



Lupus Nephritis

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**KDIGO CLINICAL PRACTICE
GUIDELINE FOR THE MANAGEMENT
OF GLOMERULAR DISEASES**





Pleural effusions

Heart problems


Lupus nephritis

Arthritis

Raynaud's phenomenon

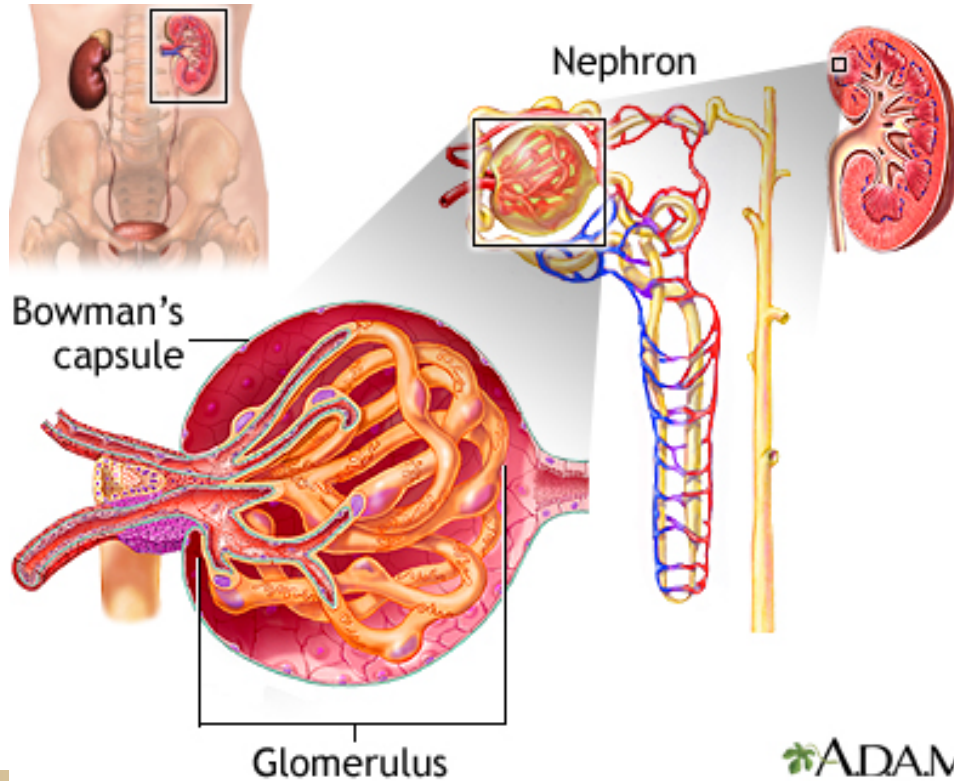
Butterfly rash

Symptoms of systemic lupus erythematosus may vary widely with the individual

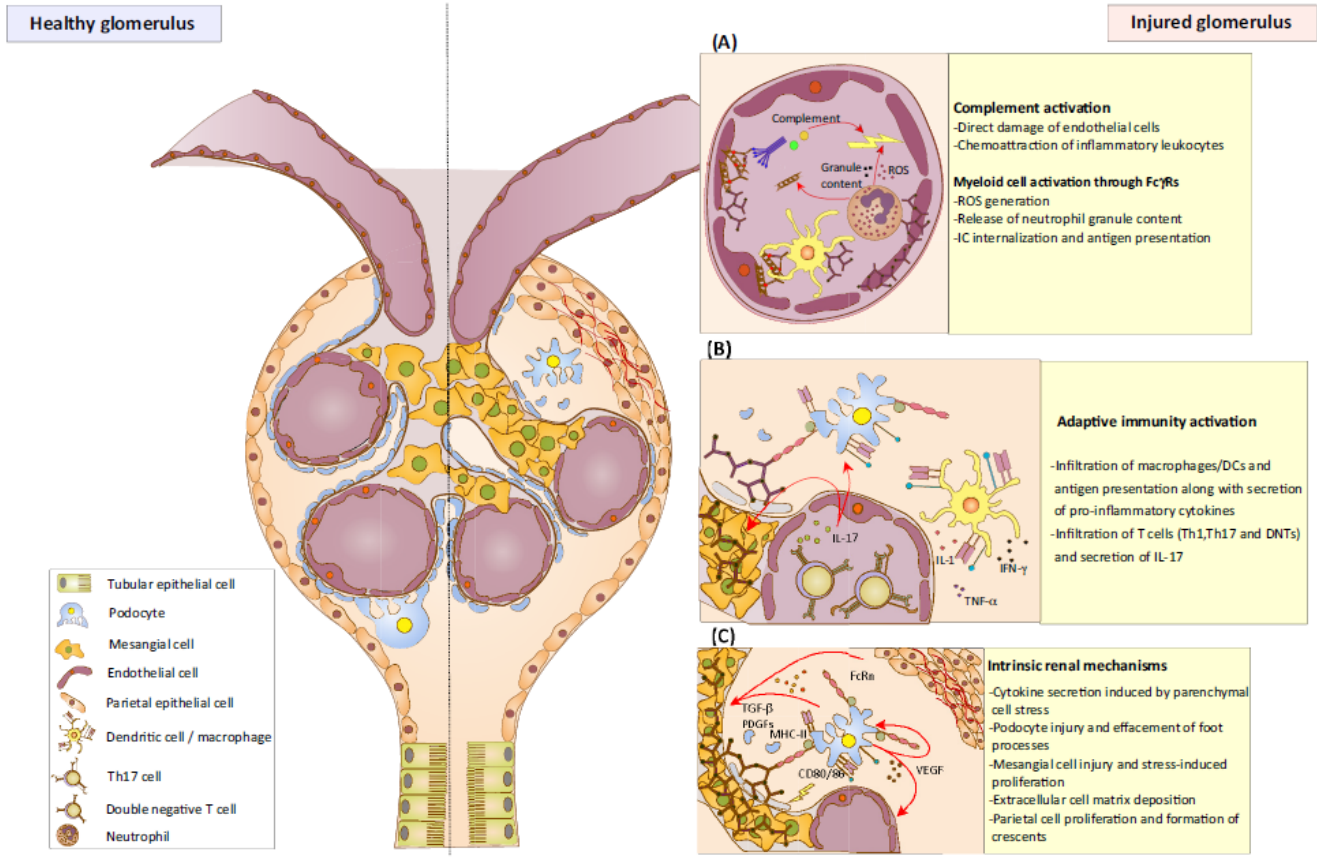




Kidney- Nephron- Glomeruli



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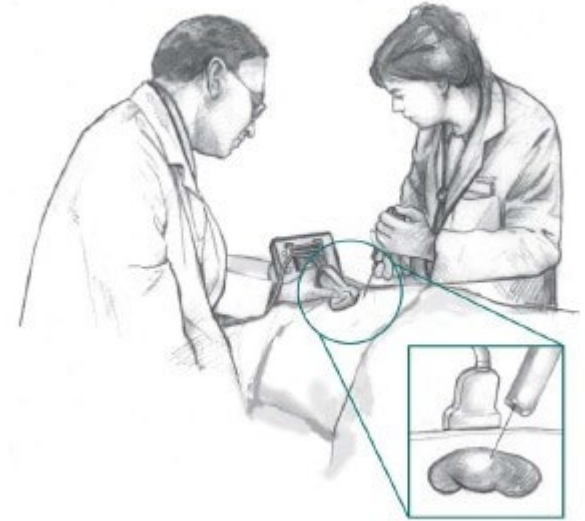


Diagnosis: Kidney Biopsy



Practice Point 1.1.1: The kidney biopsy is the “**gold standard**” for the diagnosis of Lupus Nephritis

Practice Point 1.1.3: Repeat kidney biopsy should be performed if the information will potentially alter the therapeutic plan or contribute to the estimation of prognosis



Diagnosis

Blood tests: Assessing Kidney Function

- serum creatinine and or serum cystatin C
- Calculate eGFR

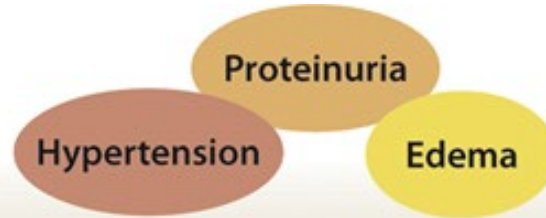
Urine tests:

- Protein in urine- either by urine protein creatinine ratio or 24-hour urine protein
- Urine microscopy for blood in urine





General treatment guidelines



Lifestyle modifications:

- Sodium restriction
- Moderate protein restriction
- Heart-healthy diet
- Target ideal body weight
- Increased physical activity
- Smoking cessation
- Reduce alcohol consumption

- Renin-angiotensin-aldosterone system inhibitors
- Diuretics
- Non-renin-angiotensin-aldosterone system blockade (e.g., calcium channel blockers)

Other considerations:

- Anticoagulation
- Contraception
- Immunizations
- Management of cardiovascular risk factors



Lifestyle Modifications

- Sodium restriction
- Increase physical activity
- Smoking cessation
- Reduce alcohol consumption



Edema

- Sodium restriction
- Diuretics- water pills
- Need monitoring of electrolytes and creatinine by blood tests



Decreasing proteinuria

- Low salt intake
- Good BP control <120/80 mm Hg
- ACE-I/ARB- lisinopril/losartan
- Consider SGLT2i- dapagliflozin, empagliflozin
- Smoking cessation
- Weight normalization (to ideal body weight)



Complications of Protein in urine

Hyperlipidemia

- Checking serum cholesterol levels
- Starting statin

Hypercoagulability

- Increased risk of blood clots
- Blood thinners if develop blood clot



Complications of protein in urine: Infections

- Pneumococcal vaccine to prevent Pneumonia
- Patients and household contacts should receive the influenza vaccine
- Shingles vaccination to prevent zoster
- Screening for tuberculosis (TB), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and syphilis in clinically appropriate patients is suggested.

Lupus Nephritis General Management

Risk	Risk attenuation
Cardiovascular risk	<ul style="list-style-type: none"> • Lifestyle modifications – smoking cessation, body weight optimization, exercise • Dyslipidemia management • Low-dose aspirin during pregnancy • Blood pressure control
Proteinuria and CKD progression (refer to Chapter 1)	<ul style="list-style-type: none"> • Avoid high-sodium diet • Optimize blood pressure • Renoprotective medications, such as RAAS blockade, SGLT2 inhibitor, etc., in stable patients without AKI • Avoid nephrotoxic insult • Prevent AKI
Infection risk	<ul style="list-style-type: none"> • Assess medical history of herpes zoster and tuberculosis • Screening for HBV, HCV, HIV, and HBV vaccination • <i>Pneumocystis jirovecii</i> prophylaxis (issue of potential adverse drug reaction discussed below) • Influenza and pneumococcal vaccination • Individualized consideration for recombinant zoster vaccine • Individualized consideration for other infectious organisms as dictated by public health concerns at the time of treatment
Bone injury	<ul style="list-style-type: none"> • Bone mineral density and fracture risk assessment • Calcium and vitamin D supplementation • Bisphosphonates when appropriate
Ultraviolet light exposure	<ul style="list-style-type: none"> • Broad-spectrum sunscreen • Limit ultraviolet light exposure
Premature ovarian failure	<ul style="list-style-type: none"> • Gonadotropin-releasing hormone agonists (i.e. leuprolide) • Sperm/oocyte cryopreservation
Unplanned pregnancy	<ul style="list-style-type: none"> • Individual evaluation and counselling for contraception type (preference, thrombosis risk, age)
Cancer	<ul style="list-style-type: none"> • Evaluate individual risk factors for malignancies • Age-specific malignancy screening • Minimize lifetime cyclophosphamide exposure to <36 g



Kidney Biopsy in Lupus Nephritis



Lupus Nephritis HISTOPATHOLOGY

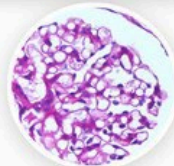
GlomCon

This infographic is based on the GlomCon fellowship session by
Dr. Anila Abraham Kuriem on Histopathology of Lupus Nephritis.
November 25, 2021

Histopathologic findings in lupus nephritis are heterogenous and affect all compartments of the kidney. The site of deposition of immune complexes determines the histological pattern. To date, the ISN/RPS 2018 Classification is used to interpret the kidney biopsy based on glomerular features.

CLASS I

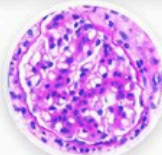
Minimal mesangial



- Normal by light microscopy [LM]
- Mesangial deposits on immunofluorescence [IF] or electron microscopy [EM]

CLASS II

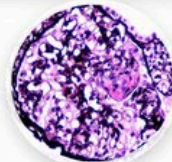
Mesangial



- Pure mesangial hypercellularity with ≥ 4 nuclei surrounded by mesangium per mesangial area, away from the hilum
- Mesangial deposits in IF & EM

CLASS III

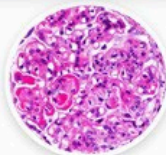
Focal proliferative



- Segmental or global endocapillary hypercellularity by LM in $< 50\%$ of glomeruli

CLASS IV

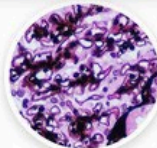
Diffuse proliferative



- Segmental or global endocapillary hypercellularity by LM in $\geq 50\%$ of glomeruli

CLASS V

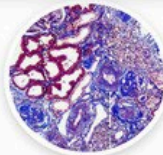
Membranous



- Segmental to global subepithelial electron dense deposits
- If endocapillary hypercellularity is also present, an additional diagnosis of Class III or IV nephritis is made

CLASS VI

Sclerotic



- $> 90\%$ glomeruli globally sclerotic
- No evidence of endocapillary proliferation in the remaining glomeruli



Lupus Nephritis

Recommendation 10.2.1.1: We recommend that patients with SLE, including those with lupus nephritis (LN), be treated with hydroxychloroquine or an equivalent antimalarial unless contraindicated (1C).





LN class 1 and 2

- Hydroxychloroquine
- Ace-i/Angiotensin receptor blocker: Lisinopril/Losartan



LN class 3 and 4

- Hydroxychloroquine
- Ace-i/Angiotensin receptor blocker: Lisinopril/Losartan
- Glucocorticoids : oral vs intravenous over 4 months



LN class 3 and 4

Initial therapy 6-9 months

- Mycophenolate Mofetil – oral medication twice daily
 - Side effects: Nausea, vomiting, diarrhea
 - Low white blood cell count
- Intravenous cyclophosphamide once every 2 – 4 weeks
 - Side effects: Nausea, vomiting, diarrhea
 - Low white blood cell count



LN class 3 and 4

Initial Therapy 6-9 months

- Mycophenolate and Belimumab
- Mycophenolate and voclosporin/tacrolimus



Blood test to monitor

- Complete Blood count
- Kidney function- serum creatinine
- Urine test – blood and protein in urine
- Lupus Markers: Serum complement levels C3/C4,
Double stranded DNA antibody levels



LUPUS NEPHRITIS – TREATMENT: CLASS III OR CLASS IV

LN: MAINTENANCE THERAPY

Recommendation 10.2.3.2.1: We recommend that after completion of initial therapy, patients should be placed on mycophenolate for maintenance (*1B*) which is to prevent flare of disease for total of 3 years



Treatment of LN

Prednisone+ MMF

Complete
remission

Partial
response

No
response



LUPUS NEPHRITIS – RESPONSE AND RELAPSE

CONSIDERATIONS: MANAGEMENT OF UNSATISFACTORY RESPONSE TO TREATMENT

1	Verify adherence to treatment
2	Ensure adequate dosing of immunosuppressive medications by measuring plasma drug levels if applicable or available (check mycophenolic acid level if on mycophenolic acid analogs/check infusion records if on cyclophosphamide)
3	Repeat biopsy if concern for chronicity or other diagnosis (e.g., thrombotic microangiopathy)
4	Consider switching to an alternative recommended treatment regimen when there is persistent active disease
5	Consider the following in patients refractory to first-line treatment regimens: <ul style="list-style-type: none">• Addition of rituximab or other biologic therapies• Extended course of i.v. pulse cyclophosphamide• Enrollment in clinical trials if eligible



enrollmypatient

Clinical Trials Patient Portal MyGlomCon

Clinical Trials

A list of currently enrolling clinical studies

1 APOLI-mediated kidney disease Learn More	2 IgA Nephropathy Learn More	3 Lupus Nephritis Learn More
4 Membranous Nephropathy Learn More	5 Complement 3 Glomerulopathy Learn More	6 Focal segmental glomerulosclerosis Learn More
7 Minimal Change Disease Learn More		

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Take Home Points

Kidney biopsy is needed to diagnose Lupus Nephritis

Prednisone with Mycophenolate are the main medications used for treatment

New FDA approved medications for treatment of Lupus Nephritis

Clinical trials are important to advance the field and find new therapies for treatment to have options

Thank you



Contact: tsingh@medicine.wisc.edu