Glomerular Diseases Part II

Elise Barney, DO

Nephrologist, Phoenix VA Health Care System

Associate Professor, University of Arizona College of Medicine

BUMC Internal Medicine Resident Lecture

January 24, 2017

PHOENIX VA HEALTH CARE SYSTEM

ARIZONA

Outline

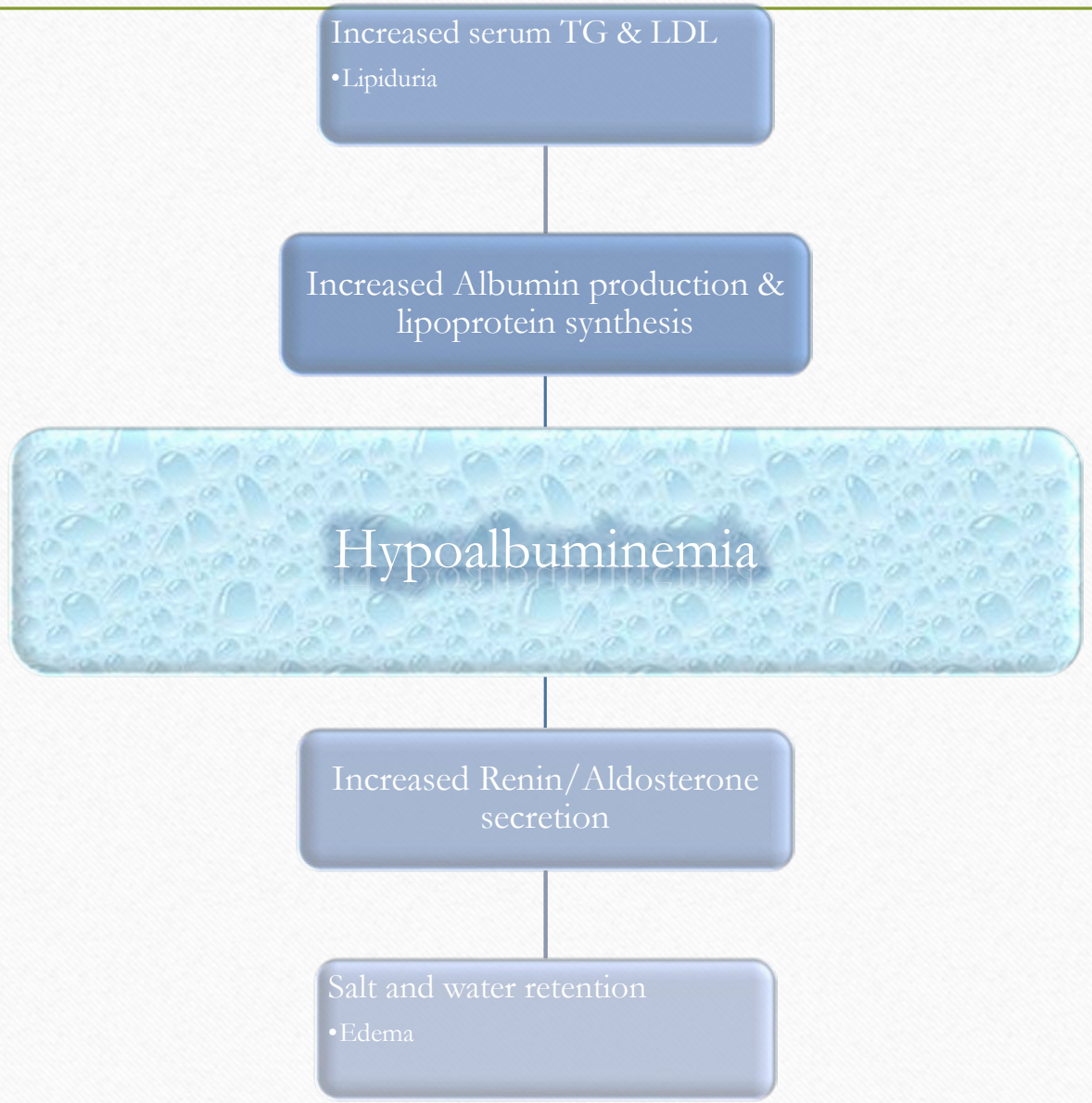
- Nephrotic syndrome
- FSGS
- Membranous glomerulonephritis
- Minimal change disease
- Systemic Diseases causing glomerulonephritis

Nephrotic Syndrome

- UPC or 24 hr urine > 3.5 grams of protein
- Edema
- Hypoalbuminemia
- Hyperlipidemia

Nephrotic Syndrome :

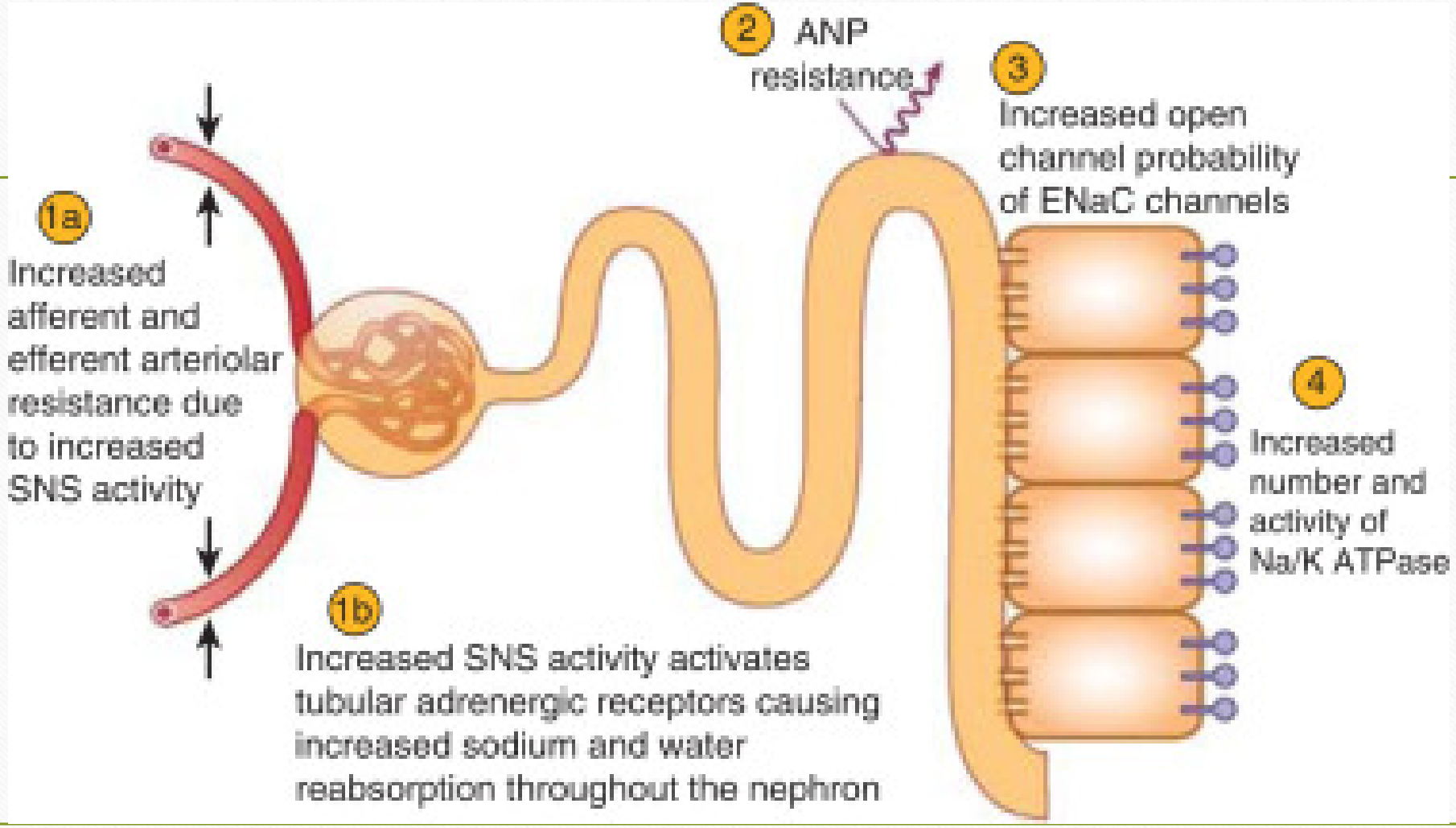
Reduced oncotic P → Loss of fluid into interstitial space



Nephrotic Syndrome (NS) Complications

- Vitamin D deficiency
- Hypercoaguable state
- Immunodeficient state
- Thyroid disorders from urinary loss of thyroxine

Mechanisms of Sodium Retention in NS

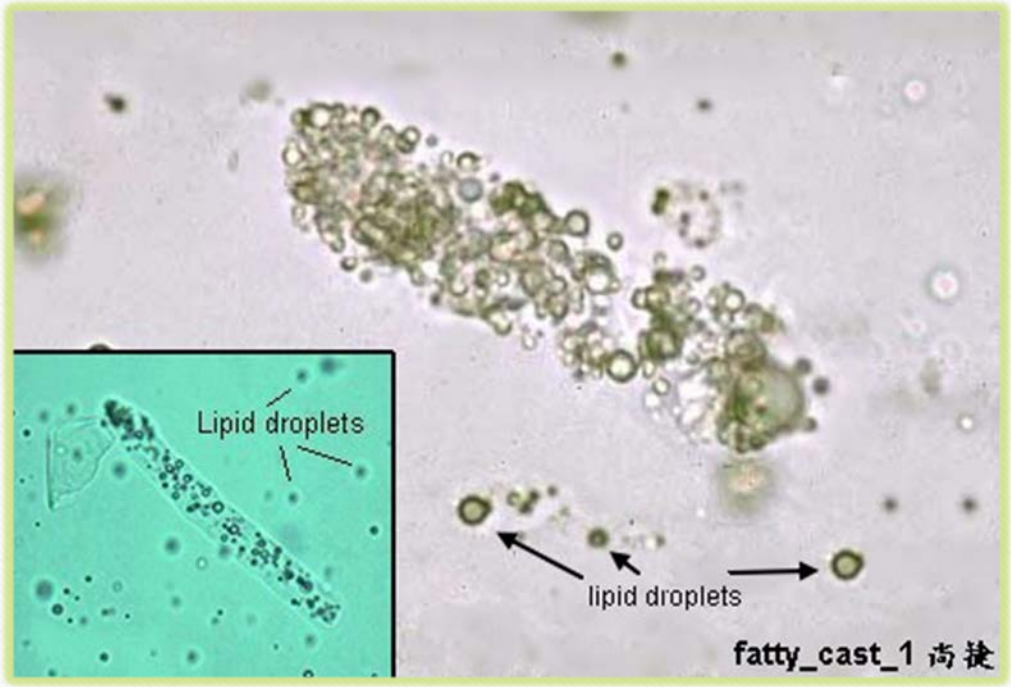


NS: Loop Diuretics

- Decreased response to loop diuretics
  - Hypoalbuminemia (95-99% protein-bound)
  - Enhanced renal metabolism of furosemide to inactive glucuronide
  - Renal failure: competition with other anions
  - Albuminuria → decreased free diuretic levels in tubular fluid

Ceiling Doses	of Loop	Diuretics
	Dose Furosemide IV	Dose Furosemide PO
NS w/normal GFR		120
GFR 21-50	120	240
GFR < 20	200	400

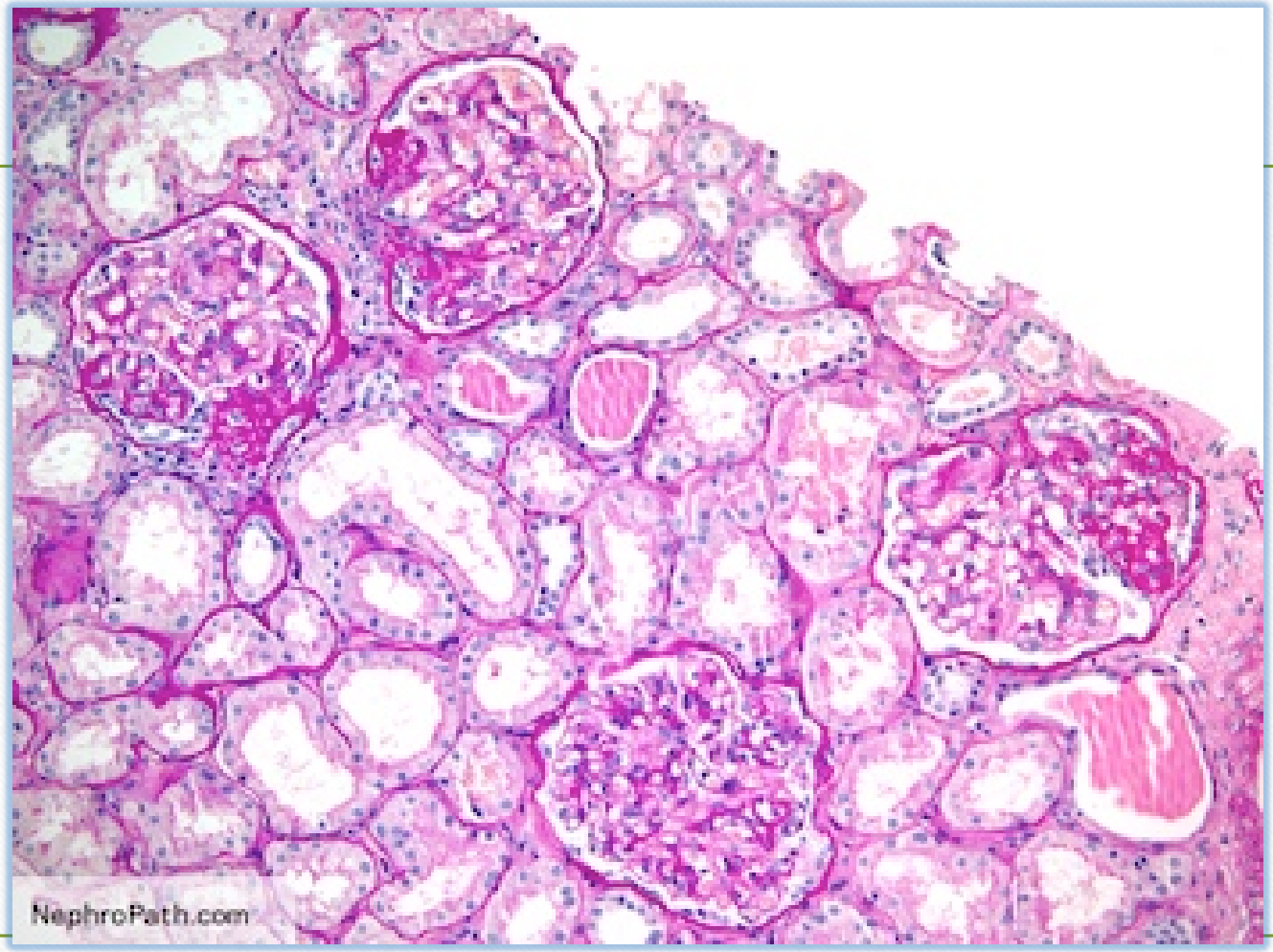
Nephrotic Syndrome: Urine microscopy



Focal Segmental Glomerulosclerosis

- A morphological / histological pattern of injury
- Sclerotic lesions in glomeruli that are focal (< 50% of all gloms on LM) and segmental (< 50% of the glomerular tuft affected)
- Podocyte effacement
- Further LM classification: tip, cellular, collapsing, perihilar, and NOS
- Most common path associated with ESRD in the US
- More common in AA, obese

FSGS



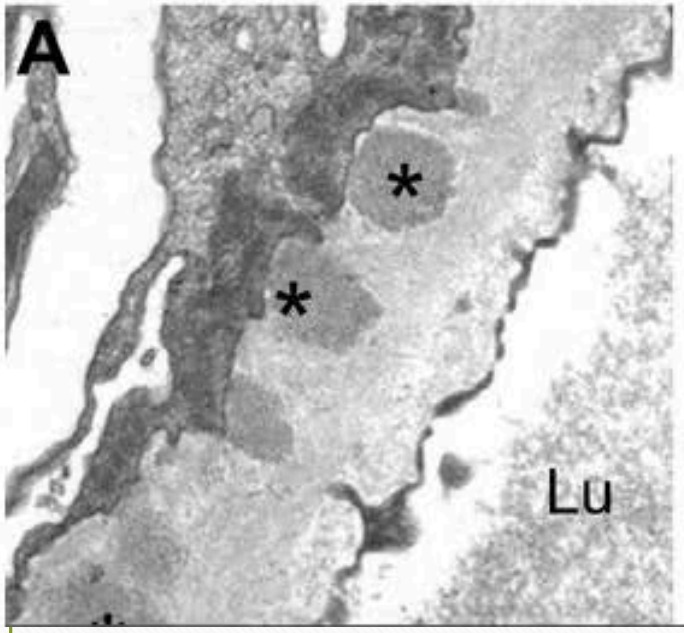
FSGS: Etiologies

- Primary / Idiopathic
  - Typically presents as NS
  - May be associated with a circulating **podocyte** toxin
- Secondary
  - Genetic: APOL1 gene, NPHS1/2
  - Viral: HIV, Parvovirus B19
  - Drugs: Heroin, Pamidronate, Interferon, Sirolimus
  - Adaptive changes: Nephron loss, Reflux nephropathy, Obesity, HTN

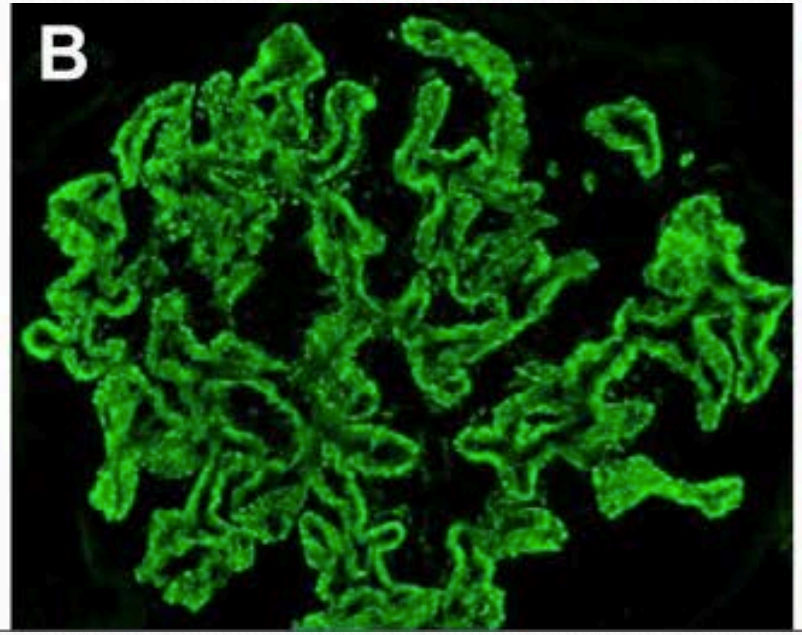
Membranous Glomerulonephritis

- Hitological lesion with thickened GBM, podocyte effacement and subepithelial immune deposits
- May be primary vs secondary
- Primary associated with PLA2 R antigen
- Secondary associated with solid tumor malignancy, HBV, penicillamine, gold

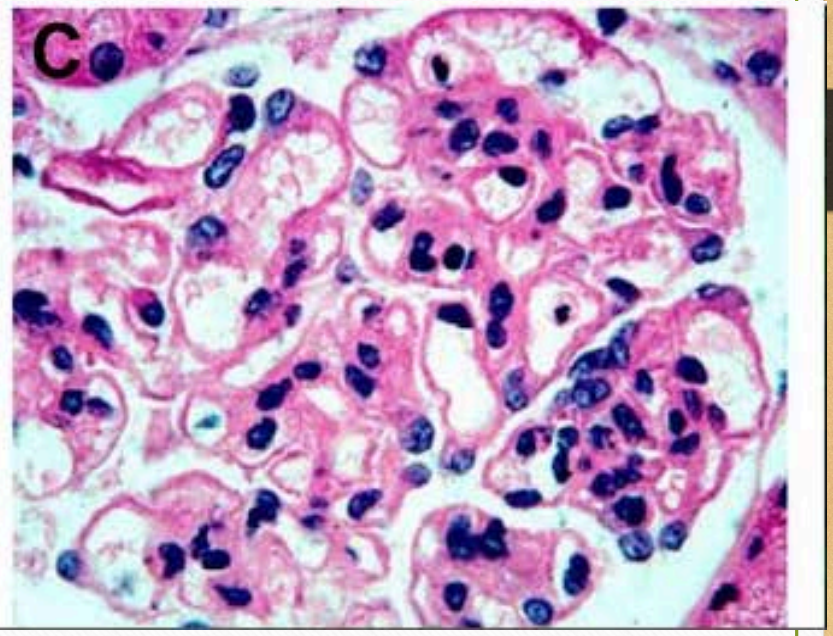
Membranous GN: EM/IF/LM



Subepithelial electron dense deposits



+IgG & Anti-PLA2R Ab along capillary wall

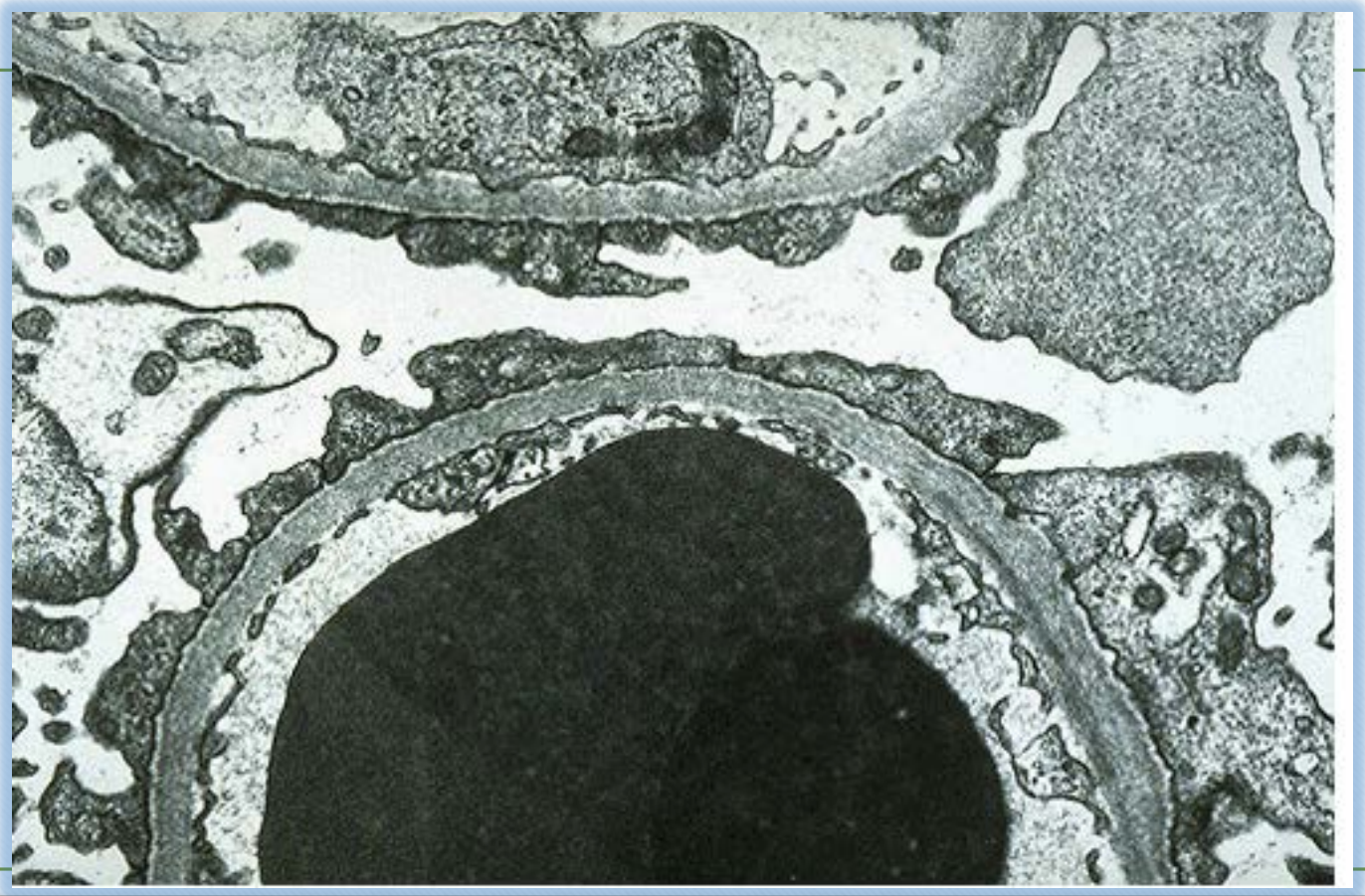


Thickened capillary walls

Minimal Change Disease

- Most common cause NS in children
- Extremes of age: young and very old
- Typically secondary in adults, from medications
  - NSAIDs, Hematologic malignancies (NHL) and Thymoma
- Typically severely nephrotic
- Steroid-responsive

Minimal Change Disease



Systemic Diseases → Glomerular Disease

- Diabetes mellitus
- Systemic lupus erythematosus
- Multiple myeloma
- Amyloidosis

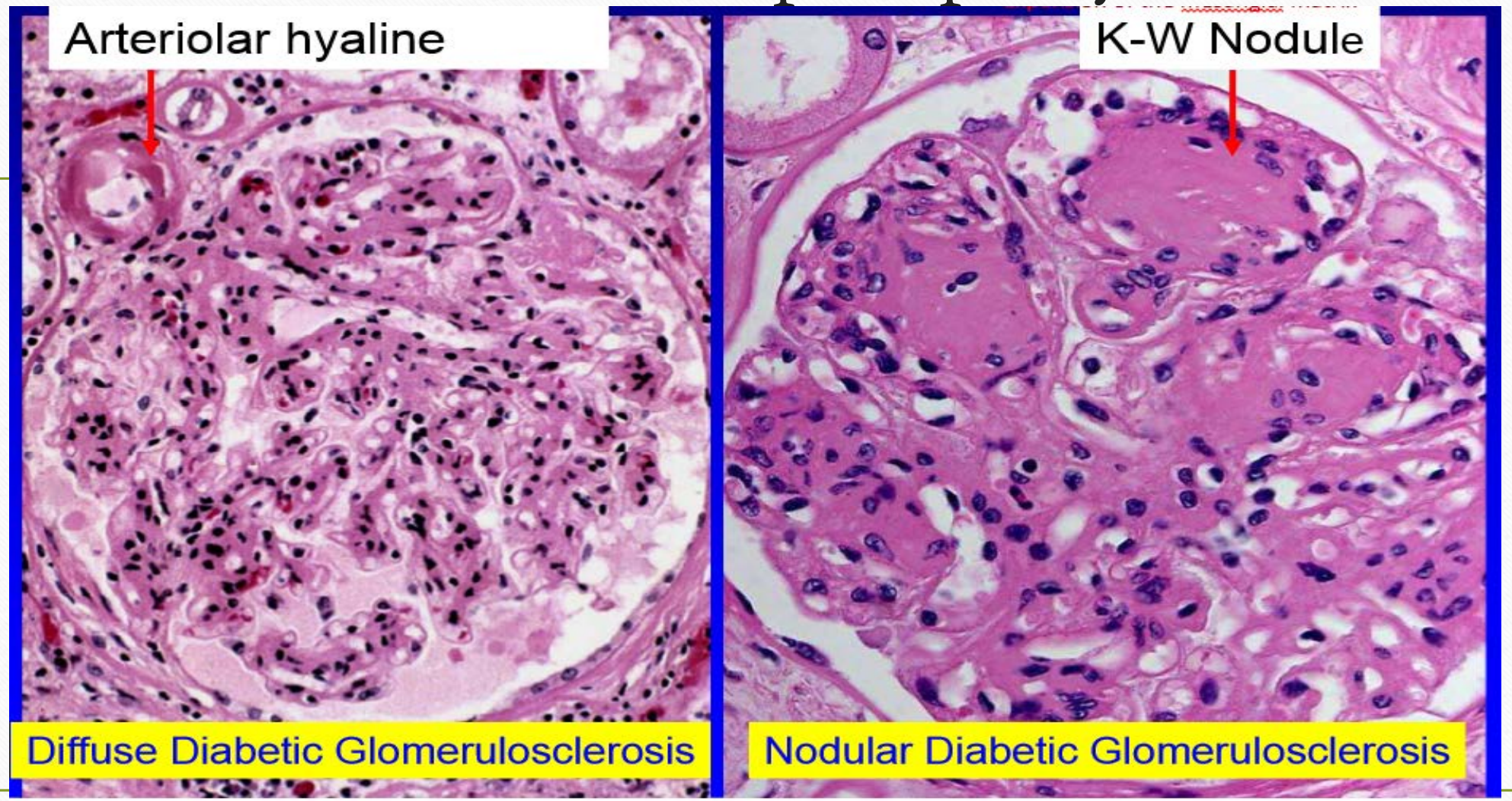
Diabetic Nephropathy

- #1 cause of kidney disease in the U.S.
- Develops after 10-12 years of diabetes Type 2; after 20 yrs in Type 1
  - Screen with UACR
  - Initially hyperfiltrative state, high GFR, "microalbuminuria"
- Clinically can be subnephrotic or nephrotic
  - Degree of proteinuria prognostic indicator

Diabetic Nephropathy: Path

- Basement membrane thickening and increased mesangial matrix
- Diffuse or Nodular glomerulosclerosis
  - ~ 50% have "Kimmelstiel-Wilson" nodules: ovoid, spherical, laminated hyaline masses in periphery of glomerulus, PAS+, **pathognomonic** for DN
- Profound hyalinization of afferent arterioles

Diabetic Nephropathy



Lupus Nephritis (LN)

- 60 % of adults with SLE will develop renal abnormalities
- Renal disease results from deposition of circulating immune complexes → complement cascade activation → comp-mediated damage, leukocyte infiltration, cytokine release
- Anti-dsDNA correlates best with renal disease
- Low C4 > C3
- 6 different histopathological classes
  - Prognosis and treatment depends on LN Class
  - May change classes over time or have >1 class on pathology

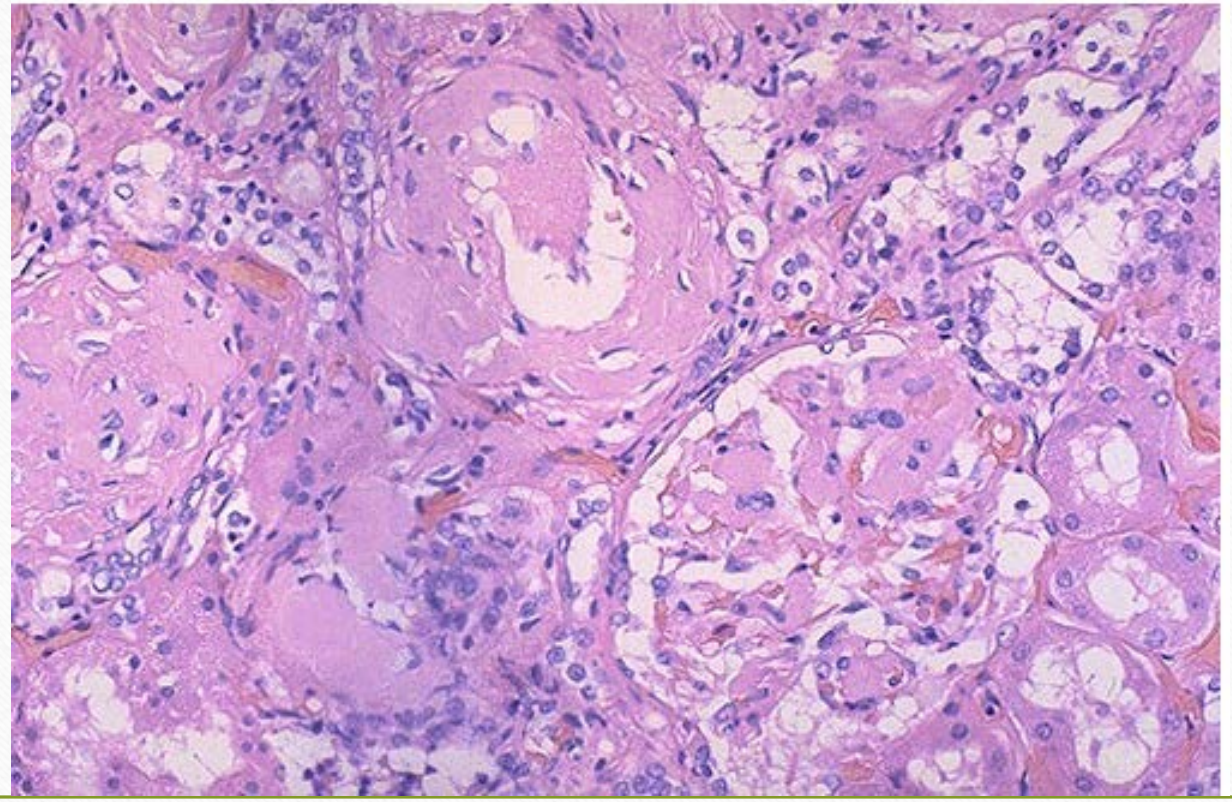
ISN / Renal Pathology Society Classification of Lupus Nephritis (2004)

Class	Renal Pathology
I	Minimal mesangial LN
II	Mesangial proliferative LN
III	Focal LN (< 50 % glomeruli)
IV	Diffuse LN (≥ 50 % glomeruli)
V	Membranous LN
VI	Advanced sclerosing LN (≥ 90% globally sclerosed glomeruli)

Gammopathies

- Diverse renal pathology, subnephrotic vs nephrotic
- Tubular vs Glomerular pathology
- Glomerular: MIDD, MPGN, C3GN, Crystalline podocytopathy
- Fibrillary GN and Immunotactoid glomerulopathy
- AL Amyloid

Renal Amyloid



Steel Magnolias: Dialysis

- https://youtu.be/oUVgUYvWKXA?t=11s

Questions?