# Lupus Nephritis

**Background**

1. Definition (if needed / appropriate)
    - Glomerular disease resulting from Systemic Lupus Erythematosus (SLE)
    - Dx based on renal biopsy

**Pathophysiology**

1. Pathology of disease
    - Multifactorial glomerular disease, largely attributed to immune complex deposition, increase in mesangial cells and matrix, basement membrane abnormalities, inflammation and cellular proliferations
2. Incidence, prevalence
    - Estimated 1.5 million people in US have SLE
        - Male to female ratio 1:12
    - Lupus nephritis occurs in patients with SLE
        - In early SLE, 25-50% will develop lupus nephritis
        - In late SLE, 60-80% will develop lupus nephritis
3. Risk factors
    - Blacks and Hispanics are at greater risk, even when controlling for socioeconomic factors
4. Morbidity / mortality
    - Proteinuria leads to nephritic syndrome in 45-65% pts
    - Despite appropriate Tx, some patients will eventually progress to end-stage renal dz
    - Race is significant
        - Whites >90% survival at 5 years after renal biopsy
        - Blacks 60% survival at 5 years after renal biopsy

**Diagnostics**

1. History
    - Weight gain
    - Dark urine
    - Edema
2. Physical exam
    - Hypertension
    - Edema
3. Diagnostic testing
    - Laboratory evaluation
        - Renal insufficiency (100% sens)
        - Microscopic hematuria (80% sens)
        - Renal insufficiency (40-80% sens)
        - Proteinuria >500mg/dl (45-65% sens)
        - Granular casts (30% sens)
        - Declining renal function (30% sens)
        - Hypertension (15-50% sens)
        - Hyperkalemia (15% sens)
        - Red cell casts (10% sens)
        - Renal failure (1-2% sens)

        - Gross hematuria (1-2% sens)
    - Diagnostic imaging
        - Renal ultrasound
    - Other studies
        - Renal biopsy - gold standard for diagnosis
4. Diagnostic "Criteria"
    - WHO classification (1995)
        - Class I: Normal biopsy
        - Class II: Mesangial deposits
        - Class III: Focal segmental proliferative nephritis
        - Class IV: Diffuse proliferative nephritis
        - Class V: Membranous nephritis
        - Class VI: Diffuse glomerulosclerosis and advanced tubulointerstitial disease
    - International Society of Nephrology / Renal Pathology Society classification (2003)
        - Class I: Minimal mesangial lupus nephritis
        - Class II: Mesangial proliferative lupus nephritis
        - Class III: Focal lupus nephritis
        - Class IV: Diffuse segmental or global lupus nephritis
        - Class V: Membranous lupus nephritis
        - Class VI: Advanced sclerosing lupus nephritis
    - Changes in proteinuria, serum creatinine, anti-ds DNA and C3 concentrations correlate with renal flares and outcome

**Differential Diagnosis**

1. Key DDx
    - Pyelonephritis
    - Urinary calculi
    - Preeclampsia
    - Intrinsic renal disease
2. Extensive DDx
    - Nephritic range proteinuria
        - Post-streptococcal glomerular nephritis (GN)
        - Crescentic GN
        - Membranoproliferative GN
        - HCV-associated cryoglobinemia
        - IgA nephropathy
        - Rapidly progressive glomerular nephritis
        - Anti-basement membrane disease
        - Systemic vasculitis
            - Henoch Schonlein Purpura
            - Wegener's granulomatosis
        - TTP / HUS
    - Nephrotic range proteinuria
        - Amyloidosis
        - Focal segmental glomerular sclerosis
        - Minimal change disease
        - Preeclampsia

- Renal and ureteral calculi
- Acute tubular necrosis

**Therapeutics**

1. Acute treatment (induction therapy)
    - Corticosteroids are the 1st-line therapy plus an immunomodulator (such as cyclophosphamide)
    - Mycophenolate mofetil
        - Alternative to cyclophosphamide for induction
        - Newer agent with emerging data supporting its use
        - Intensification considered after six months if inadequate response (proteinuria >1g/day)
2. Long-term care
    - Therapeutic options:
        - Corticosteroids
            - Recommended option: Methylprednisolone IV in combination with either cyclophosphamide or azathioprine
        - Cyclophosphamide (Cytoxan, Neosar)
            - May cause irreversible ovarian failure in young women
        - Azathioprine
        - Mycophenolate mofetil (CellCept)
            - Insufficient evidence to recommend for long-term use but data is emerging supporting its use
        - Rituximab (Rituxan)
            - Small, short-term trials suggest that up to 50% of refractory patients to cyclophosphamide may respond to rituximab
            - Additional data is emerging showing potential use in maintenance
        - Dialysis
        - Kidney transplant
            - Superior long-term survival compared to dialysis for ESRD
    - Considerations
        - Long-term efficacy has only be shown for cyclophosphamide but this has considerable side effects
        - Mycophenolate has had similar or better efficacy but only in short- to medium-term trials
            - It also has a more favorable side effect profile

**Follow-Up**

1. Return to office every 3-6 mo
2. Recommendations for earlier follow-up
    - Refer to nephrology or interventional radiology for renal biopsy
    - Refer to nephrology for recommendations
3. Laboratory studies
    - Complete blood count
    - Inflammatory markers (ESR, CRP)
    - 24 hour urine collection for protein and creatinine clearance
    - Urine sediment analysis
    - Chemistry to include evaluation of renal function
4. Admit to hospital

- Induction of therapy
- Acute worsening of renal function, including proteinuria and drop in GFR

**Prognosis**

1. Variable course and pattern
    - Chronicity of nephritis (as determined by biopsy) is a stronger prognostic factor than nephritis classification
        - Patients with active lesions have minimal progression with effective therapy
        - Those with active and chronic lesions are much more likely to have worsening nephritis as identified by increasing proteinuria, active urinary sediment, and doubling of the serum creatinine

**Prevention**

1. Routine screening of pts with SLE
    - Serum creatinine
    - Urinary sediment, urinalysis, protein
    - Renal biopsy in patients with renal abnormalities

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**Author: Bill Kriegsman, MD,** *Tacoma FM, WA*

**Editor: Elizabeth Steiner, MD,** *Oregon Health & Sciences University*