

SLE · Systemic Lupus Erythematosus

Lupus is your own antibodies attacking many parts of you. The picture changes over time as different organs flare up.

THE ONE-LINE TRUTH

In lupus, the immune system loses its brake and makes antibodies (immune proteins) that attack the body's own tissues — skin, joints, kidneys, blood, brain, and heart lining — causing swelling and damage wherever the antibodies land.

The chain — how it unfolds

1. Loss of immune tolerance lets self-reactive B cells and T cells survive and multiply — why: Normally, the thymus (behind your breastbone) and bone marrow delete or silence any immune cell that recognizes your own proteins. In lupus, genetic variants (especially in HLA-DR2, HLA-DR3, complement genes C1q/C4, and genes controlling apoptosis and interferon signaling) weaken those checkpoints. Environmental triggers — ultraviolet (UV) light, Epstein-Barr virus (EBV), smoking, and estrogen (which is why lupus hits women nine times more than men) — push the system over the edge. Self-reactive B cells escape into the bloodstream and start making antibodies against your own nuclear DNA (anti-dsDNA), RNA-binding proteins (anti-Sm, anti-Ro/SSA, anti-La/SSB), and cell membranes (antiphospholipid antibodies).
2. Plasmacytoid dendritic cells flood the body with type I interferons (especially interferon-alpha) — why: When self-reactive antibodies grab onto your own DNA or RNA, they form immune complexes that get swallowed by dendritic cells (special antigen-presenting cells in your blood and tissues). Inside the dendritic cell, these complexes trigger pattern-recognition receptors — TLR7 (which normally detects viral RNA), TLR9 (which normally detects viral DNA), and the cGAS-STING pathway — even though no virus is present. The dendritic cells pour out interferon-alpha, a chemical alarm that tells the whole immune system to stay activated. This interferon signature is the engine of lupus: it keeps B cells making more autoantibodies, activates more T cells, and makes your tissue cells display more self-antigens on their surface, creating a vicious cycle.

3. Autoantibodies bind to self-antigens and form immune complexes that deposit in small blood vessels — why: Anti-dsDNA antibodies latch onto DNA released from dying cells (especially in sun-damaged skin and inflamed kidneys). Anti-Sm and anti-Ro/La antibodies grab onto ribonucleoproteins (the machinery that reads your genes). Antiphospholipid antibodies stick to phospholipids on cell membranes. All of these antibody-antigen pairs clump together into large immune complexes. When blood flow slows down in tiny capillaries — especially in the skin (face, scalp), kidney glomeruli (the filters), joint synovium (lining), pleura (lung sac), and pericardium (heart sac) — these clumps get stuck in the vessel walls.
4. Complement proteins coat the immune complexes and call in neutrophils and macrophages, causing tissue damage — why: The complement system (a cascade of blood proteins: C1q, C4, C3, C5-C9) is supposed to tag germs for destruction. In lupus, complement lands on the immune complexes stuck in your tissues and marks them as targets. Neutrophils (the most common white blood cells) and macrophages (tissue scavenger cells) rush in, release enzymes (proteases, elastase), and spray oxygen radicals trying to dissolve the clumps. But because the target is your own tissue, the collateral damage causes inflammation, bleeding, protein leak, and eventually scar tissue (fibrosis). Low complement levels (low C3, low C4) in the blood mean complement is being consumed at the sites of attack — a marker of active lupus.
5. Skin shows a malar (butterfly) rash, photosensitivity, and discoid lesions — why: UV light damages skin cells (keratinocytes) on your face, neck, and arms, causing them to die and spill their nuclear contents. Anti-dsDNA, anti-Ro/SSA, and anti-La/SSB antibodies bind to that DNA and RNA, forming immune complexes in the upper dermis (the layer just under the skin surface). Complement and white cells attack, causing a red, raised, butterfly-shaped rash across the cheeks and nose (malar rash), sun-triggered rashes (photosensitivity), or thick, scaly, coin-shaped patches (discoid lesions) that can scar. The dermoepidermal junction (the glue layer between skin layers) breaks down, which you see on biopsy as vacuolar interface dermatitis.
6. Joints hurt and swell, but the bone does NOT erode (non-erosive arthritis) — why: Immune complexes deposit in the synovium (the thin lining inside joints, especially in the hands, wrists, and knees). The synovium swells and releases inflammatory chemicals (IL-6, TNF-alpha), causing pain, morning stiffness, and sometimes swelling that looks like rheumatoid arthritis. But lupus arthritis is driven by antibodies and complement, not by the direct cellular attack (T cells and macrophages releasing enzymes) that eats away bone in rheumatoid arthritis. X-rays show swelling but no erosions. Over time, ligament laxity can cause Jaccoud arthropathy (reversible joint deformity without bone damage).

7. Kidneys develop lupus nephritis with protein and blood spilling into the urine (proteinuria and blood in the urine (hematuria)) — why: Anti-dsDNA and anti-C1q antibodies form immune complexes that lodge in the glomeruli (the kidney's tiny filters made of capillary loops and podocytes). Complement activation and neutrophil attack punch holes in the glomerular basement membrane (the filter barrier) and damage the podocytes (the cells that hug the capillaries and keep protein in the blood). Protein leaks into the urine (proteinuria), red blood cells squeeze through (hematuria), and white blood cells appear (pyuria). If enough glomeruli scar (glomerulosclerosis), the kidney loses its ability to filter waste, and creatinine rises (renal insufficiency → kidney failure). Lupus nephritis is classified by biopsy into six classes (WHO/ISN): class III (focal), class IV (diffuse), and class V (membranous) are the most serious and need aggressive immunosuppression (cyclophosphamide or mycophenolate plus steroids).
8. The pleura (lung sac) and pericardium (heart sac) become inflamed, causing serositis with chest pain and fluid buildup — why: Immune complexes deposit in the thin mesothelial linings of the pleura (around the lungs) and pericardium (around the heart). Inflammation causes sharp, position-dependent chest pain (pleuritic pain that hurts more when you breathe in; pericarditic pain that eases when you lean forward). Fluid leaks into the pleural space (pleural a fluid collection (effusion)) or pericardial space (pericardial a fluid collection). You hear a friction rub on exam (a scratchy sound as the inflamed layers rub). Large effusions can compress the lung or heart, causing shortness of breath or, rarely, cardiac tamponade (the heart squeezed by fluid around it) (fluid squeezes the heart so it can't fill).

Spot it — what you see, and why

- Malar rash (butterfly rash across the nose and cheeks): The immune system mistakenly attacks skin cells, especially where sunlight (ultraviolet light) hits. UV light triggers the skin cells to show certain proteins on their surface, and the confused immune system sees those proteins as invaders and attacks them, causing red swelling and a rash.
- Joint pain and swelling (arthritis), especially in hands, wrists, and knees: The immune system releases inflammatory signals (cytokines like IL-6 and TNF-alpha) into the joints. These signals tell white blood cells to rush in and attack the joint lining (the synovium), causing pain, warmth, and swelling — even though there is no real infection to fight.
- Extreme tiredness (fatigue) that does not go away with rest: Chronic inflammation floods the body with cytokines (chemical messengers like interferon-alpha and IL-1) that signal the brain to slow down and conserve energy — the same 'sick feeling' you get with the flu. Also, anemia (low red blood cells from immune attack or kidney loss) means less oxygen reaches the muscles and brain, making every task feel heavy.

- Photosensitivity (rashes or feeling sick after sun exposure): Ultraviolet (UV) light from the sun damages skin cells, and damaged cells release their DNA and proteins into the tissue. In lupus, the immune system mistakes this cell debris for foreign germs and launches an attack, triggering a new rash or a whole-body flare within hours or days.
- Fever without infection: Cytokines (especially IL-1, IL-6, and TNF-alpha) released during immune flares travel through the blood to the hypothalamus (the brain's thermostat) and reset the body's temperature set-point higher, just as they would during a real infection — even though no bacteria or virus is present.
- Mouth or nose sores (usually painless): The immune system attacks the delicate lining (mucosa) of the mouth and nose, where cells turn over quickly. The chronic low-grade inflammation causes small ulcers or sores, often on the roof of the mouth or inside the nose, and they usually do not hurt because the nerve endings are not as inflamed as in infectious sores.

Red flags — act now

- New seizure, severe headache, confusion, or sudden weakness on one side of the body (possible brain lupus or stroke)
- Sudden shortness of breath, chest pain, or coughing up blood (possible blood clot in the lung, heart inflammation, or lung bleeding)
- Swelling of the legs and face with foamy urine or much less urine than usual (kidney failure may be starting)
- Fever over 100.4°F (38°C) — could be infection (lupus suppresses immunity and treatments do too) or a severe lupus flare
- Severe abdominal pain, especially with nausea or vomiting (possible inflammation of blood vessels in the gut, which can cause bleeding or tissue death)

Treat it — in this order

1. Hydroxychloroquine 200–400 mg daily (all patients, indefinitely) → Blocks Toll-like receptors (immune alarm switches) inside cells and stops type I interferon production, which turns down autoantibody factories in B cells. It cuts flare rate by about half, prevents organ damage over years, and improves survival. This is the backbone drug — it targets the broken self-tolerance upstream.
2. Low-dose corticosteroids during flares (prednisone 0.5–1 mg/kg/day, then taper over weeks) → Shuts down the entire immune response fast — stops cytokine release, calms inflamed tissues (joints, skin, serous membranes), and reduces autoantibody production right now. Symptoms improve in days.

3. Mycophenolate mofetil 1–3 g/day or cyclophosphamide IV (induction for lupus nephritis), then mycophenolate or azathioprine for maintenance → Kills or blocks B cells and plasma cells that make anti-dsDNA antibodies. This stops immune complex formation and deposition in kidney glomeruli (the filters), so proteinuria and blood in the urine (hematuria) drop and kidney function stabilizes or improves. Mycophenolate is preferred because it works as well as cyclophosphamide with fewer side effects.
4. Belimumab 10 mg/kg IV every 4 weeks (or 200 mg subcutaneous weekly) for active skin, joint, or serosa disease despite standard therapy → Blocks BLyS (B-lymphocyte stimulator, also called BAFF), a survival signal for B cells. This shrinks the pool of B cells making autoantibodies, reduces flare frequency, and lets you lower steroid doses. Works best in patients with high disease activity and positive anti-dsDNA.
5. Rituximab 1 g IV on days 1 and 15 (for refractory lupus nephritis or severe cytopenias) → Targets CD20 on B cells and wipes them out, stopping autoantibody production for months. Used when mycophenolate or belimumab fail. Effective for nephritis and severe blood cell destruction.

Your top priorities at the bedside

1. Check urine dipstick for protein and blood, and monitor daily weights — why: Lupus nephritis (kidney inflammation) can progress silently to kidney failure; proteinuria (protein in urine) and blood in the urine (hematuria) (blood in urine) are early warning signs that need urgent nephrologist referral and aggressive immunosuppression
2. Assess for signs of infection before assuming symptoms are a lupus flare — why: Immunosuppressed lupus patients get serious infections easily; fever and fatigue can mean infection or flare, but treating a flare with more steroids when infection is present can be fatal
3. Monitor blood pressure every 4 hours and report systolic over 140 or diastolic over 90 — why: Lupus nephritis causes high blood pressure (hypertension) (high blood pressure) which damages kidneys further; corticosteroids also raise blood pressure and increase cardiovascular risk