PRIMEVIEW

LUPUS NEPHRITIS

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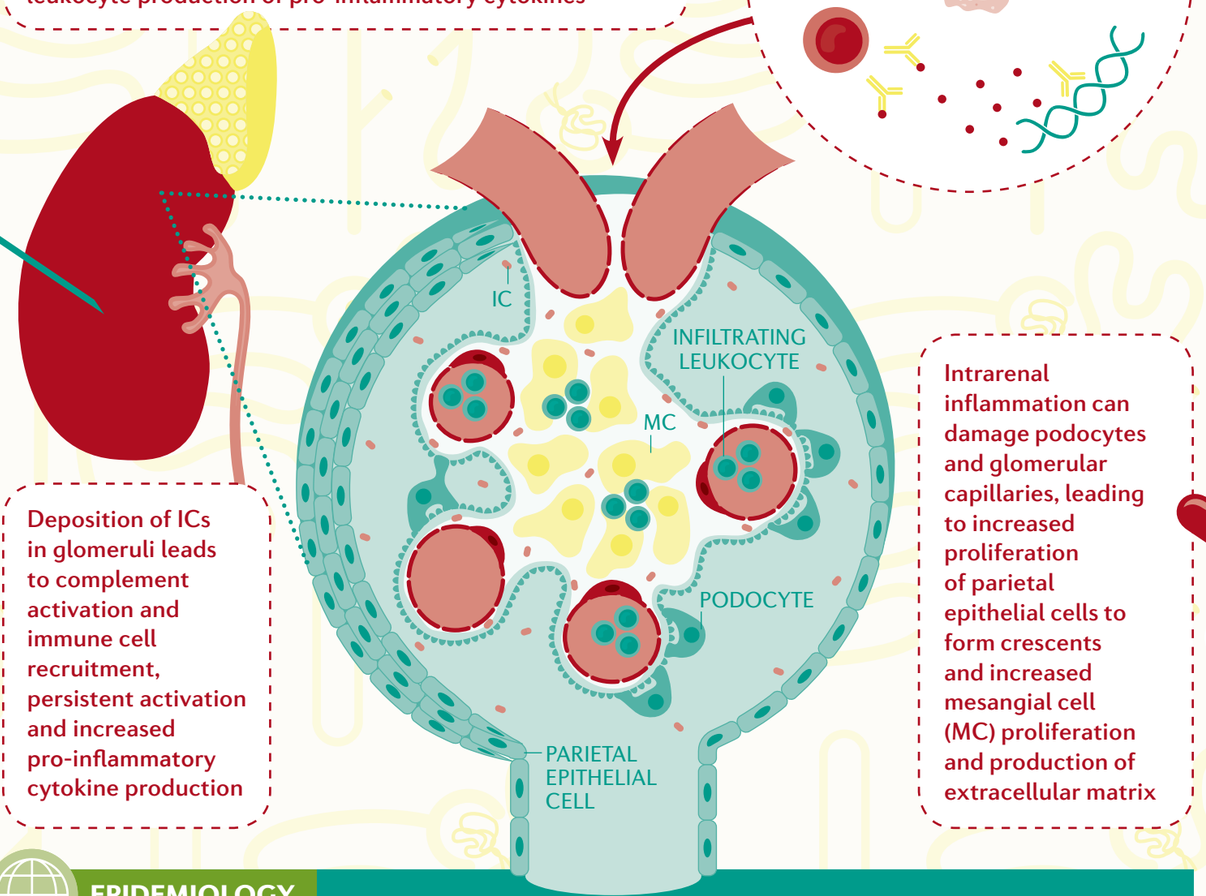
Lupus nephritis (LN) is inflammation of the kidneys caused by the autoimmune disease systemic lupus erythematosus (SLE). LN severity can range from asymptomatic disease to nephrotic syndrome to severe kidney damage resulting in end-stage kidney disease.

DIAGNOSIS

Diagnosis of LN relies on blood tests to measure serum creatinine levels, urine analysis to measure proteinuria and detect haematuria, and histological analysis of kidney biopsy specimens to determine the proportion of glomeruli affected and type of kidney injury (intraglomerular, extraglomerular and/or tubulointerstitial). Features of LN include immune complex (IC) deposition, endocapillary hypercellularity and the presence of glomerular lesions termed crescents. The 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) histological classification system is the most widely used and defines six classes of LN (class I-VI) using light microscopy and immunofluorescence or electron microscopy of kidney biopsy specimens. Furthermore, a renal pathology scoring system is used to assess disease activity and chronic tissue damage, resulting in activity and chronicity indices, respectively, which have prognostic value and guide management decisions.

MECHANISMS

In SLE, a chronic loss of immune tolerance results in increased abundance of autoreactive lymphocytes, leading to increased B cell production of autoantibodies and leukocyte production of pro-inflammatory cytokines



Deposition of ICs in glomeruli leads to complement activation and immune cell recruitment, persistent activation and increased pro-inflammatory cytokine production

Intrarenal inflammation can damage podocytes and glomerular capillaries, leading to increased proliferation of parietal epithelial cells to form crescents and increased mesangial cell (MC) proliferation and production of extracellular matrix

EPIDEMIOLOGY

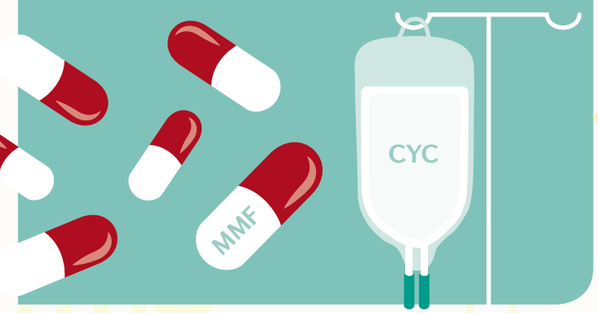
LN is a common and severe organ complication in patients with SLE, with 25-50% of patients presenting with kidney disease symptoms at SLE disease onset. Although SLE is 6–13 times more prevalent in females than males,

LN is slightly more prevalent in male than in female patients with SLE. LN is also more prevalent in black (34-51%), Hispanic (31-49%) and Asian (33-82%) patients with SLE than in white patients with SLE (14-23%).

Most of the risk factors for LN overlap with those for SLE, and include genetic polymorphisms and environmental factors, such as smoking, exposure to industrial agents or pesticides, and infections.

MANAGEMENT

Treatment of LN is based on the histological classification of the disease. All patients with LN should receive adjunctive treatment and supportive care to treat comorbidities. Patients with active disease initially receive induction immunosuppressive therapy (with glucocorticoids and either mycophenolate mofetil (MMF) or cyclophosphamide (CYC)) to rapidly reduce acute renal inflammation (termed a flare). If there is a partial or complete response, then maintenance therapy is initiated with low-dose immunosuppressants to treat residual inflammation, prevent renal flares and reduce their duration. Patients with advanced sclerotic LN should receive standard management for chronic kidney disease.



OUTLOOK

To improve diagnosis of LN, renal histology findings will need to be complemented with molecular insights into the pathogenesis of the disease, and deep learning algorithms might reduce subjectivity in renal histopathology assessment. Potential therapeutic advances based on insights from preclinical studies have not been successfully translated to the clinic. However, potential immunomodulatory therapies are being tested in clinical trials, including inhibitors of complement activation, B cell function, lymphocyte crosstalk and inflammatory signalling pathways.

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