

Kidney Disease in Lupus

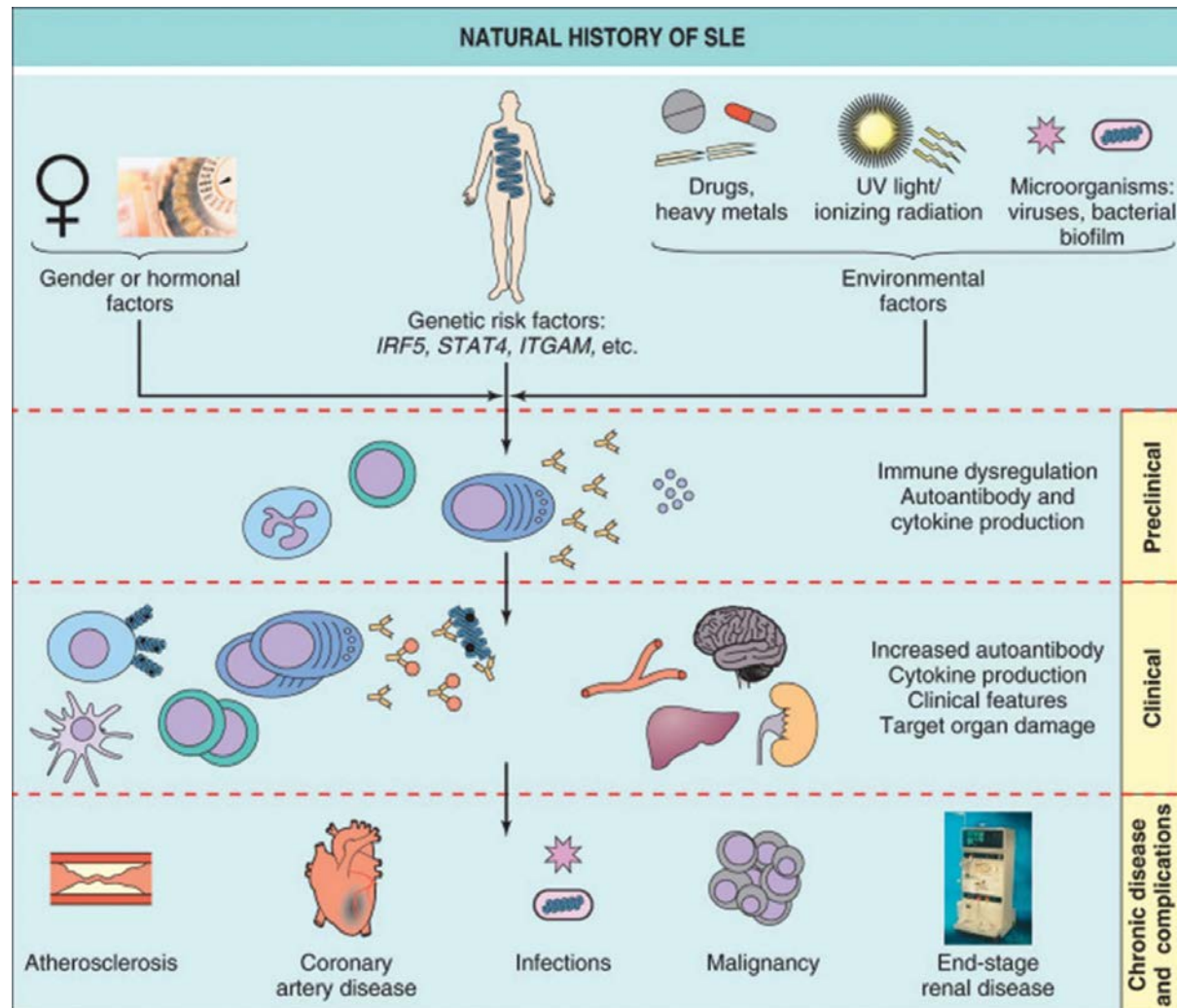
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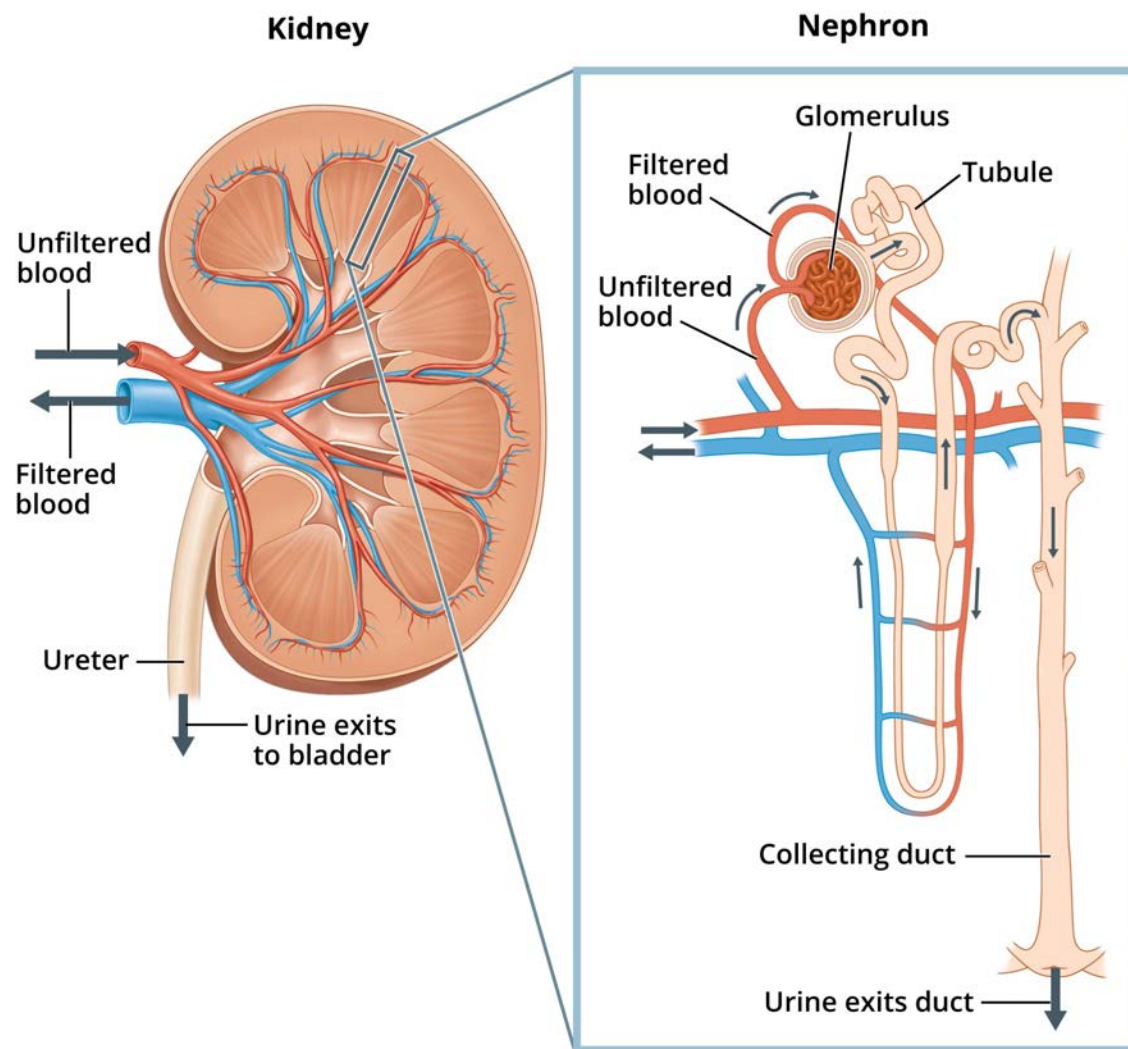




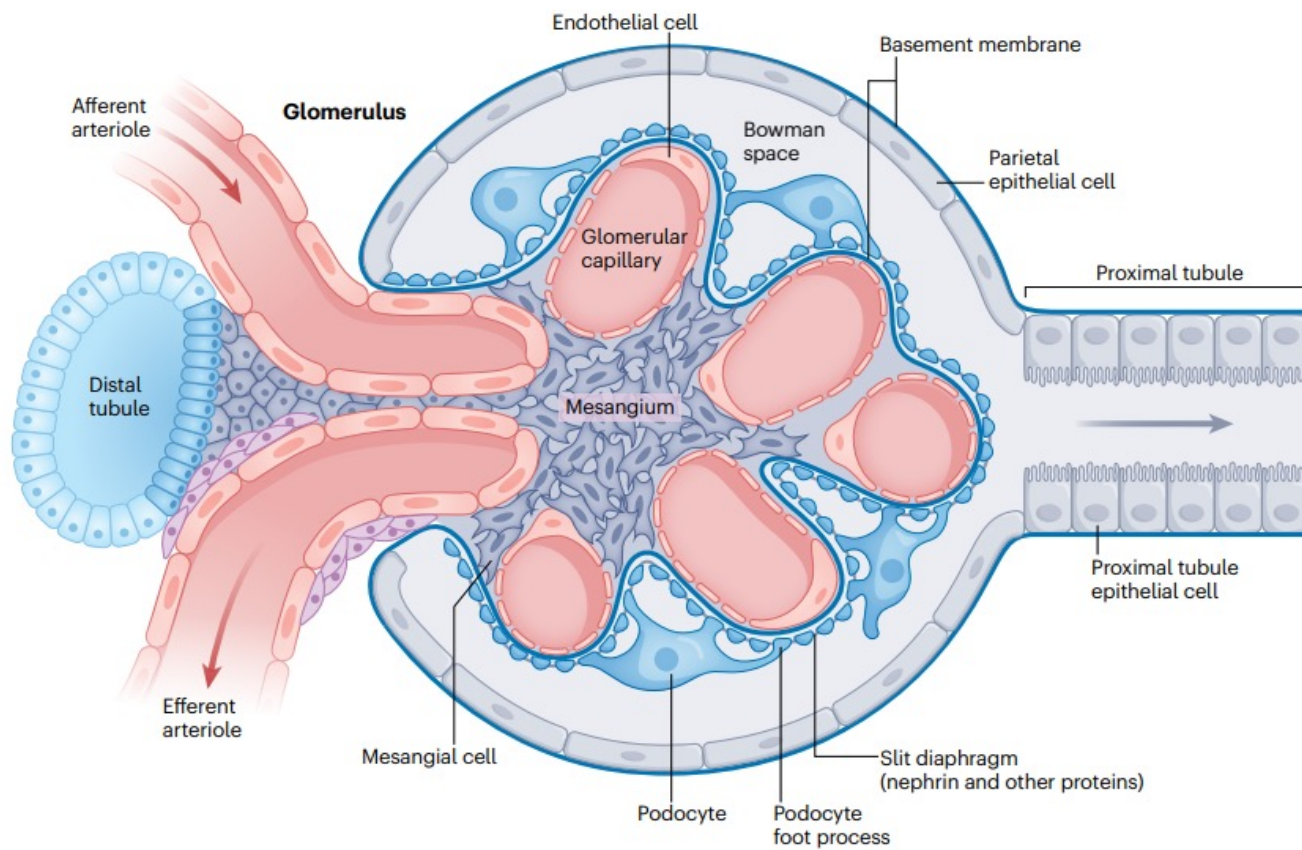
Rheumatology, Hochberg. 2023

Epidemiology of Lupus Nephritis

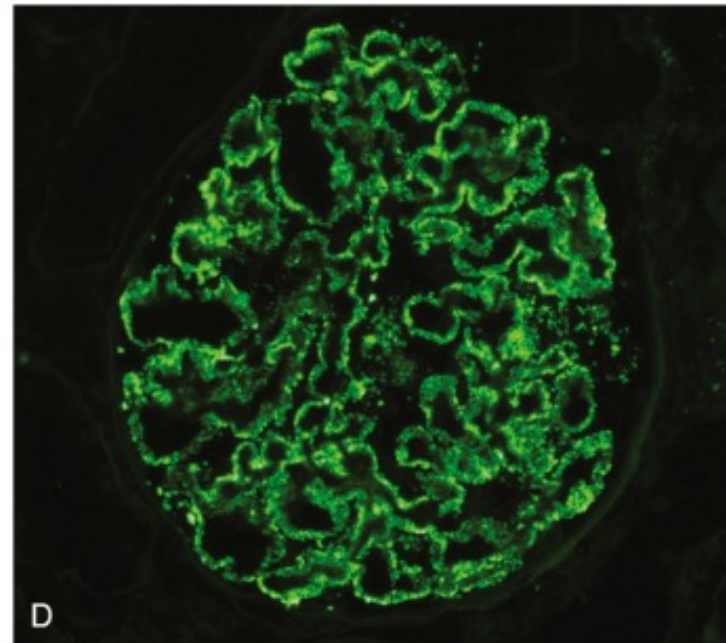
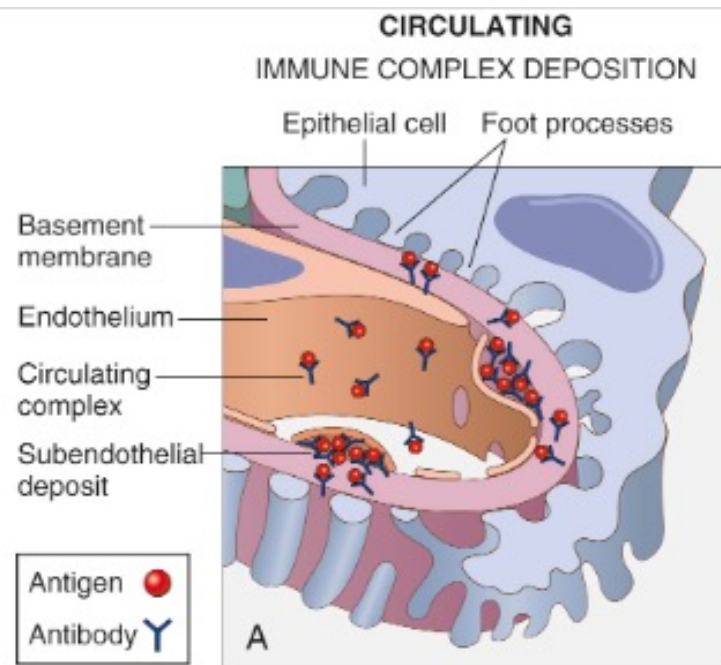
- LN is found in 20% to 60% of patients with SLE, and occurs most often within 6 months of the SLE diagnosis. LN can be the first manifestation of lupus.
- The risk of LN diminishes with age, and there is a higher incidence of LN in childhood compared with adult-onset SLE.
- LN occurs more often (40%–70%) in patients of Asian, African, Hispanic, or Native American origin than those of European origin (up to 30%).
- Currently progression to ESRD 5, 10, and 15 years after the diagnosis of LN occurs in about 11%, 17%, and 22% of patients in developed countries
- Progression to ESRD is higher among black, Asian, and Hispanic patients compared with white patients.

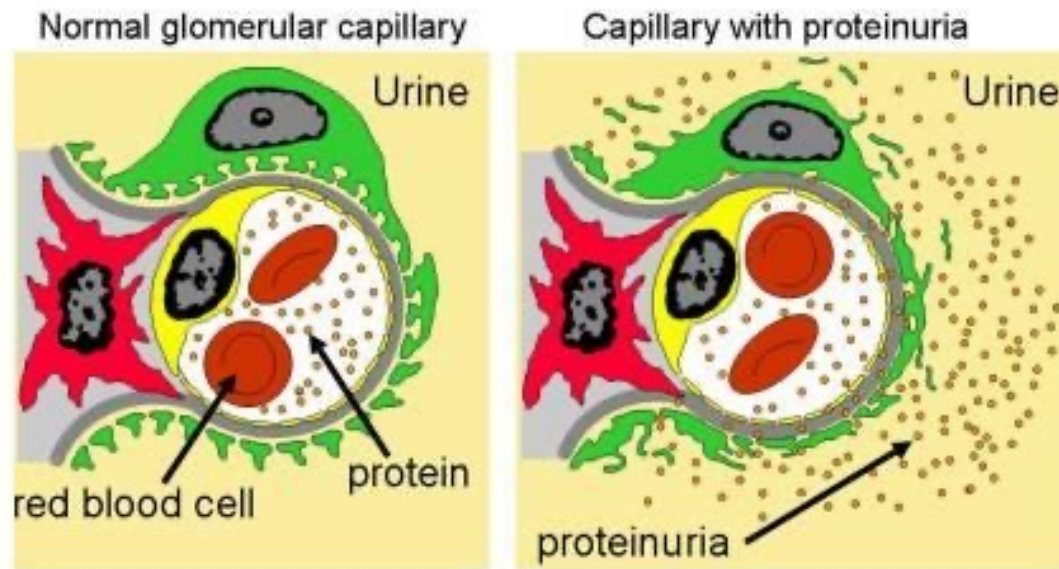


<https://www.niddk.nih.gov/news/media-library/11236>



Hans-Joachim Anders, et al. Nature Reviews Immunology 2023





1. Glomerular immune complexes cause a protein leak.
(Severe protein loss leads to edema.)
2. Glomerular inflammation cause leak of red blood cells.
3. Multiple factors lead to hypertension.

Common finding in lupus nephritis

- Blood and protein in the urine (earliest findings)
- High blood pressure (important contribution to kidney failure)
- Decreased kidney function = increased creatinine
- Swelling of the face, hands, feet, and belly

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-
- In early disease there are no symptoms!!

Why do a kidney biopsy?

- There may be other diseases causing kidney problems that mimic lupus nephritis.
- There are different type of lupus nephritis and they are treated differently.

Membranous

Diffuse Proliferative

Focal proliferative

Mesangial

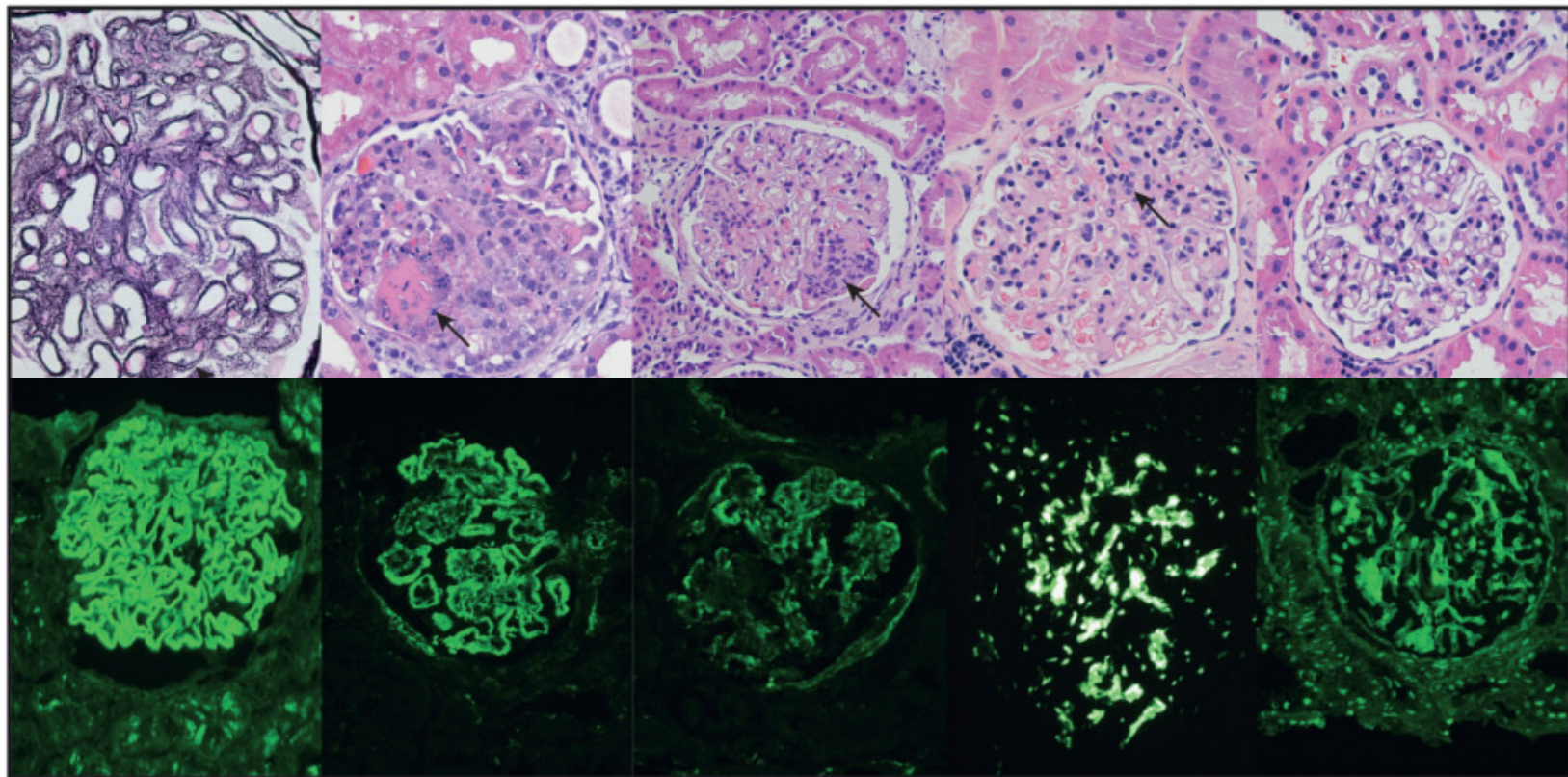
Class 5

Class 4

Class 3

Class 2

Class 1



Light microscopy

Immunofluorescence

Intermediate risk

High risk

Low risk

Treatment of Proliferative Lupus Nephritis

- Induction

- High dose steroids
- Mycophenolate or cyclophosphamide
- Rituximab

- Maintenance

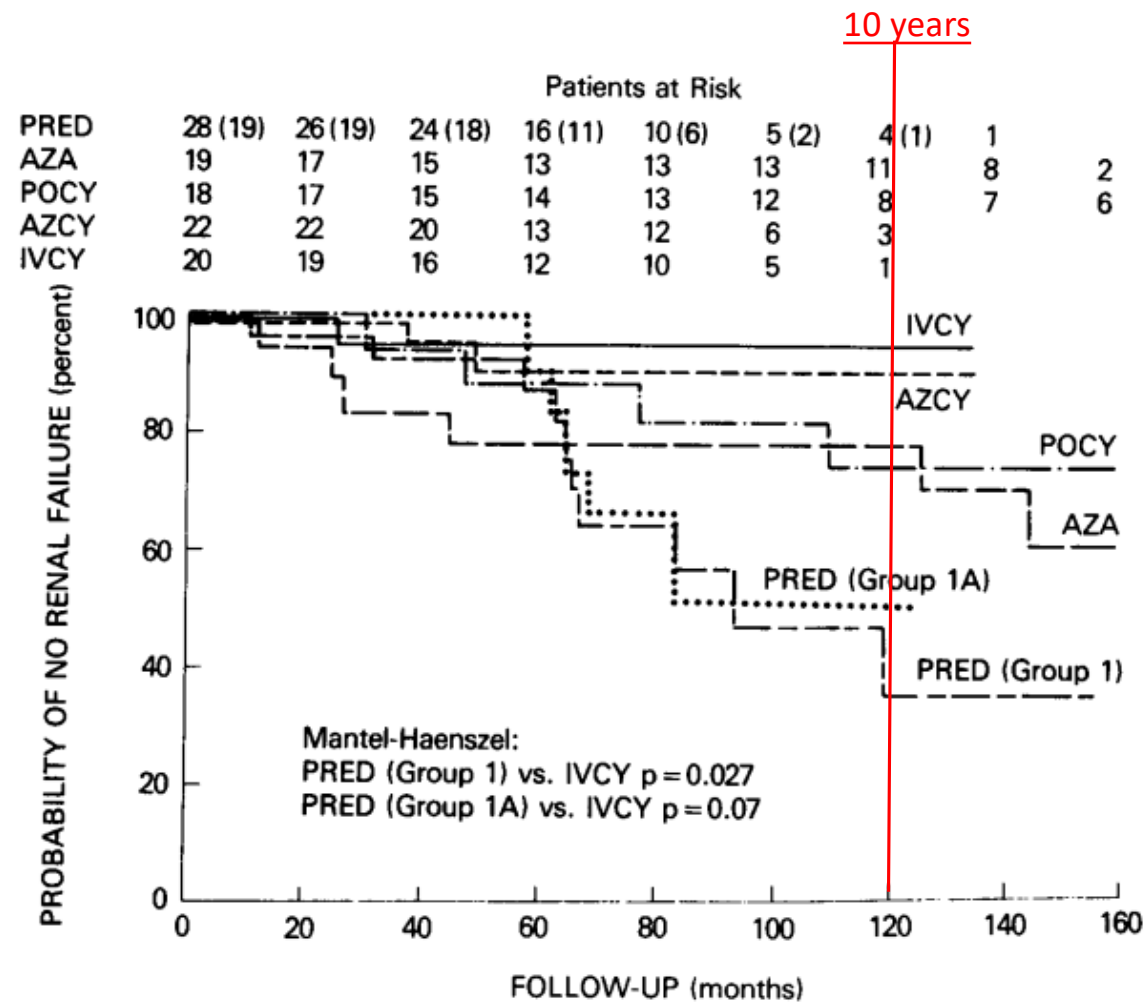
- Mycophenolate or azathioprine
- Cyclosporine or tacrolimus or **vocolosporin**
- **Belimumab**
- Hydroxychloroquine

- Adjuvant

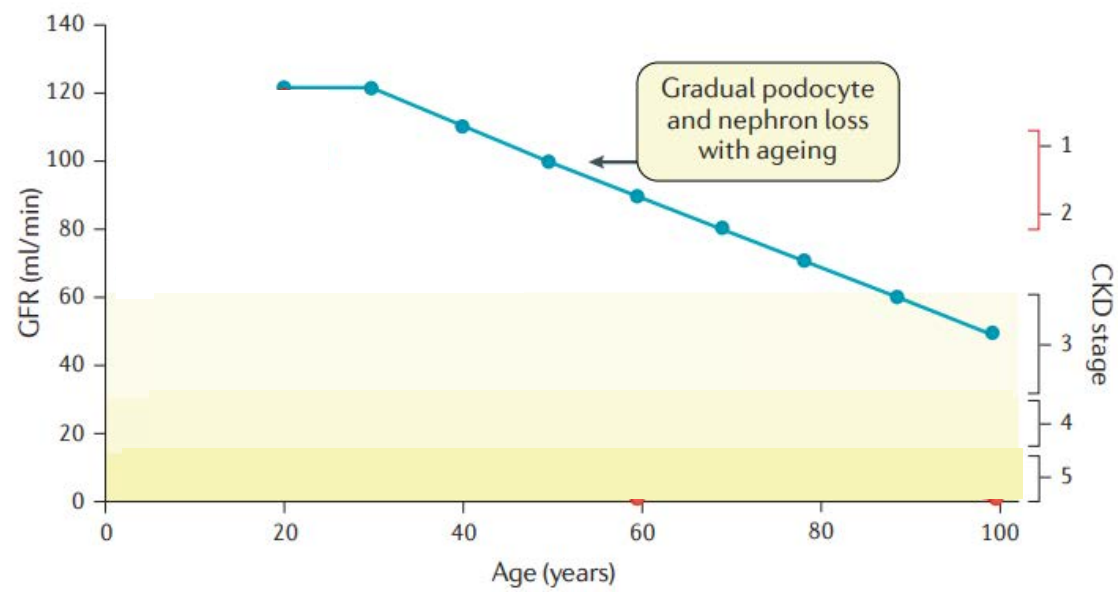
- ACE-Inhibitors, ARB, and other BP medications
- Health diet especially low sodium diet
- Smoking cessation

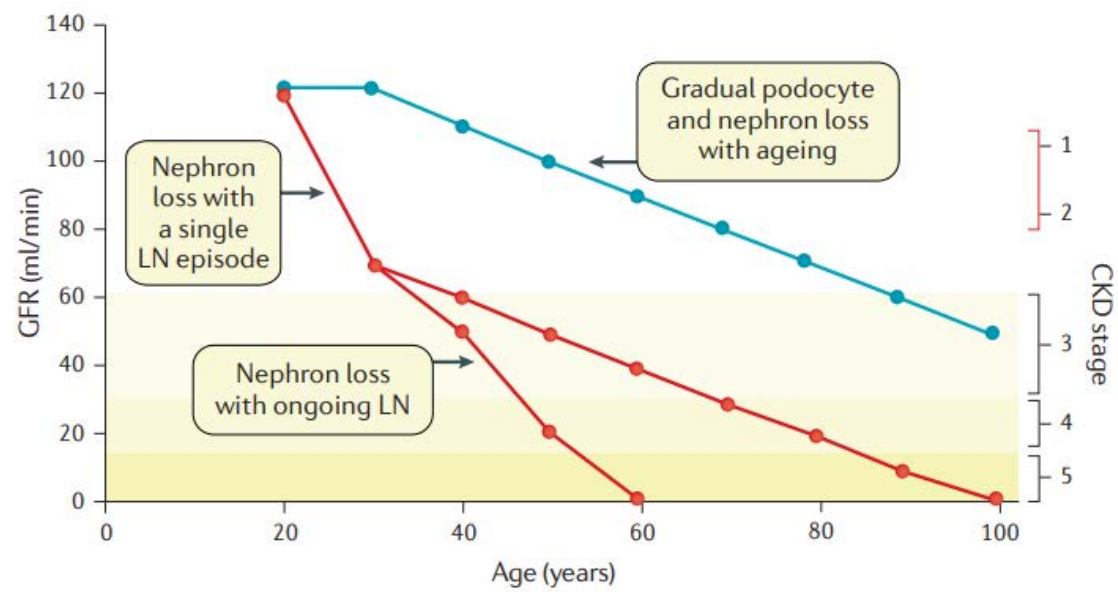
1. Targeting autoimmunity

2. Protecting the kidney

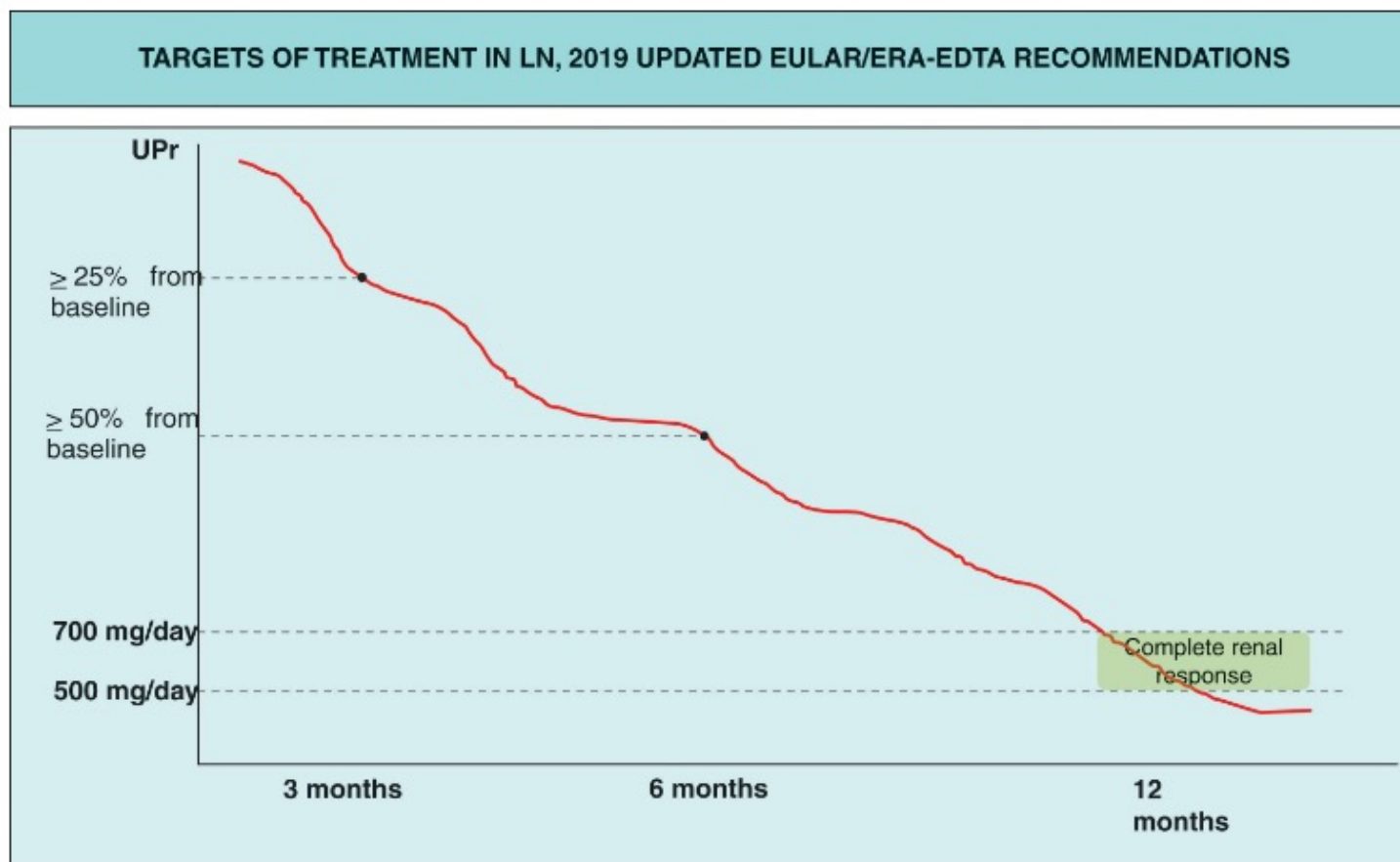


Howard A. Austin, et al, NEJM 1986





Right now proteinuria is our best measure of renal response



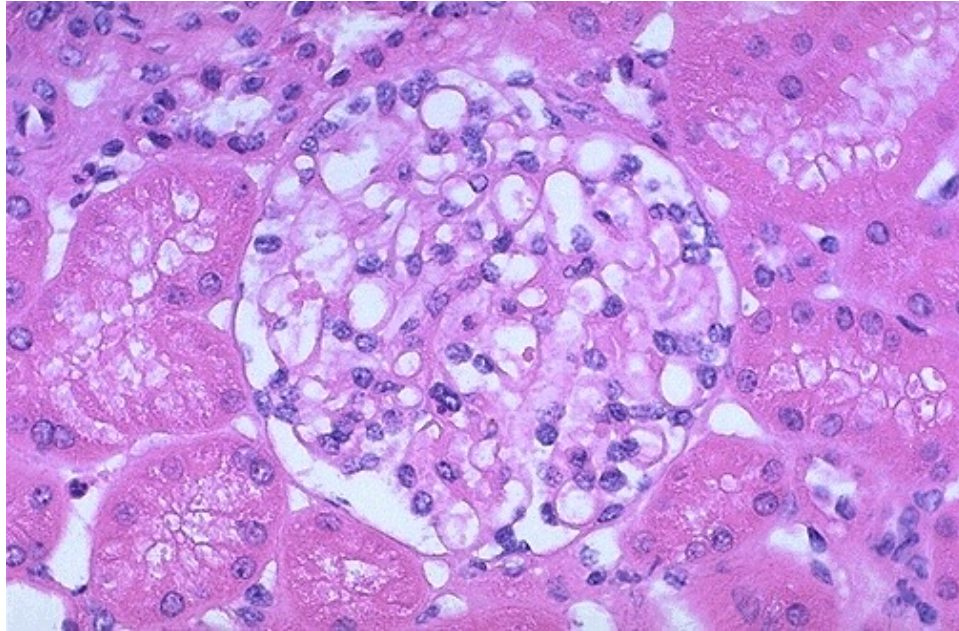
Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				Persistent albuminuria categories		
				Description and range		
				A1	A2	A3
				Normal to mildly increased < 30 mg/g < 3 mg/mmol	Moderately increased 30–300 mg/g 3–30 mg/mmol	Severely increased > 300 mg/g > 30 mg/mmol
GFR categories (ml/min/1.73 m ²) Description and range	G1	Normal or high	≥ 90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	< 15			

Green, low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk.

GFR, glomerular filtration rate

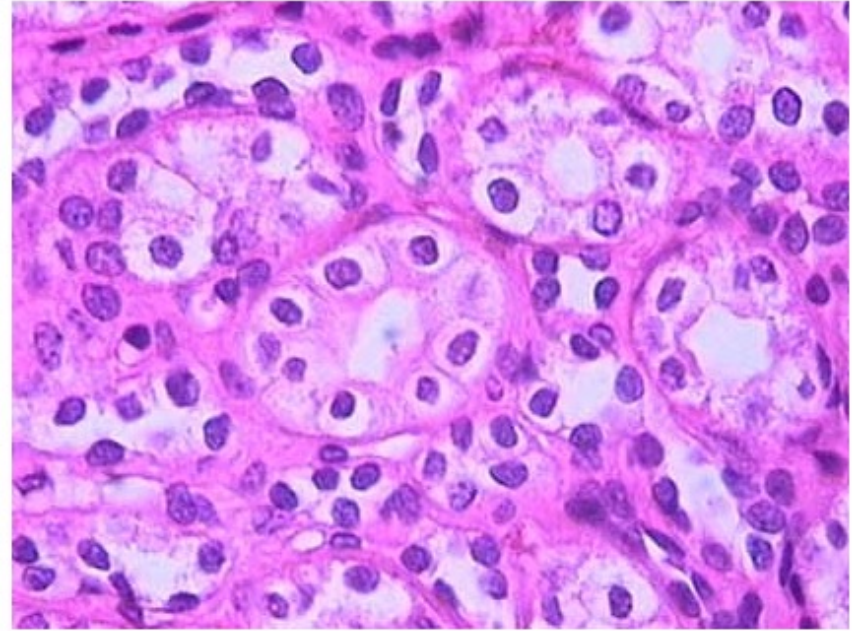
KDIGO 2023 CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF LUPUS NEPHRITIS

Glomerulus



Filters the blood
Protects blood proteins

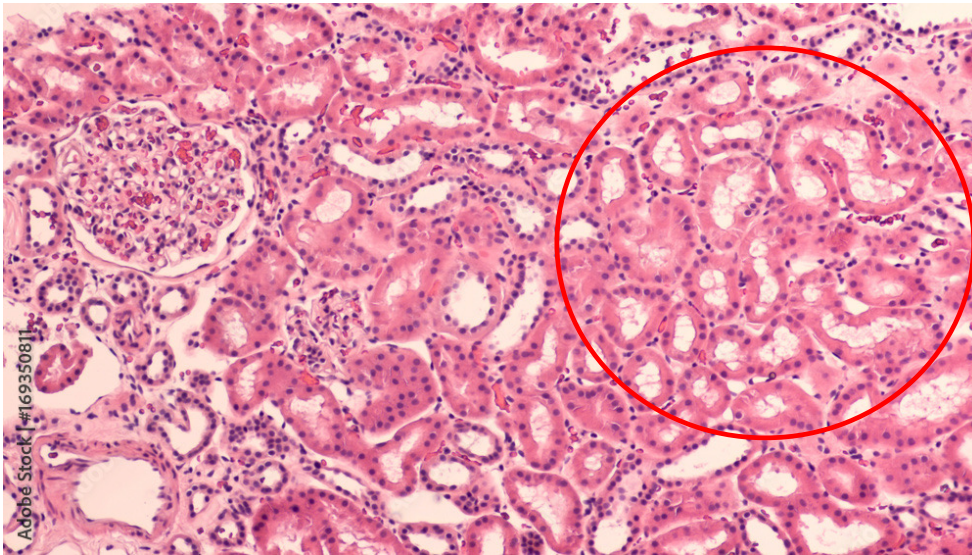
Tubules



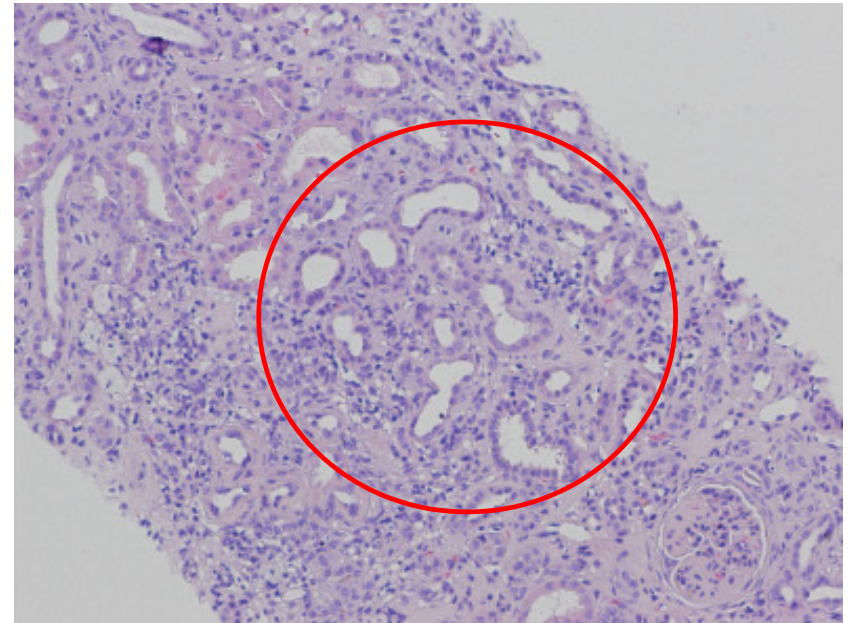
Processes the urine
Retains glucose and sodium

New approaches to prevent progression target the tubules

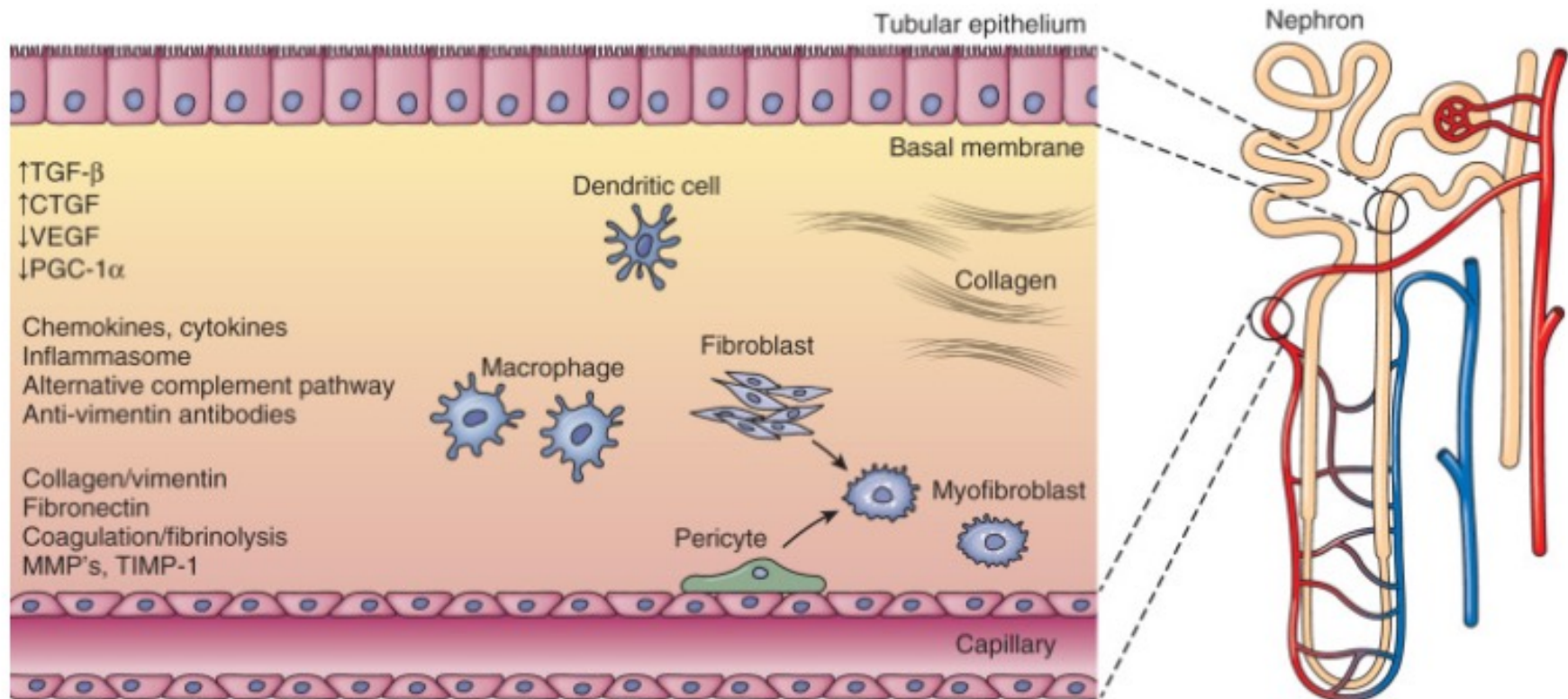
Normal Tubules



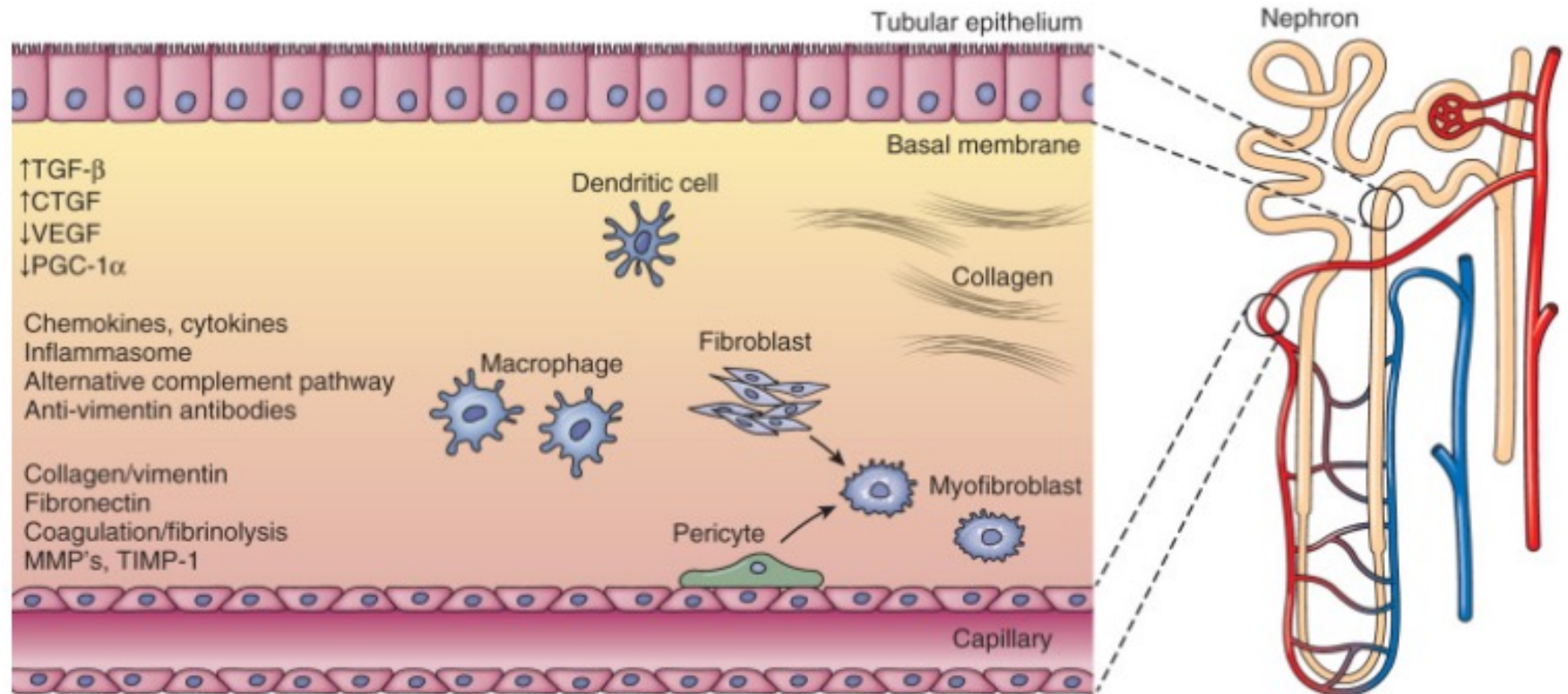
Lupus Tubules



Link between damage and progression to renal failure

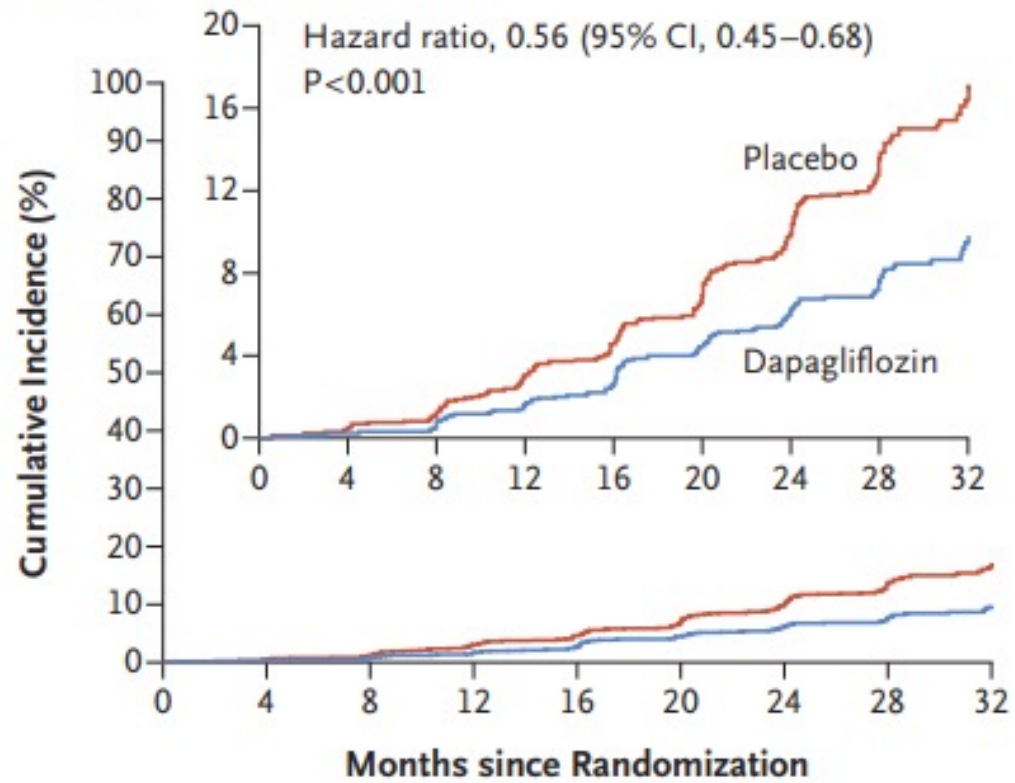


Stress due to proteinuria



Stress due to inflammation and decreased blood supply

B Renal-Specific Composite Outcome



No. at Risk

Placebo	2152	1993	1936	1858	1791	1664	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309

Keys for successful outcomes

1. Early diagnosis
2. Well informed patients who actively participate in their treatment
3. Starting treatment early and staying on treatment
4. Frequent evaluation of response and adjustment of treatment
5. Treating comorbidities such as hypertension and diabetes
6. Healthy lifestyles
7. Providers who listen to patients

Thinking about Rochester's future

1. Programs to identify patients at risk (education and screening)
2. Access and support (IQ Lupus*: Dr. Shah)
3. Equity for underserved patient populations (Dr. Edith M. Williams)
4. More effective less toxic treatment (LuCIN: Drs. Anolik, Abeles, Shah)
5. Better biomarkers (NIH AMP Network: Drs. Anolik and Barnas)
6. Medications to protect the kidney and prevent progression (LRA: Drs. Anolik and Rangel-Moreno)
7. Prevent lupus - linking lifestyle, microbiome, diet, environmental factors and other potentially modifiable factors to the risk for autoimmunity (and allergic diseases)

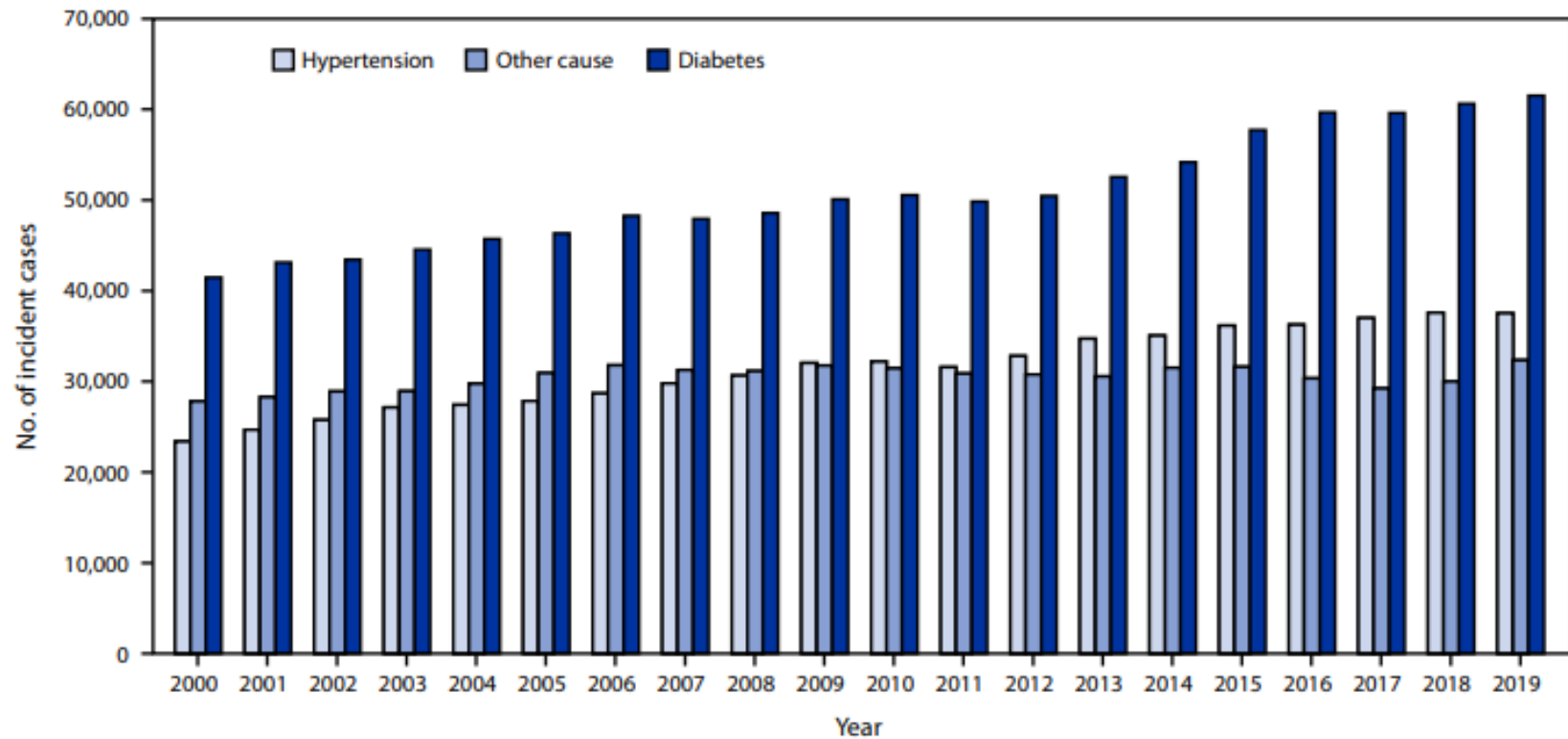
* Started by Dr. Anandarajah



Thank You!

The importance of hypertension and diabetes

FIGURE 1. Number of reported incident cases of end-stage kidney disease, by primary cause — United States, 2000–2019*



* Data from United States Renal Data System, 2021 Annual Data Report, Reference Tables. <https://adr.usrds.org/2021/reference-tables>