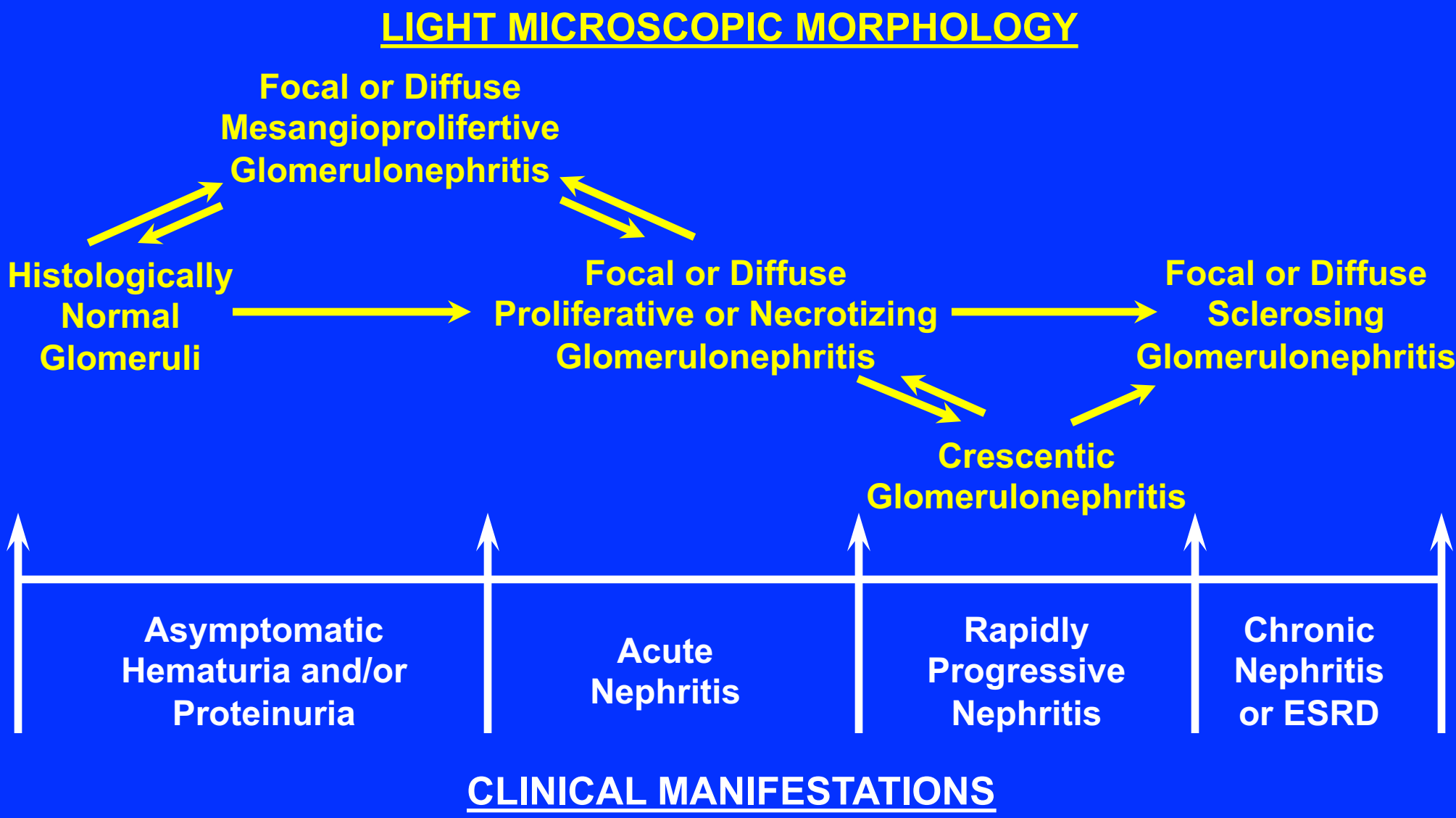


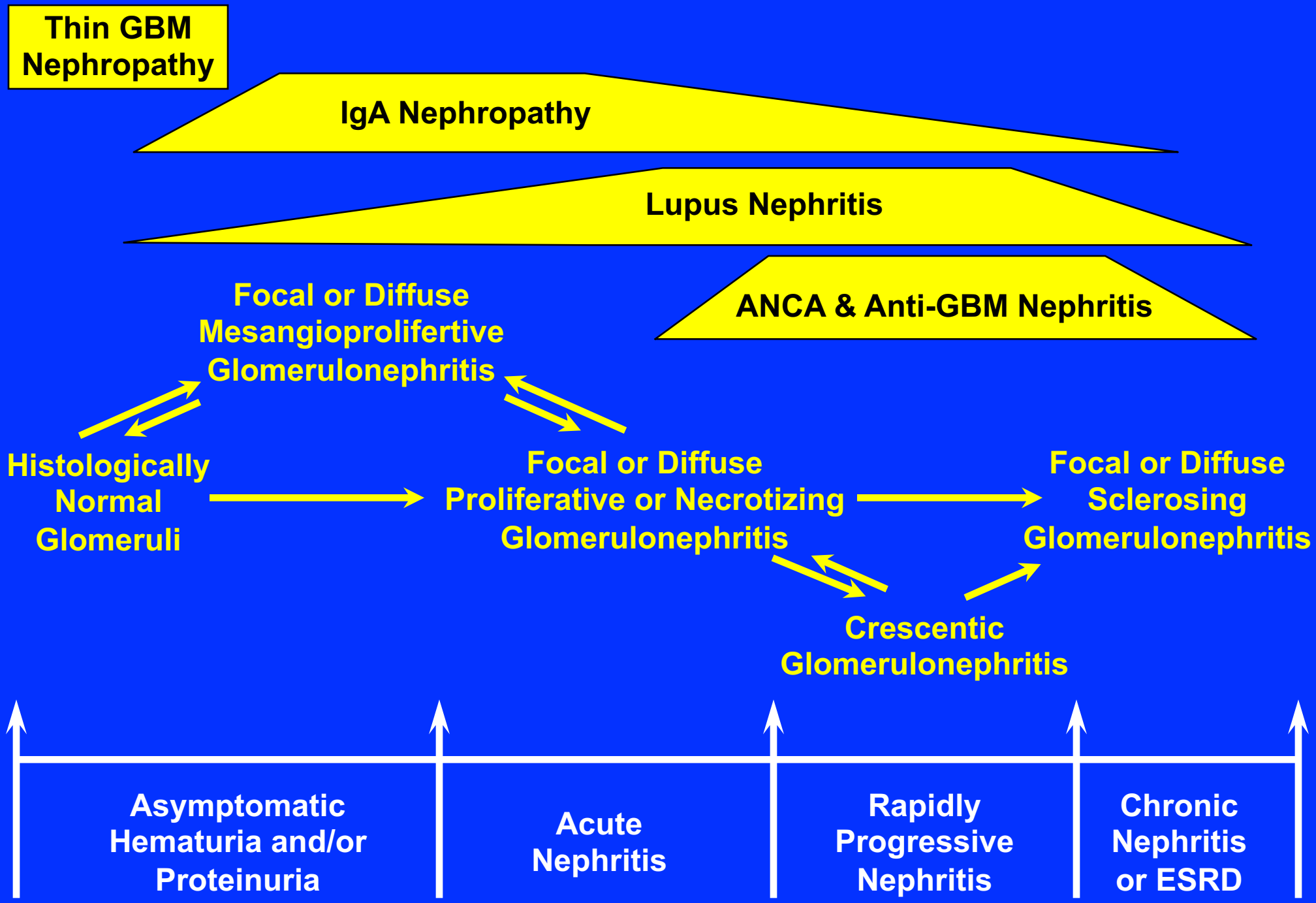
Necrotizing GN
(slight hypercellularity)

Crescentic GN
(extracapillary hypercellularity)



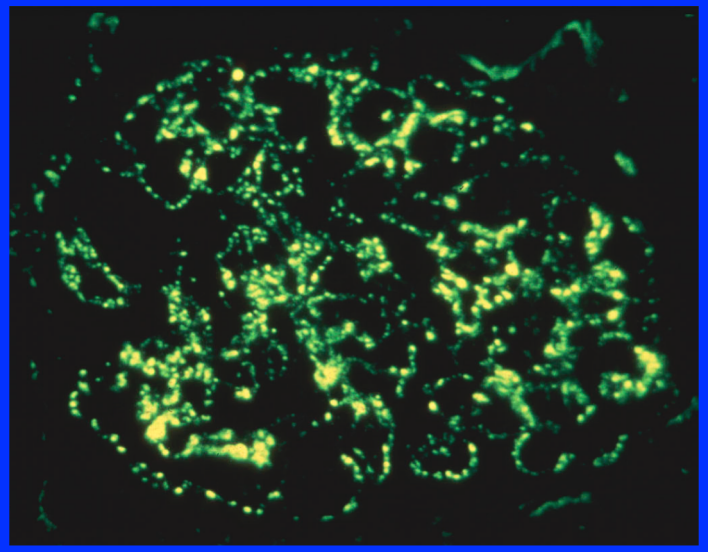
Συσχέτιση ευρημάτων από τη βιοψία νεφρού με τις κλινικές εκδηλώσεις της νόσου



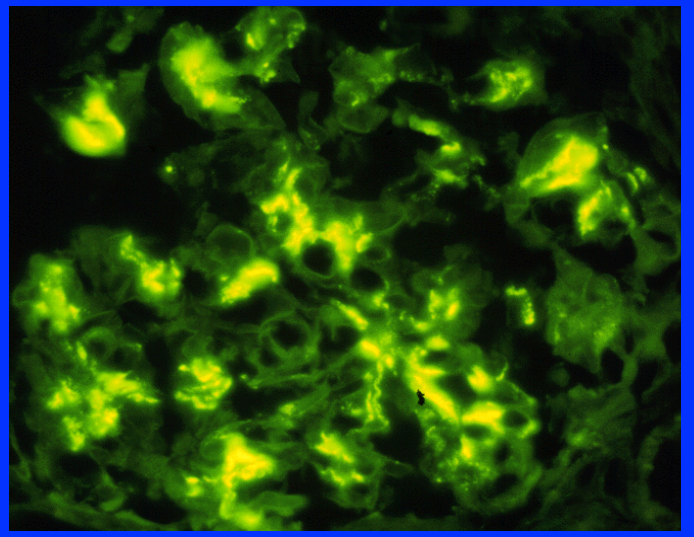

Thin GBM Nephropathy
IgA Nephropathy
Lupus Nephritis
ANCA & Anti-GBM Nephritis
Focal or Diffuse Mesangioprolifertive Glomerulonephritis
Histologically Normal Glomeruli
Focal or Diffuse Proliferative or Necrotizing Glomerulonephritis
Focal or Diffuse Sclerosing Glomerulonephritis
Crescentic Glomerulonephritis
Asymptomatic Hematuria and/or Proteinuria
Acute Nephritis
Rapidly Progressive Nephritis
Chronic Nephritis or ESRD

Υπάρχουν διαφορετικοί τύποι σπειραματικών παθήσεων από ανοσοσυμπλέγματα

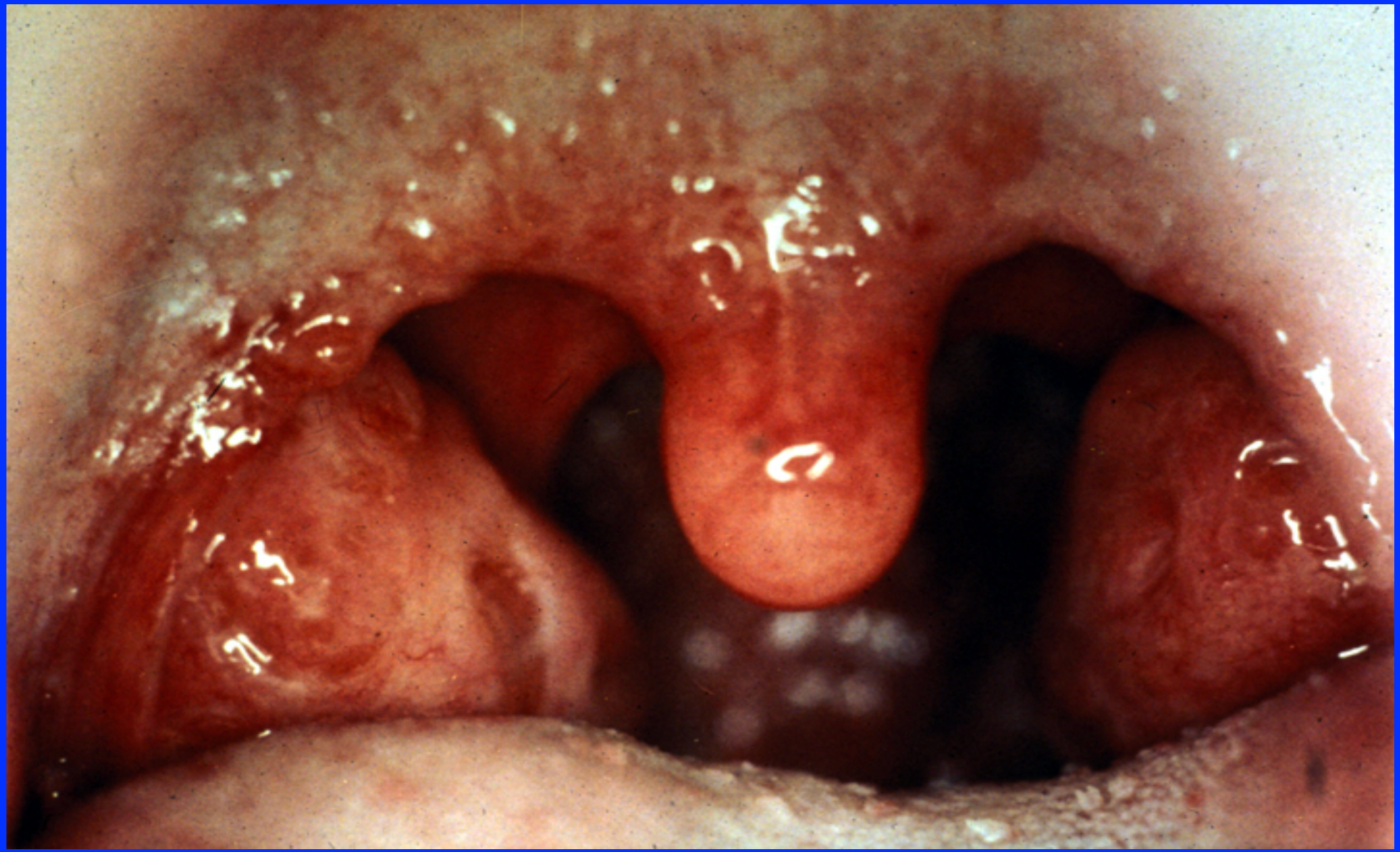
GLOMERULONEPHRITIS



Granular glomerular IF staining due to immune complex localization

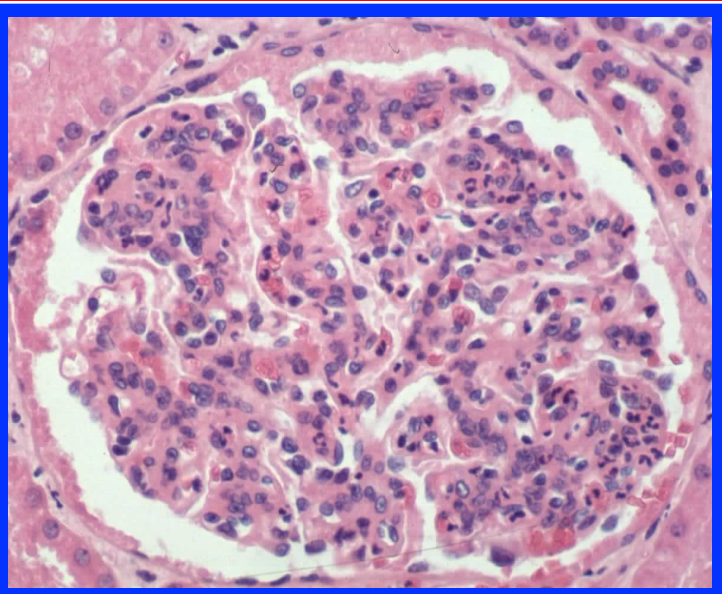


IgA dominance and no vasculitis	IgA and systemic vasculitis	IgG/IgM/IgA and SLE clinically	subepithelial humps by EM and infection clinically	mesangio-capillary changes by EM	GBM dense deposits by EM	numerous subepithelial deposits by EM	20nm fibrils by EM	other features
IgA Nephropathy	**H-S Purpura**	**Lupus Nephritis**	**Acute Post-Infectious GN**	**Type I MPGN**	**Type II MPGN**	**Membranous GN**	**Fibrillary GN**	**Many Others**

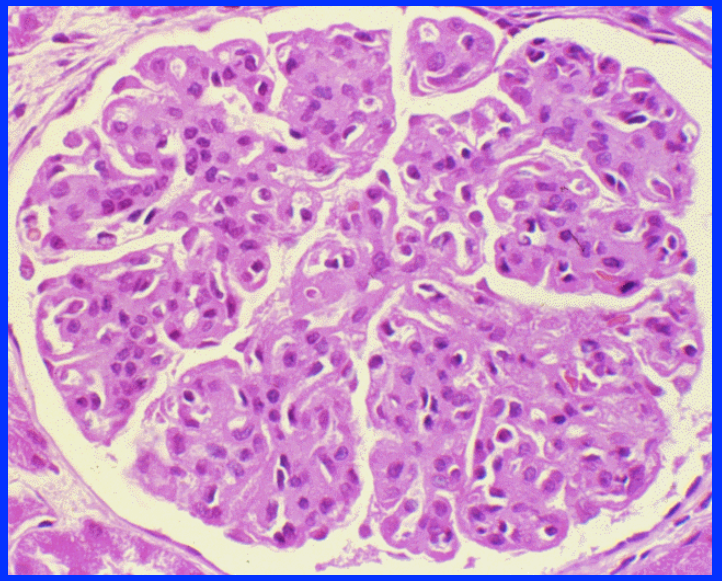


Μεταλοιμώδης Σπειραματονεφρίτιδα

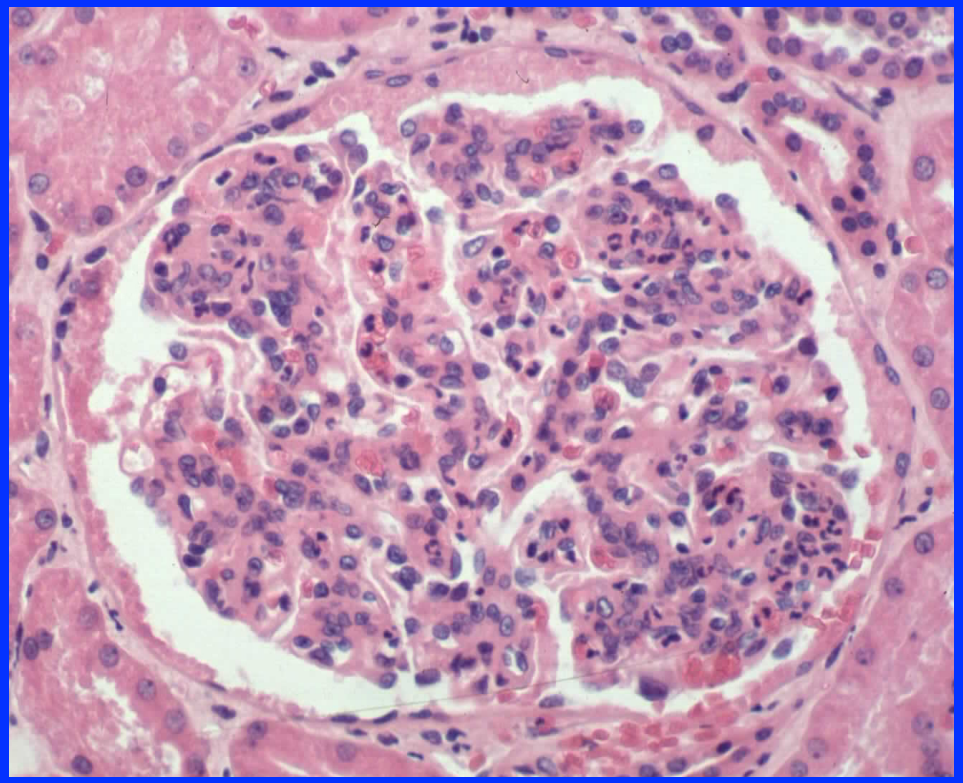
Acute (especially self-limited) infections (e.g. streptococcal pharyngiitis and pyoderma) may cause an immune complex mediated **acute postinfectious glomerulonephrits**

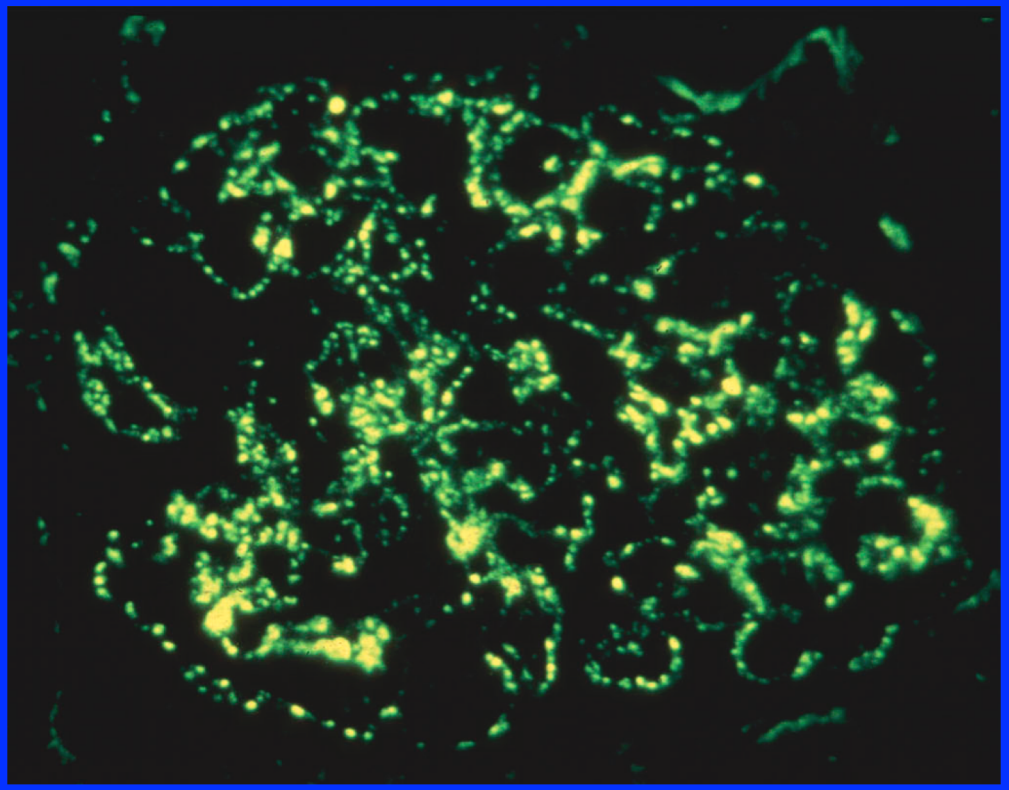


Chronic (persistent) infections (e.g. hepatitis C, SBE) may cause an immune complex mediated **chronic membranoproliferative glomerulonephrits**



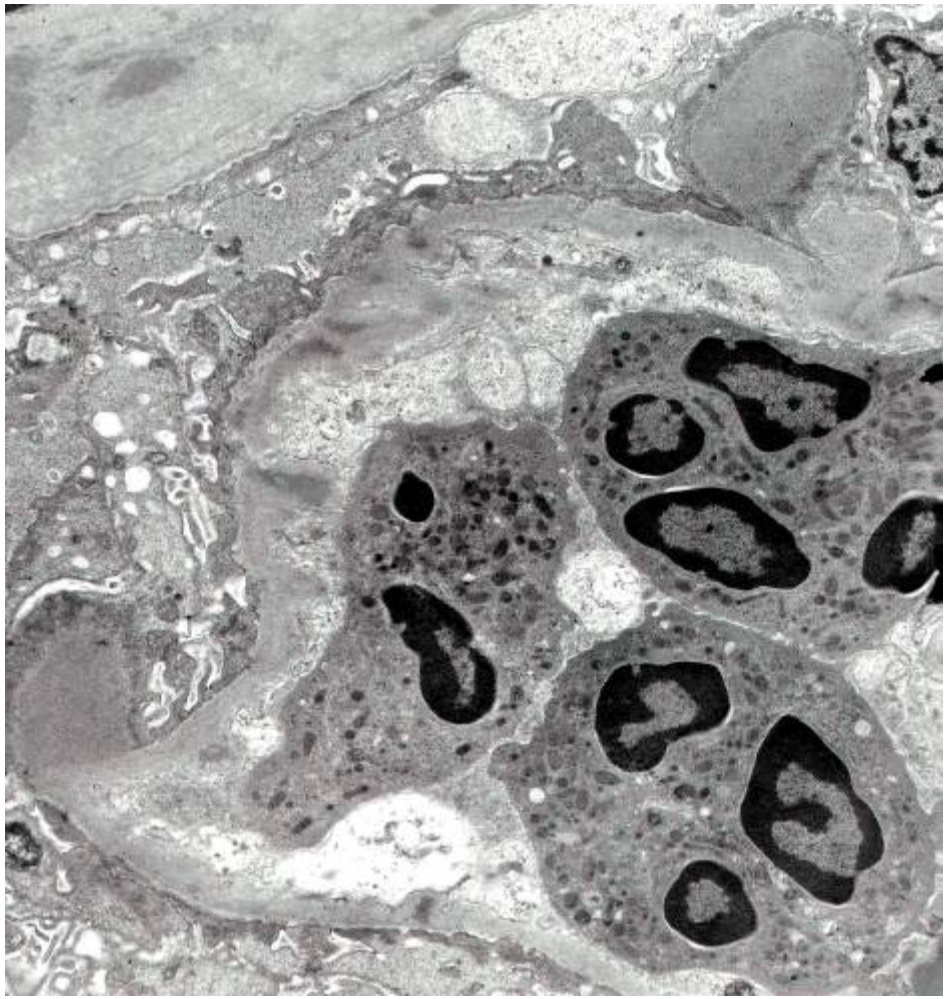
ΟΞΕΙΑ ΜΕΤΑΛΟΙΜΩΔΗΣ ΣΠΕΙΡΑΜΑΤΟΝΕΦΡΙΤΙΔΑ

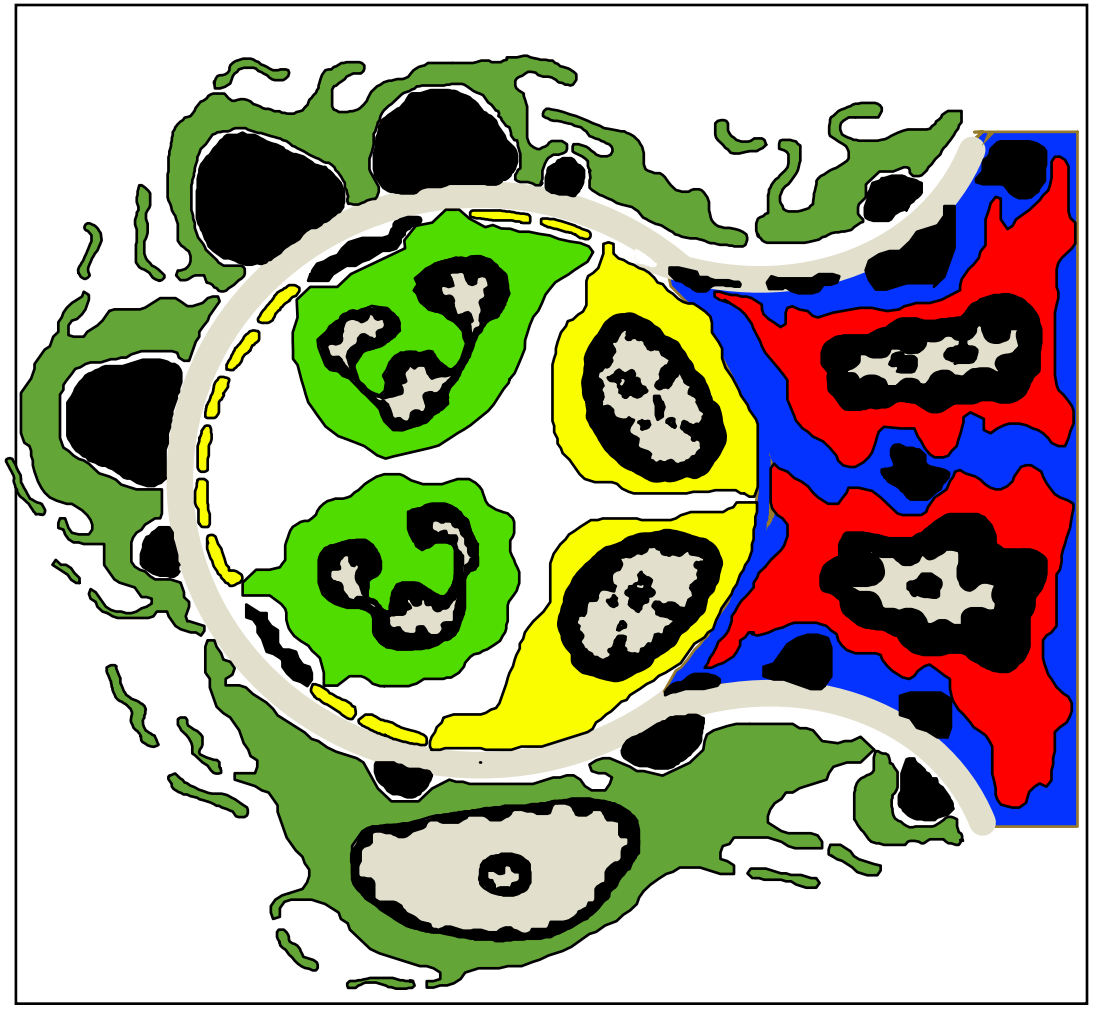


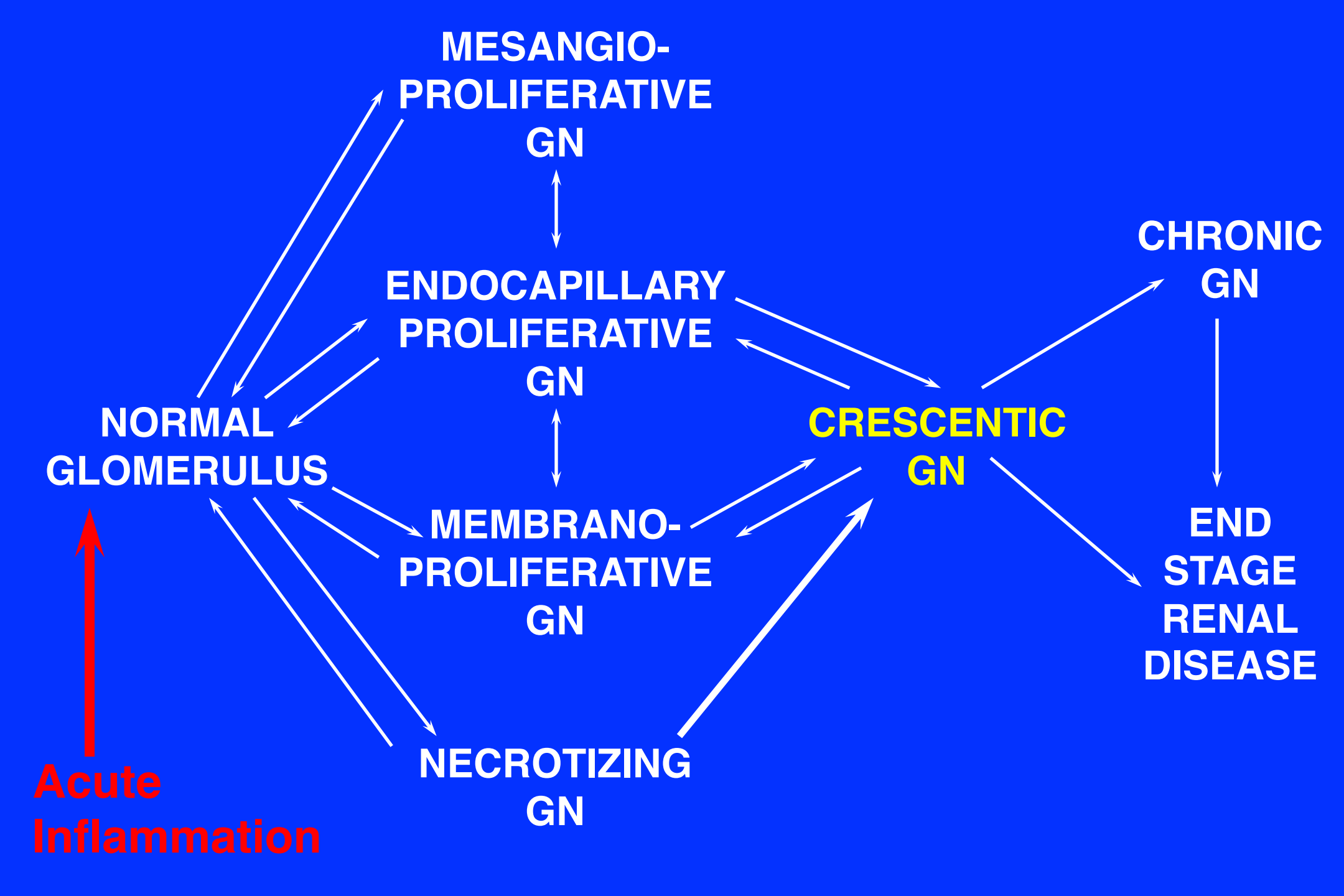


Nephritis usually begins 1 or 2 weeks following the onset of pharyngiitis or pyoderma, usually is accompanied by hypocomplementemia, and typically resolves within weeks to months.

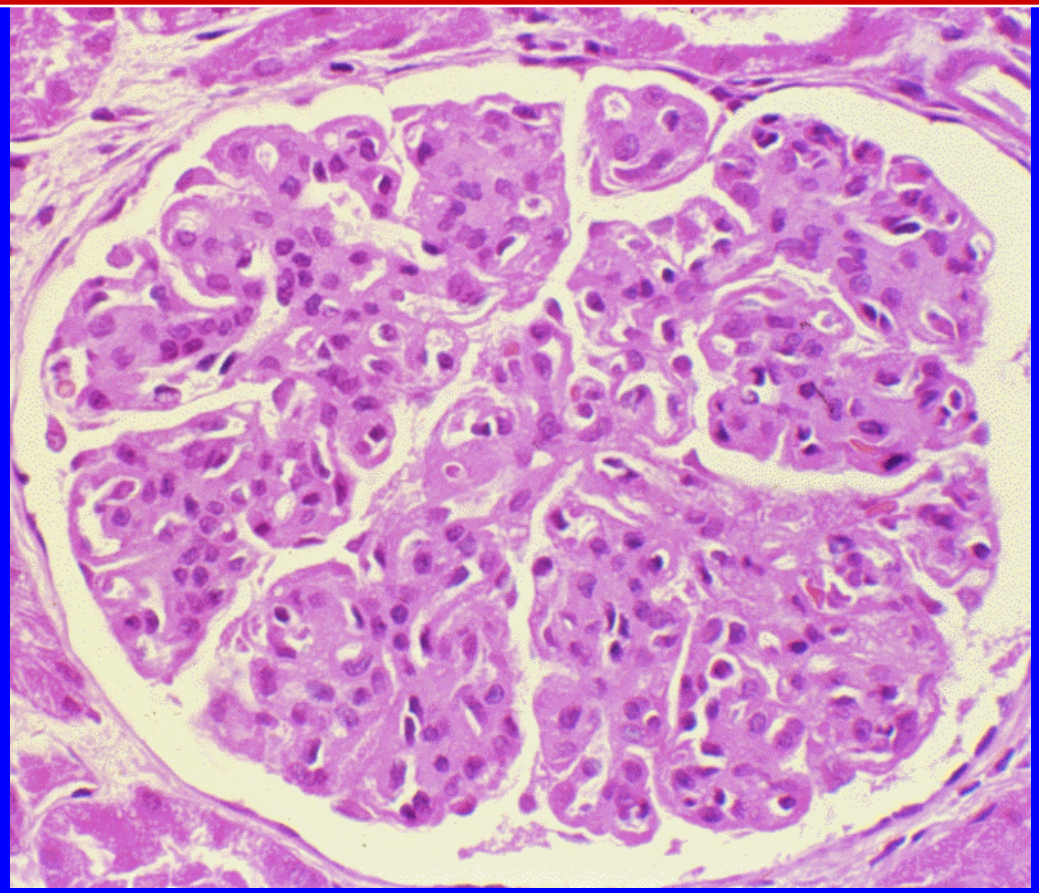
ΟΞΕΙΑ ΜΕΤΑΛΟΙΜΩΔΗΣ ΣΠΕΙΡΑΜΑΤΟΝΕΦΡΙΤΙΔΑ

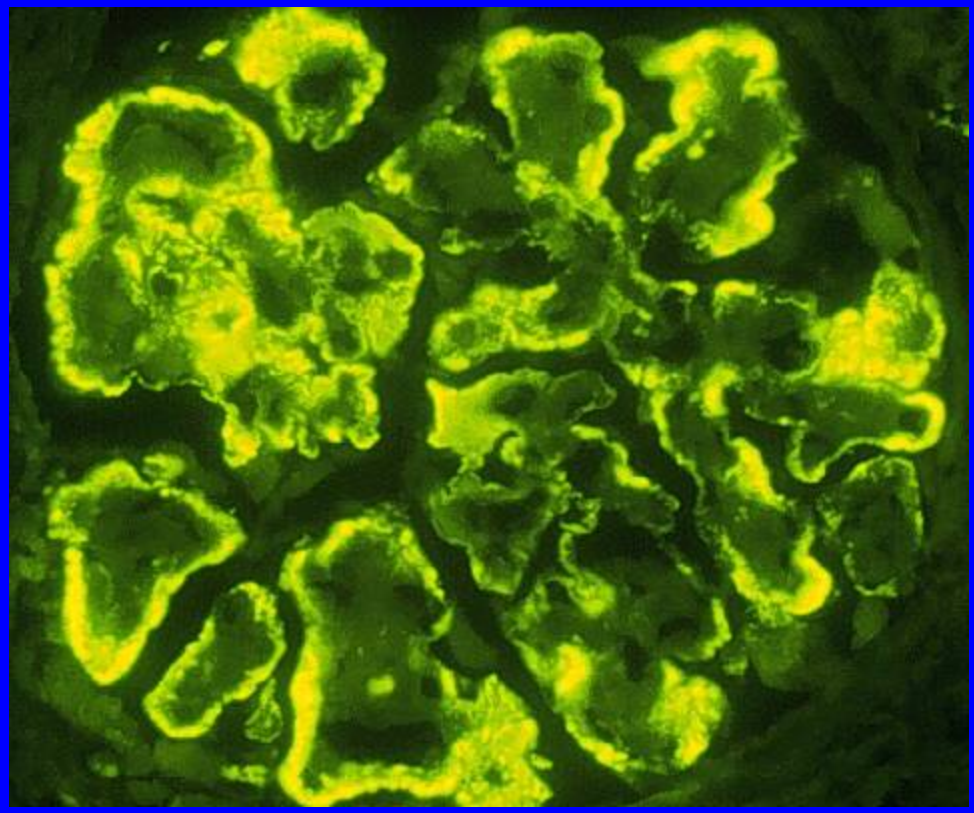




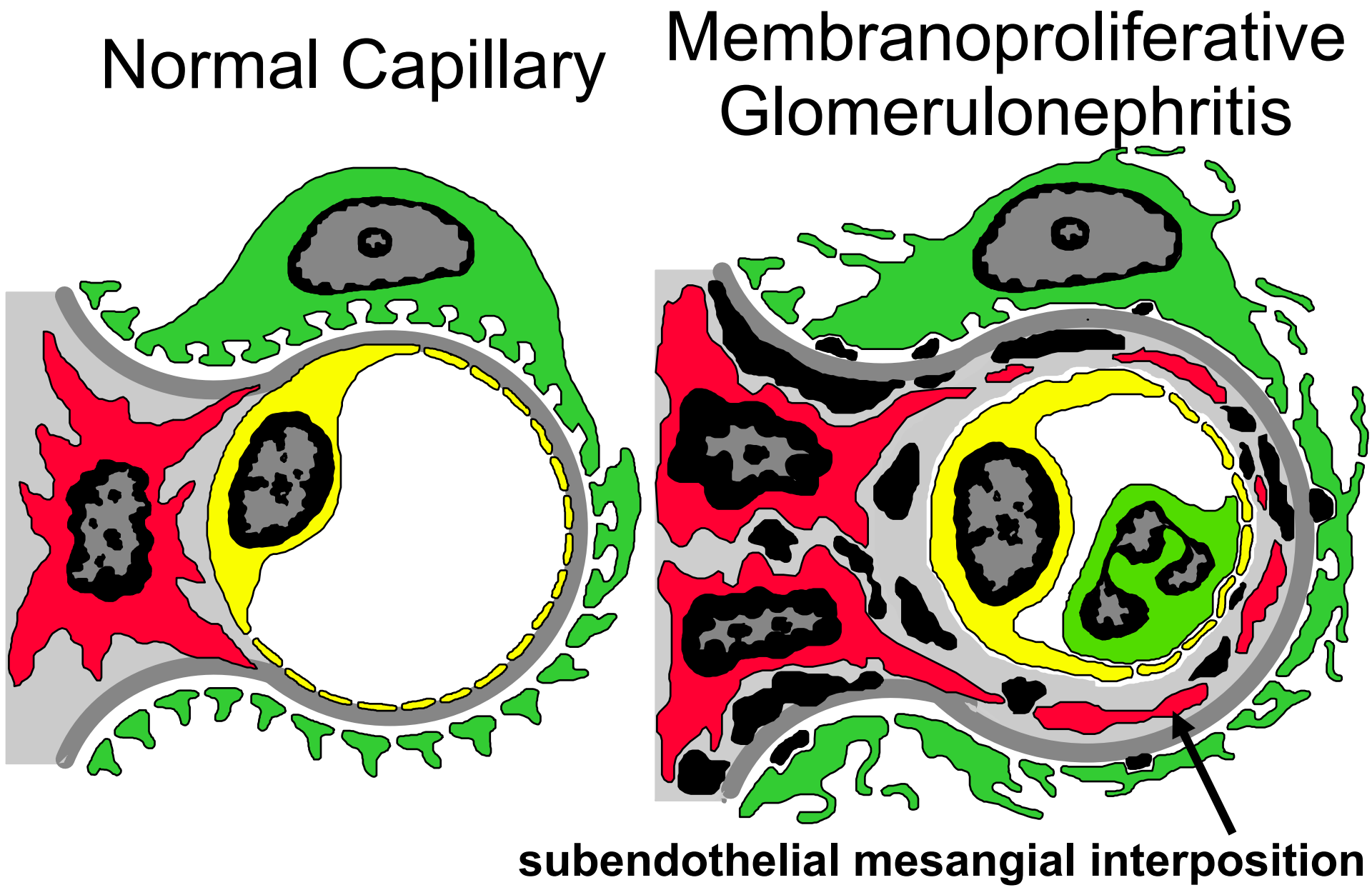

MESANGIO-
PROLIFERATIVE
GN
ENDOCAPILLARY
PROLIFERATIVE
GN
NORMAL
GLOMERULUS
MEMBRANO-
PROLIFERATIVE
GN
NECROTIZING
GN
CRESCENTIC
GN
CHRONIC
GN
END
STAGE
RENAL
DISEASE
Acute
Inflammation

Membranoproliferative Glomerulonephritis

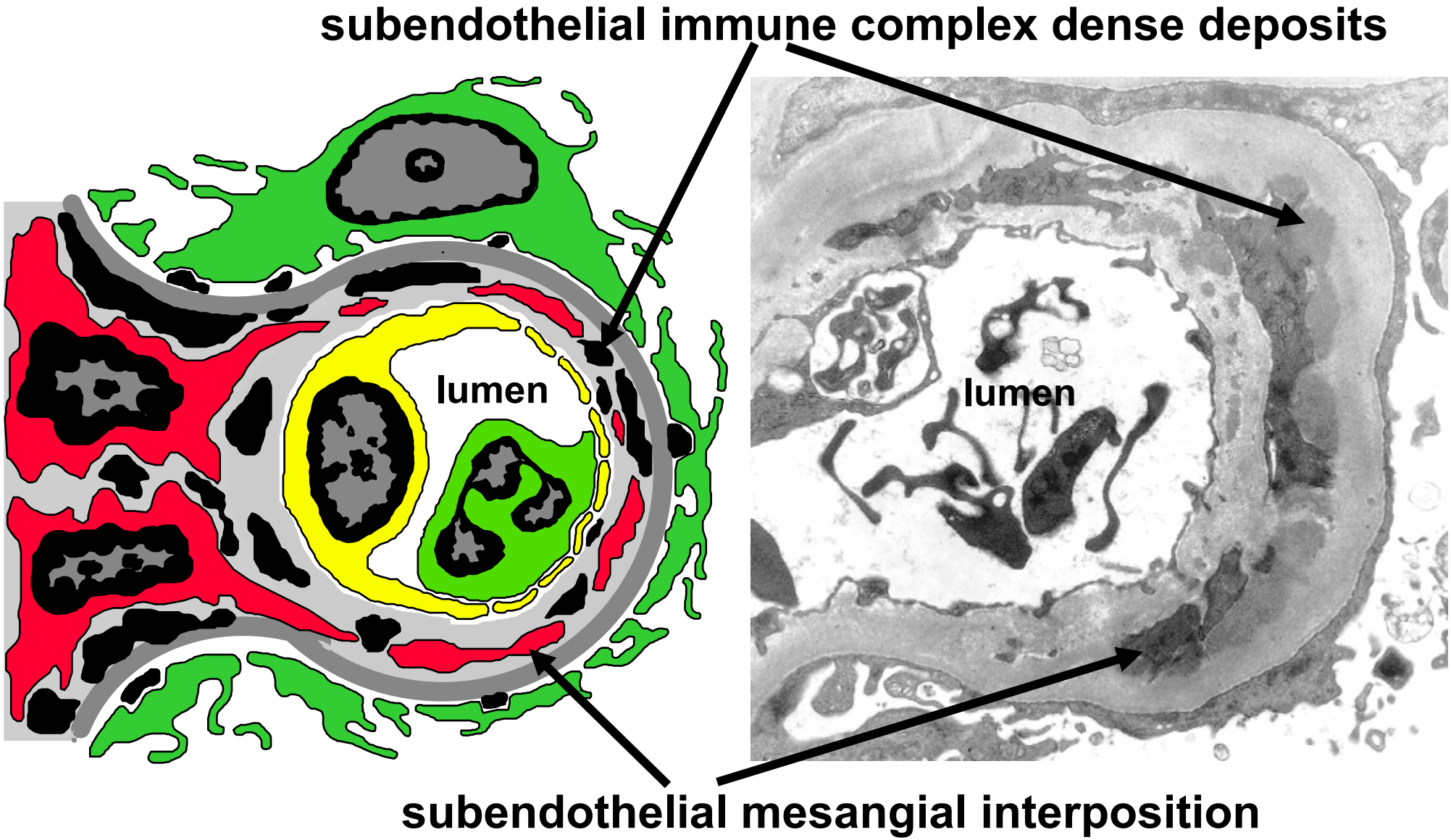




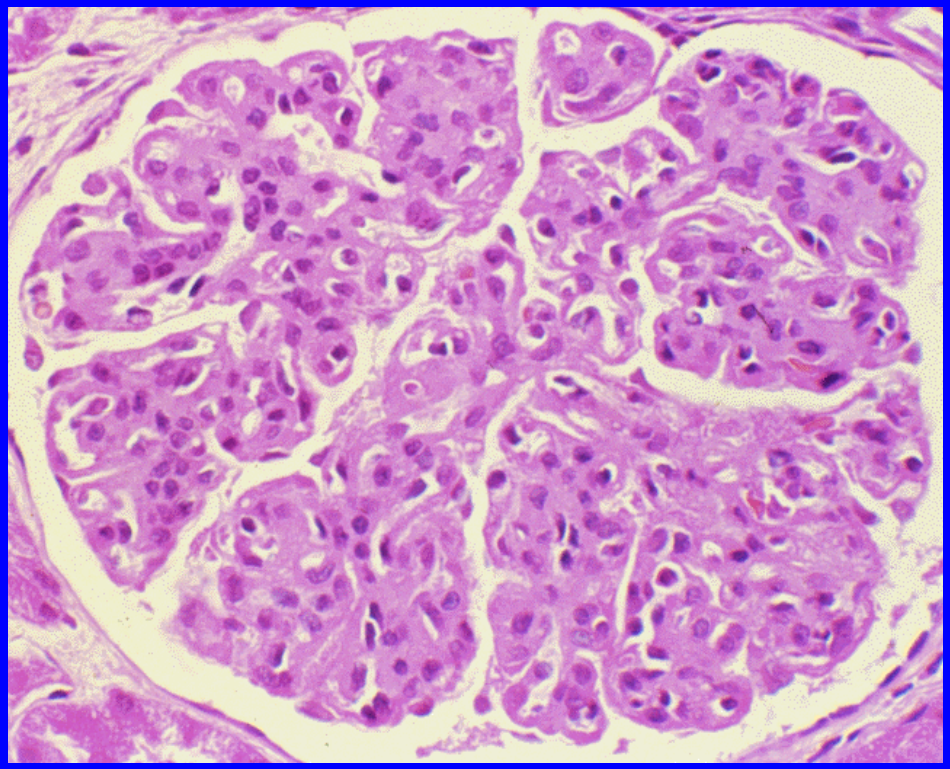
Mixed nephritis/nephrosis often but not always accompanied by hypocomplementemia. May be caused by persistent infections (e.g. hepatitis C, SBE) or neoplasms but often is idiopathic.

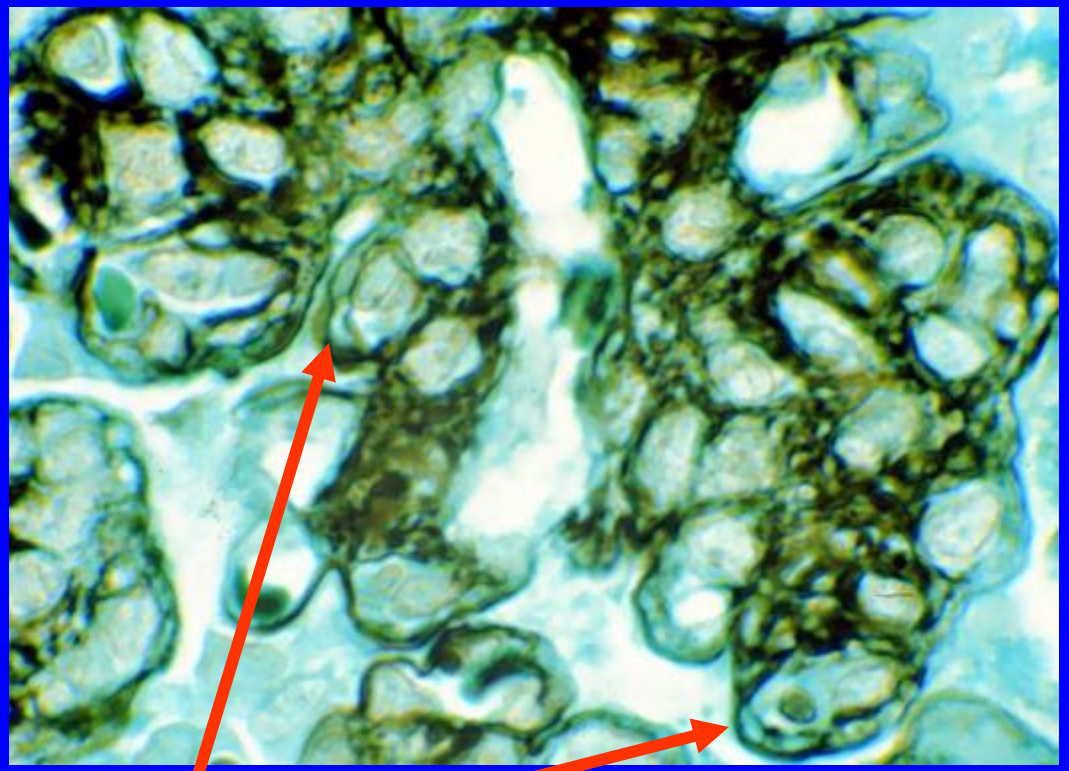

Normal Capillary
Membranoproliferative Glomerulonephritis
subendothelial mesangial interposition

Membranoproliferative Glomerulonephritis



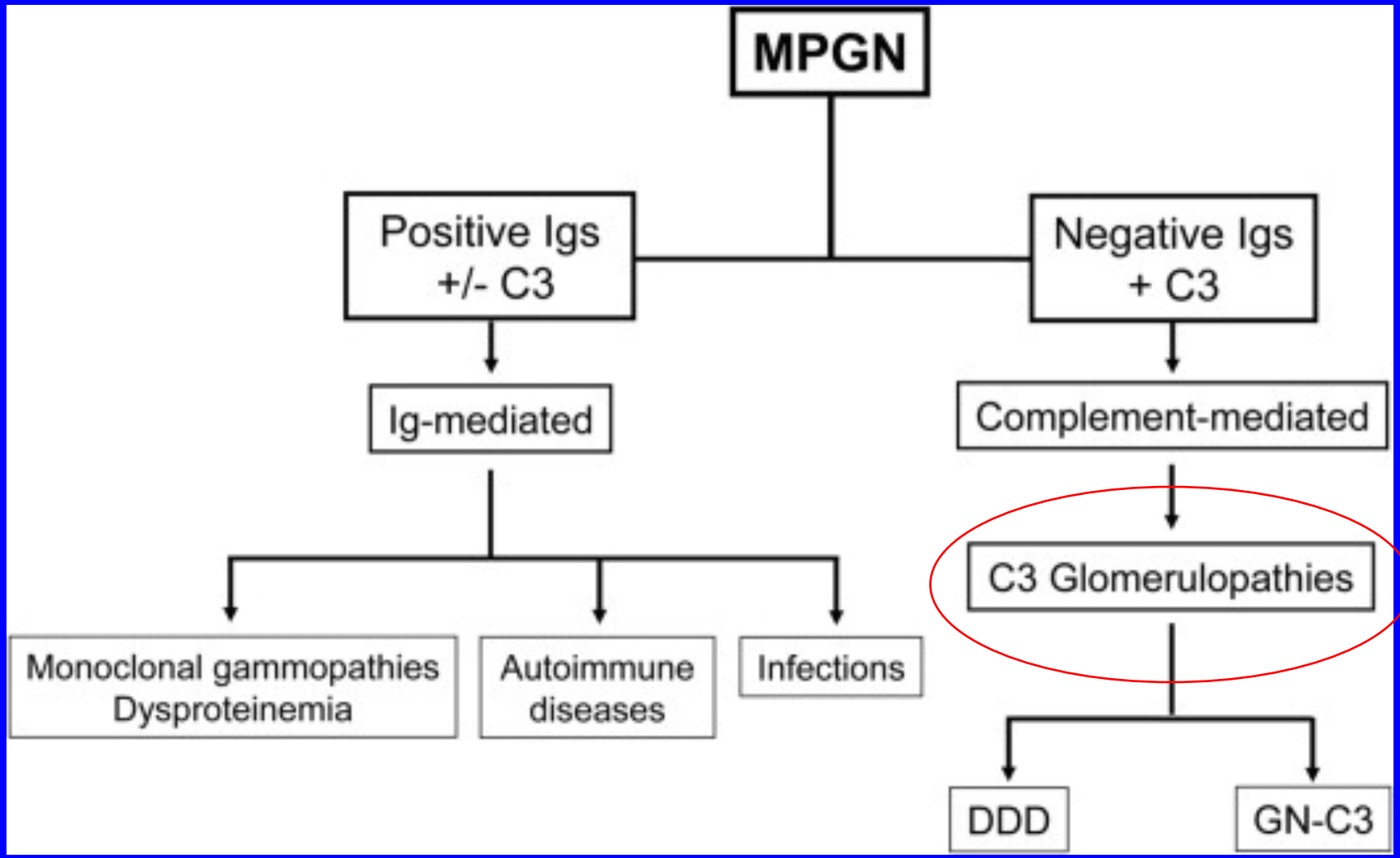
Membranoproliferative Glomerulonephritis





GBM replication

Μεμβρανουπερπλαστική ΣΝ-Ταξινόμηση



Παθογένεια C3 σπειραματοπαθειών

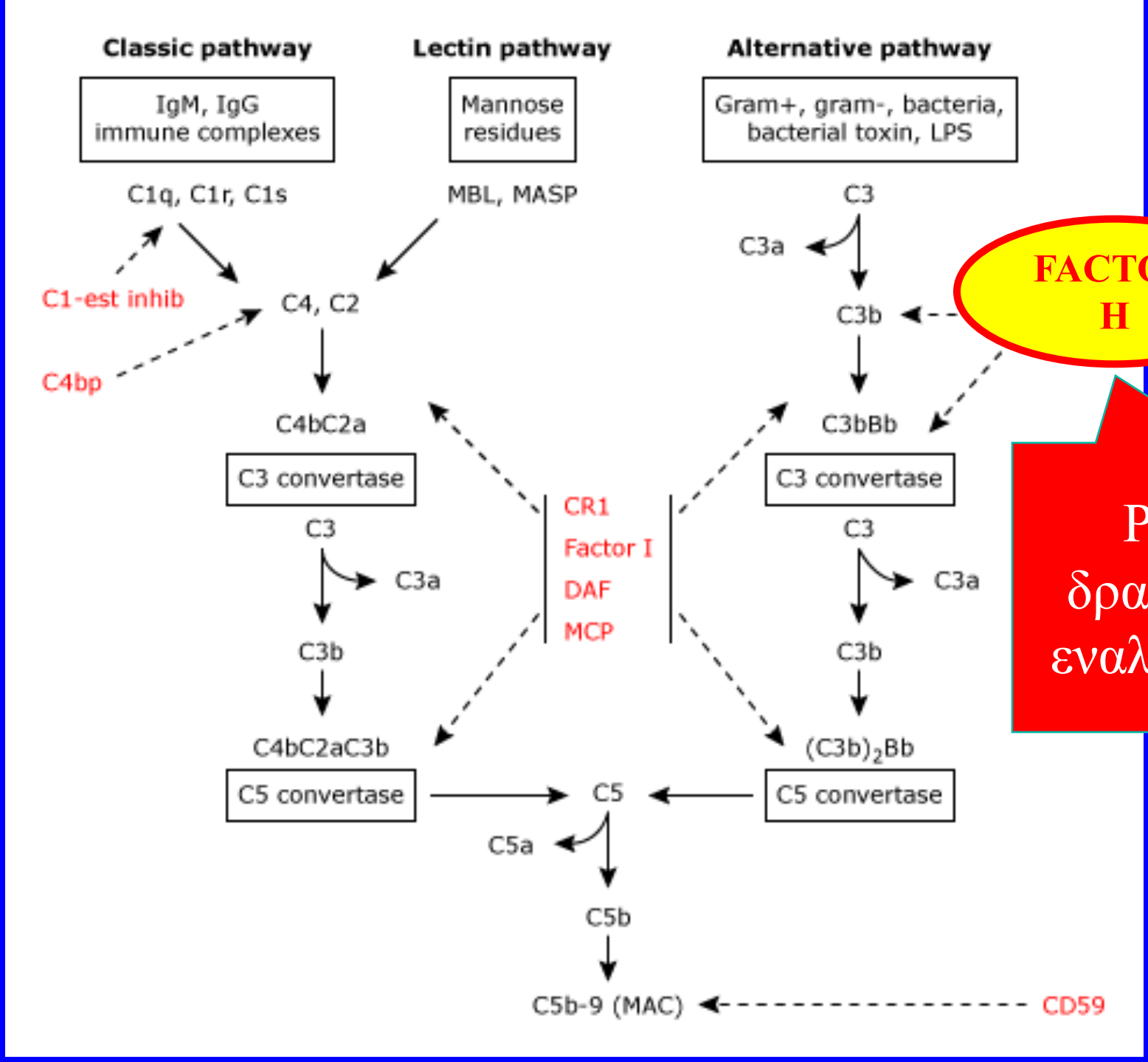
- ↑ Δραστηριότητα της εναλλακτικής οδού του συμπληρώματος.
- Εναπόθεση στοιχείων του συμπληρώματος στο σπείραμα.

- **Ανεπάρκεια του παράγοντα Η**

-Κληρονομική

-Επίκτητη (αυτοαντίσωμα)

- **↑ Δραστηριότητα C3 κονβερτάσης**


Classic pathway
Lectin pathway
Alternative pathway
IgM, IgG immune complexes
Mannose residues
Gram+, gram-, bacteria, bacterial toxin, LPS
C1q, C1r, C1s
MBL, MASP
C3
C3a
C1-est inhib
C4, C2
C3b
C4bp
C4bC2a
C3bBb
C3 convertase
C3 convertase
CR1
Factor I
DAF
MCP
C3
C3a
C3
C3a
C3b
C3b
C4bC2aC3b
(C3b)2Bb
C5 convertase
C5
C5 convertase
C5a
C5b
C5b-9 (MAC)
CD59
FACTOR H
Ρυθμίζει την
δραστικότητα
εναλλακτικής ο

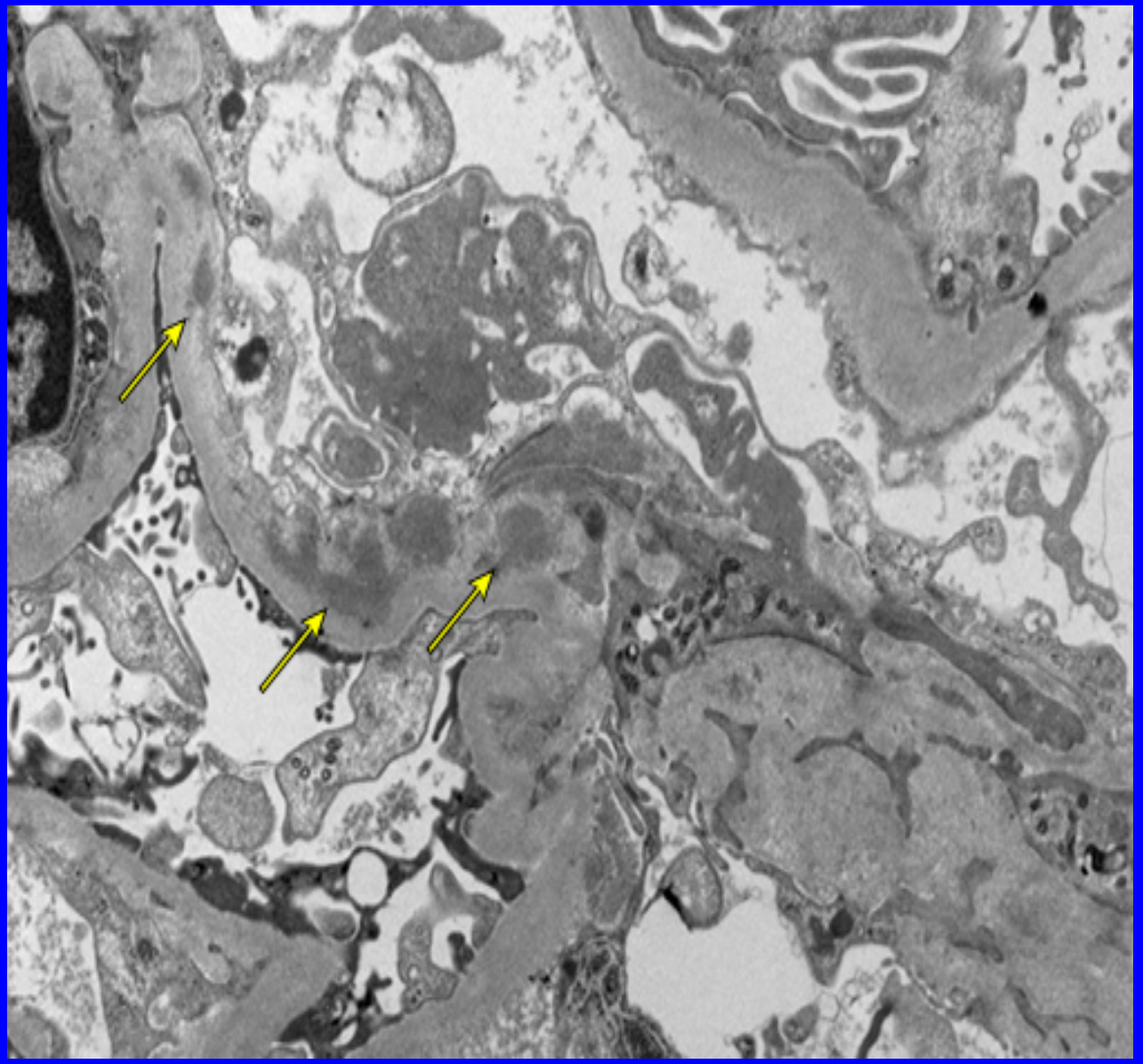
↑ Δραστικότητα της C3 κονβερτάσης

- Αυτοαντίσωμα έναντι της C3 κονβερτάσης, συνήθως IgG (C3NeF).
- (+) 80% των ασθενών με Νόσο πυκνών εναποθέσεων.
- (+) 40% των ασθενών με C3 σπειραματονεφρίτιδα.
- Ανευρίσκεται και σε φυσιολογικά άτομα ή ασθενείς με μηνιγγιτιδικοκκική λοίμωξη.

Νόσος των πυκνών εναποθέσεων

C3

Σπειραματονεφρίτιδα



IgA Νεφροπάθεια

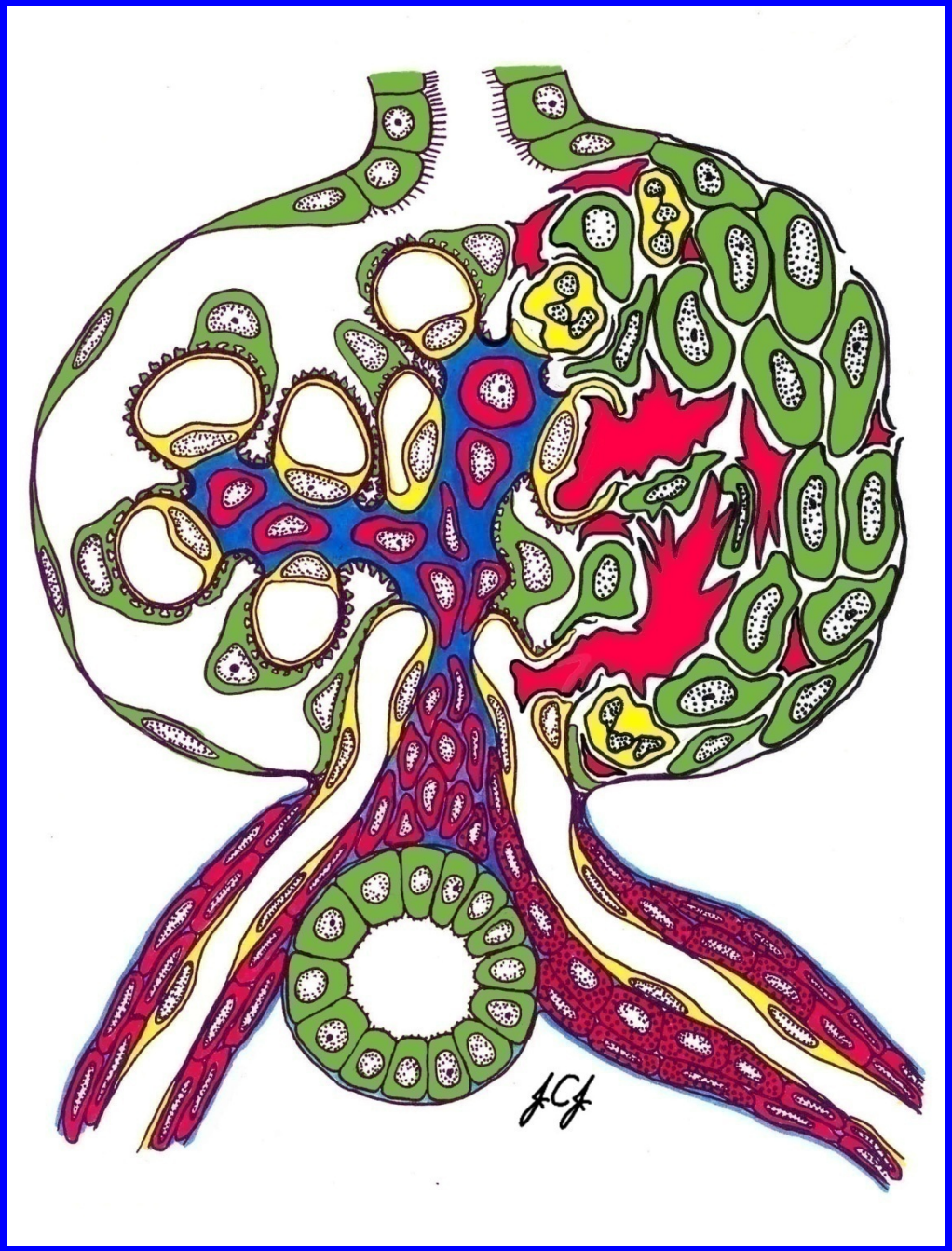
- Ίσως η συχνότερη ΣΝ παγκοσμίως (ειδικά στον αναπτυσσόμενο κόσμο)
- Συνήθως αφορά άτομα 15-30 ετών

  Asian>Caucasian>African

  Males>Females

- Η κλινική εικόνα έχει μεγάλη ετερογένεια:

•40% ασυμπτωματική αιματουρία
•40% επεισόδια μακροσκοπικής αιματουρίας
•10% νεφρωσικό σύνδορμο
•10% νεφρική ανεπάρκεια (ενίοτε ΤΕΣΝ)



Μηνοειδής Σχηματισμός

Ευχαριστώ!