

SLE · Systemic Lupus Erythematosus

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THE STORY IN ONE SENTENCE

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

Normal anatomy — the body's job

Normally, your immune system has a built-in safety brake called immune tolerance that stops it from attacking your own cells, and type I interferons (chemical alarms that fight viruses) stay quiet unless a real germ invades. Keep that picture in mind, because every lupus symptom is a break from that normal quiet state.

BODY'S JOB

Your thymus (a small training school for immune cells behind your breastbone) and bone marrow teach young T cells and B cells to recognize the difference between 'you' and 'not you.' Any cell that grabs onto your own proteins gets deleted or shut off. Meanwhile, sensors in your cells watch for viral DNA and RNA; when they spot a virus, they release type I interferons (especially interferon-alpha) that tell nearby cells to go into antiviral mode. In a healthy person, these interferons turn off quickly so they don't keep the immune system buzzing after the threat is gone. Regulatory T cells (special calming immune cells) patrol your blood and tissues, releasing chemicals like TGF-beta and IL-10 that hush overactive immune responses. Together, these checkpoints keep your immune system aimed outward at germs, not inward at you.

1. Young immune cells form in the bone marrow and thymus and go through tolerance training — any cell that reacts to your own proteins is deleted or turned off permanently.

2. Mature T cells and B cells circulate in your blood and lymph nodes, watching for foreign invaders (bacteria, viruses, fungi) but ignoring your own tissue markers.
3. If a virus enters a cell, pattern sensors (like TLR7, TLR9, and cGAS-STING) detect viral DNA or RNA and trigger a burst of type I interferons (interferon-alpha and interferon-beta).
4. Those interferons tell neighboring cells to make antiviral proteins, ramp up their germ-killing tools, and call in more immune cells — but only for a few days, then the signal fades.
5. Regulatory T cells release calming messengers (TGF-beta, IL-10) that dampen the immune response once the threat is cleared, preventing collateral damage to your own tissues.
6. B cells that recognize foreign proteins turn into plasma cells and make antibodies (immune proteins) that tag germs for destruction — but tolerance checkpoints block any B cell that would make antibodies against your own DNA, proteins, or cell surfaces.

What breaks

In lupus, the immune system's safety brake fails. Cells that should have been deleted or silenced during training survive and start making autoantibodies — immune proteins that attack your own DNA, cell surfaces, and tissues. At the same time, your cells keep pouring out type I interferons (especially interferon-alpha) even when no virus is present, which revs up the whole immune system nonstop. Those autoantibodies clump together with your own proteins into immune complexes that get stuck in tiny blood vessels, especially in the skin, kidneys, joints, and the thin sacs around the heart and lungs. White blood cells swarm to those clumps and release chemicals that cause swelling, bleeding, and scarring. Triggers like UV light, Epstein-Barr virus, cigarette smoke, and hormones (especially estrogen) can flip this switch in someone whose genes already set the stage.

CLINICAL TERM

Loss of immune tolerance in systemic lupus erythematosus (SLE)

How the body compensates

Early in a lupus flare, your body tries to wall off the damage, recruit repair cells, and keep vital organs running — so blood pressure, heart rate, and oxygen levels can look normal even while kidneys, brain, or lungs are quietly failing. That is the dangerous window, because the patient

looks stable until suddenly they crash into kidney failure, stroke, pulmonary bleeding (hemorrhage), or catastrophic clotting. Your job is to see the slow burn before it explodes.

1. {'what': 'The renin-angiotensin-aldosterone system (RAAS) kicks in to protect blood pressure', 'why': 'When immune complexes clog kidney glomeruli (the filters), less blood flows through, so the kidney releases renin (an enzyme that raises blood pressure). Aldosterone (a hormone from the adrenal glands above the kidneys) tells the kidney to hold onto salt and water, keeping blood volume up. Blood pressure stays normal for weeks or months, masking the fact that the kidney is losing filter units (nephrons) one by one.'}
2. {'what': 'The bone marrow ramps up production to replace destroyed blood cells', 'why': 'Autoantibodies attack red blood cells (causing destroying red blood cells (hemolytic) anemia), white blood cells (leukopenia), and platelets (thrombocytopenia). The marrow tries to keep up by churning out young cells (reticulocytes, band neutrophils), but if the attack is faster than production, counts drop. Early on, you might see a normal or only slightly low count even though destruction is happening.'}
3. {'what': 'The liver makes more clotting factors to counteract antiphospholipid antibodies', 'why': 'In antiphospholipid syndrome (APS), antibodies against phospholipids on cell membranes cause paradoxical clotting (thrombosis) in veins and arteries, even though lab tests like PTT look prolonged. The liver cranks out extra fibrinogen and clotting factors trying to balance the system, but this can tip into either clots (stroke, pulmonary embolism (a clot lodging in a lung artery), a clot in a deep leg vein (deep vein thrombosis)) or, rarely, bleeding if factors get consumed.'}
4. {'what': 'The heart pumps harder to deliver oxygen when anemia or lung inflammation cuts oxygen delivery', 'why': 'If destroying red blood cells (hemolytic) anemia drops your red cell count or if immune complexes cause alveolitis (lung air-sac inflammation) or pleuritis (lung-lining inflammation), less oxygen reaches the blood. The heart responds by beating faster (tachycardia) and squeezing harder to push more blood per minute. Oxygen saturation might stay above 90% at rest, hiding the fact that the lungs or blood are failing — until you walk across the room and it drops.'}
5. {'what': 'The brain redistributes blood flow to protect critical centers', 'why': 'If lupus causes cerebral vasculitis (inflammation of brain blood vessels) or microthrombi (tiny clots), blood flow to some brain regions drops. The brain shunts blood to the brainstem (breathing, heart control) and away from the cortex (thinking, memory, mood). Early signs are subtle: brain fog, word-finding trouble, mood swings, headache. By the time you see seizures, stroke, or psychosis, compensation has failed.'}

6. {'what': 'Anti-inflammatory pathways try to calm the storm — but they also hide the damage', 'why': "Your body releases cortisol (the main stress hormone from the adrenal glands) and anti-inflammatory cytokines (IL-10, TGF-beta) to dampen the immune attack. This can mask fever, reduce pain, and keep lab markers like CRP (C-reactive protein) lower than you'd expect. A patient with active lupus nephritis might have only mild a run-down, unwell feeling (malaise) and a trace of protein in the urine, even though glomeruli are being destroyed."}
7. {'what': 'Watch for the crash point: lupus nephritis progressing to end-stage renal disease (ESRD), catastrophic antiphospholipid syndrome (CAPS), severe pulmonary bleeding (hemorrhage), or stroke', 'why': "Once the kidney loses enough filter units, creatinine shoots up and fluid overload causes pulmonary edema (fluid flooding the lungs) (lungs fill with water). Once antiphospholipid antibodies trigger widespread clots, organs fail in hours (CAPS has >50% mortality even with treatment). Once alveolar capillaries rupture, you cough up bright red blood and oxygen saturation plummets. Once a clot or vasculitis cuts off a brain artery, stroke symptoms appear in minutes. All of these can happen while yesterday's vital signs looked fine."}
8. {'what': 'Infection from immunosuppression is the other crash point', 'why': 'Lupus itself suppresses white cell counts (leukopenia, lymphopenia), and the drugs used to treat it (cyclophosphamide, mycophenolate, azathioprine, rituximab, high-dose steroids) knock down immune defenses further. Opportunistic infections — Pneumocystis jirovecii pneumonia (PJP), cytomegalovirus (CMV), tuberculosis (TB), fungal infections — can explode quickly. Fever in a lupus patient on immunosuppression is an emergency until proven otherwise.'}
9. {'what': 'Trend the trajectory, not the snapshot', 'why': "A patient with stable creatinine today but rising protein in the urine (nephrotic-range proteinuria >3.5 g/day) is on a downhill slope toward kidney failure. A patient with a platelet count of 80,000 today who had 120,000 last week is heading toward dangerous bleeding. A patient who feels 'fine' but has new livedo reticularis (purple net-like skin pattern) and a prolonged PTT is brewing antiphospholipid syndrome. Look at the curve, not the point."}

Domino effect

1. Loss of immune tolerance lets self-reactive B cells and T cells survive and multiply — 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) — 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 — 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 — 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 — 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) — 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)) — 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 — 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).

- 9.** Blood counts drop: red cells (anemia), white cells (leukopenia, lymphopenia), and platelets (thrombocytopenia) — Autoantibodies directly attack blood cells. Anti-red-cell antibodies coat red blood cells, marking them for destruction by splenic macrophages (autoimmune destroying red blood cells (hemolytic) anemia, Coombs-positive). Anti-neutrophil and anti-lymphocyte antibodies destroy white cells, leaving you prone to infection (leukopenia $<4000/\mu\text{L}$, lymphopenia $<1500/\mu\text{L}$). Anti-platelet antibodies tag platelets for removal (immune a low platelet count (thrombocytopenia), platelets $<100,000/\mu\text{L}$), raising bleeding risk. The bone marrow tries to compensate by making more cells, so you see young forms (reticulocytes, band neutrophils), but if the attack is faster than production, counts fall. Severe anemia or a low platelet count can trigger transfusion or even splenectomy.
- 10.** The brain and nervous system are attacked, causing neuropsychiatric lupus (NPSLE): headache, seizures, psychosis, cognitive dysfunction, or stroke — Lupus can hit the brain in two ways. First, immune complexes and anti-neuronal antibodies (including anti-ribosomal-P and anti-NMDA-receptor antibodies) cross the blood-brain barrier (the tight seal around brain capillaries) and activate microglia (the brain's immune cells) and astrocytes (support cells). This causes diffuse brain inflammation (encephalitis), leading to confusion, memory loss (cognitive dysfunction), mood swings, depression, or frank psychosis (hearing voices, paranoia). Second, vasculitis (inflammation of brain blood vessels) or antiphospholipid-antibody-driven clots block blood flow, causing transient blood-starved (ischemic) attacks (TIAs, mini-strokes) or full strokes with weakness, vision loss, or loss of language ability (aphasia) (language trouble). Seizures happen when inflamed or blood-starved cortex becomes electrically unstable. Spinal cord inflammation (transverse myelitis) can cause leg weakness or bladder trouble. MRI may show white-matter lesions or infarcts; lumbar puncture may show high protein or white cells in the cerebrospinal fluid (CSF).
- 11.** Lungs suffer from alveolitis, interstitial lung disease, pulmonary high blood pressure (hypertension), or life-threatening pulmonary bleeding (hemorrhage) — Immune complexes deposit in the alveolar walls (the air sacs where oxygen enters the blood) and in pulmonary capillaries. Inflammation causes alveolitis (air-sac swelling), which shows up on CT as ground-glass opacities and causes shortness of breath and low oxygen. Chronic inflammation leads to fibrosis (scar tissue), shrinking lung capacity (interstitial lung disease). Vasculitis in the lung vessels raises pressure in the pulmonary arteries (pulmonary high blood pressure (hypertension)), forcing the right heart to pump harder; over time, right heart failure develops. In acute lupus pneumonitis or diffuse alveolar bleeding (hemorrhage) (DAH), capillaries rupture and blood fills the alveoli. You see sudden severe shortness of breath, dropping oxygen, and coughing up bright red blood (hemoptysis). Chest X-ray shows white-out infiltrates. DAH has high mortality and needs immediate high-dose steroids, cyclophosphamide, and sometimes plasmapheresis (filtering antibodies out of the blood).

- 12.** Antiphospholipid antibodies cause paradoxical blood clots (thrombosis) in veins and arteries, miscarriages, and catastrophic antiphospholipid syndrome (CAPS) — About 30–40% of lupus patients make antiphospholipid antibodies: lupus anticoagulant (LA), anti-cardiolipin (aCL), and anti-beta-2-glycoprotein-I (anti- β 2GPI). Despite prolonging clotting tests in the lab (prolonged PTT that doesn't correct with mixing), these antibodies cause clotting in the body by activating platelets and endothelial cells (the lining of blood vessels). Clots form in veins (deep vein clot formation (thrombosis), pulmonary embolism (a clot lodging in a lung artery)) and arteries (stroke, heart attack, limb starved blood flow (ischemia)). In pregnancy, clots in placental vessels cause recurrent miscarriages (usually after 10 weeks). Catastrophic antiphospholipid syndrome (CAPS) is a medical emergency: widespread small-vessel clots hit multiple organs at once (kidneys, lungs, brain, heart, gut) over days, causing multi-organ failure. CAPS has >50% mortality even with aggressive treatment (anticoagulation, steroids, plasma exchange, IVIG). Patients with antiphospholipid syndrome need lifelong anticoagulation (warfarin with target INR 2–3, or sometimes 3–4 for arterial clots; newer DOACs are less effective and not first-line).

Symptoms · what the patient feels, 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.
- Kidney problems (proteinuria, blood in urine, or rising creatinine) with little or no pain: Antibodies and immune complexes (clumps of antibody stuck to self-proteins) lodge in the tiny filters of the kidney (the glomeruli). White blood cells then attack these clumps, damaging the filter walls so that protein and red blood cells leak into the urine. Over time, scar tissue replaces working kidney tissue, raising waste levels (creatinine) in the blood.
- Seizures, headache, confusion, or stroke-like symptoms: Inflammation can directly injure brain tissue (cerebritis) through cytokines crossing the blood-brain barrier, or antibodies can attack neurons and their support cells. Separately, blood clots may form in brain vessels if antiphospholipid antibodies are present, blocking blood flow and causing stroke or transient blood-starved (ischemic) attacks (mini-strokes where brain cells do not get enough oxygen).
- Chest pain that gets worse with deep breathing (pleuritis or pericarditis): The immune system attacks the thin linings around the lungs (the pleura) or heart (the pericardium), causing them to swell and rub against each other with every breath or heartbeat. That friction creates sharp, stabbing pain — pleurisy when it is the lungs, pericarditis when it is the heart sac.
- Low blood counts (anemia, low white cells, or low platelets): Autoantibodies directly tag red blood cells, white blood cells, or platelets as 'foreign,' so the spleen (which filters the blood) traps and destroys them. The bone marrow tries to make replacements, but if the immune attack is faster than production, counts drop — leading to anemia (fatigue, pale skin), a low white blood cell count (leukopenia) (more infections), or a low platelet count (thrombocytopenia) (easy bruising and bleeding).

Focused exam

- Malar rash (butterfly shape across cheeks and nose): In lupus, the immune system makes antibodies that attack the person's own skin cells. UV light from the sun wakes up those antibodies and makes them attack even more, so the rash appears most where sun hits. Seeing this butterfly rash is one of the earliest clues that the body has lost the ability to tell 'self' from 'foreign'.
- Photosensitivity (rash gets worse after sun exposure): UV light triggers the immune system in lupus to release type I interferons (alarm proteins that turn up inflammation). When a patient's rash flares after being outside, lupus moves to the top of the list because this sun-triggered pattern is a hallmark of autoantibody attack on skin.

- Non-erosive arthritis (swollen, tender joints with no bone damage on X-ray): Lupus antibodies attack the synovium (the slippery lining inside joints), causing swelling and pain, but they do not eat away the bone itself. If X-ray shows erosions, think rheumatoid arthritis instead. No erosions is a strong clue this is lupus.
- Proteinuria or blood in the urine (hematuria) on urine dipstick (protein or red blood cells in urine): Lupus nephritis means immune complexes (clumps of antibody stuck to pieces of DNA) are jamming the kidney's tiny filters, letting protein and blood leak into the urine. This is the danger zone — untreated kidney inflammation in lupus can lead to kidney failure. Check urine in every lupus patient at every visit.
- Pleural friction rub or sharp chest pain that gets worse with breathing: Serositis means the pleura (the thin membrane wrapping the lungs) is inflamed by autoantibodies. When you hear a rub with your stethoscope or the patient says deep breaths hurt like a knife, lupus affecting the lining of the lungs or heart is high on the list.
- Low complement levels (C3 < 90 mg/dL, C4 < 10 mg/dL) with high ANA and anti-dsDNA: Complement proteins (C3 and C4) get used up when immune complexes form and stick to tissues. Low C3 and C4 plus high antibody levels mean lupus is flaring right now and actively damaging organs, especially the kidneys. This pattern tells you to treat urgently.

Diagnostics · every test answers a question

- ANA (antinuclear antibody) by immunofluorescence → Does the patient have antibodies against their own cell nuclei, the hallmark of lupus?
- Anti-dsDNA antibody (anti-double-stranded DNA) → Is there a highly specific antibody that confirms lupus and tracks disease activity?
- Anti-Smith (anti-Sm) antibody → Is there an antibody that is nearly unique to lupus, even if it does not track activity?
- Complement levels (C3 and C4) → Is the immune system actively forming complexes and consuming complement proteins right now?
- Urinalysis with microscopy and urine protein-to-creatinine ratio → Are the kidneys leaking protein or blood because immune complexes are clogging the filters?
- Complete blood count (CBC) with differential → Is the immune system attacking blood cells themselves?
- Anti-phospholipid antibodies (lupus anticoagulant, anti-cardiolipin, anti- β 2-glycoprotein I) → Does the patient have antibodies that make blood clot in arteries and veins, raising stroke and miscarriage risk?
- Kidney biopsy (if proteinuria or rising creatinine) → What class of lupus nephritis is present, and how much damage is reversible versus scarred?

Treatment logic

- 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.
- 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.
- 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.
- 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.
- 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.
- Warfarin with target INR 2–3 (or 3–4 for arterial clots) in antiphospholipid syndrome with lupus → Blocks vitamin K-dependent clotting factors (II, VII, IX, X), preventing clots in veins and arteries caused by anti-phospholipid antibodies. Prevents strokes, DVT, pulmonary embolism (a clot lodging in a lung artery), and miscarriage.
- Strict photoprotection (broad-spectrum SPF 50+ sunscreen daily, avoid sun 10 AM–4 PM, wear long sleeves and wide-brim hats) → UV light triggers keratinocytes (skin cells) to release autoantigens and type I interferons, which wake up the immune attack. Blocking UV reduces skin flares and may lower systemic disease activity.

Medications

Hydroxychloroquine · Antimalarial immunomodulator

Hydroxychloroquine calms the overactive immune system that attacks the body's own tissues in lupus. It works by changing the pH (acid level) inside certain immune cells, which slows down the cells that present 'targets' to attack and quiets the release of inflammatory signals. Think of it like turning down the volume on an alarm system that's going off too much. This medicine reduces flares, protects organs, and helps people with lupus live longer.

1. Hydroxychloroquine enters immune cells and raises the pH inside compartments called endosomes and lysosomes (tiny sacs where cells break down materials).
2. The higher pH stops antigen-presenting cells from cutting up proteins and showing fragments to T cells (the immune system's attack troops).
3. It also blocks Toll-like receptors 7, 8, and 9, which are alarm sensors that detect DNA and RNA and trigger interferon production (a powerful inflammatory signal in lupus).
4. With fewer alarm signals, the immune system makes less interferon and fewer inflammatory cytokines like TNF-alpha and IL-6.
5. Over weeks to months, this reduces inflammation in the skin, joints, and organs, and lowers the chance of flares and serious organ damage.

SAFETY WATCH

Eye damage (retinal toxicity): rare, but can happen with long-term use (usually after 5+ years). Get a baseline eye exam and yearly checks with an ophthalmologist to catch any changes early. · Low blood sugar (hypoglycemia): can happen, especially in people with diabetes or kidney problems. · Heart rhythm changes (QT prolongation): rare, but important if the person takes other medicines that affect heart rhythm. · Skin color changes or rash: some people develop darker skin patches or blue-gray discoloration with years of use. · Stomach upset: nausea or diarrhea can happen; taking it with food helps. · Muscle weakness (myopathy or cardiomyopathy): very rare, but stop the medicine if new muscle weakness appears.

Prednisone (or other corticosteroids) · Corticosteroid (synthetic version of cortisol, the body's natural anti-inflammatory hormone)

Prednisone is a powerful brake on inflammation. It mimics cortisol, a hormone the adrenal glands make to shut down the immune system's attack response. Prednisone enters cells and turns on genes that reduce inflammation and turns off genes that make inflammatory

chemicals. It is used for flares or when organs are actively inflamed, but because long-term use causes serious side effects, doctors aim to use the lowest dose for the shortest time.

1. Prednisone is absorbed in the gut and converted by the liver into prednisolone, the active form.
2. Prednisolone enters cells and binds to glucocorticoid receptors inside the cytoplasm.
3. The receptor-steroid pair moves into the nucleus and attaches to DNA.
4. It turns on genes that make anti-inflammatory proteins (like lipocortin-1, which blocks the enzyme that creates inflammatory chemicals) and turns off genes for cytokines (IL-1, IL-2, IL-6, TNF-alpha) and enzymes like COX-2.
5. Immune cells become less active, blood vessels tighten and leak less, and inflammation throughout the body drops quickly—often within hours to days.

SAFETY WATCH

Infections: steroids weaken the whole immune system, so infections (like pneumonia, urinary tract infections, fungal infections) are more likely and can be more serious. · High blood sugar and diabetes: prednisone raises blood sugar; long-term use can cause diabetes. · Weight gain and fluid retention: increased appetite and salt/water retention are common. · Weak bones (osteoporosis) and fractures: long-term use pulls calcium out of bones. People on prednisone ≥ 3 months should take calcium, vitamin D, and often a bone-protecting medicine (bisphosphonate). · Mood and sleep changes: anxiety, irritability, insomnia, or (rarely) severe mood swings or psychosis can happen. · High blood pressure: steroids can raise blood pressure. · Cataracts and glaucoma: long-term use increases risk of eye problems. · Adrenal suppression: if used for weeks or more, the adrenal glands stop making their own cortisol. NEVER stop prednisone suddenly—taper slowly under a doctor's guidance to let the adrenals wake back up. · Skin thinning, easy bruising, and slow wound healing. · Muscle weakness (steroid myopathy) with long-term use.

Mycophenolate mofetil (or mycophenolic acid) · Immunosuppressant (inosine monophosphate dehydrogenase inhibitor)

Mycophenolate slows down the multiplication of B cells and T cells (the immune cells that make antibodies and attack tissues). It does this by blocking a key enzyme those cells need to make DNA building blocks. Because B and T cells rely heavily on this pathway, mycophenolate selectively suppresses the overactive immune response in lupus without shutting down the whole immune system as much as steroids do. It is a mainstay for lupus kidney inflammation (lupus nephritis) and is used for maintenance therapy to keep the disease quiet.

1. Mycophenolate mofetil is absorbed and converted to mycophenolic acid, the active form.
2. Mycophenolic acid enters B cells and T cells and blocks the enzyme IMPDH.

3. IMPDH normally makes guanosine nucleotides, one of the four letters of DNA. Blocking it starves the cells of this building block.
4. B and T cells cannot copy their DNA and cannot multiply as quickly.
5. Over weeks to months, the number of active, attacking immune cells drops, inflammation in the kidneys and other organs decreases, and the immune system's assault on the body's own tissues slows.

SAFETY WATCH

Infections: especially viral infections (like cytomegalovirus, herpes zoster) and common bacterial infections, because immune defenses are lowered. · Stomach and gut upset: diarrhea, nausea, vomiting, and stomach pain are common. Taking it with food or switching to the enteric-coated form (mycophenolic acid) can help. · Low blood counts: can lower white blood cells (increasing infection risk), red blood cells (causing anemia), or platelets (increasing bleeding risk). Regular blood tests are needed. · Birth defects (teratogenic): **MUST NOT** be used during pregnancy—causes severe birth defects. Women of childbearing age must use effective birth control and have pregnancy tests before starting and regularly during treatment. · Increased cancer risk: long-term immunosuppression slightly raises the risk of skin cancers and lymphoma. Use sun protection and get regular skin checks. · Progressive multifocal leukoencephalopathy (PML): extremely rare but serious brain infection caused by JC virus reactivation.

Cyclophosphamide · Immunosuppressant and alkylating agent (chemotherapy drug repurposed for severe autoimmune disease)

Cyclophosphamide is a powerful medicine that kills rapidly dividing cells, especially B cells and T cells that are multiplying and attacking the body. It works by damaging the DNA inside these cells so they cannot divide and eventually die off. This resets the immune system and is used for the most severe lupus, particularly life-threatening kidney inflammation (lupus nephritis) or brain/lung involvement. Because it is so strong and has serious side effects, it is used for induction (the first few months to get severe disease under control), then switched to a gentler medicine like mycophenolate for maintenance.

1. Cyclophosphamide is given intravenously (through an IV) or by mouth and is inactive when first absorbed.
2. The liver converts it into active metabolites (phosphoramidate mustard and acrolein).
3. These metabolites enter immune cells and attach to DNA strands, forming cross-links that glue the two strands together.
4. When the cell tries to divide, it cannot separate the DNA strands, and the cell dies.
5. B cells (which make autoantibodies) and activated T cells die off rapidly, leading to a sharp drop in the immune attack on kidneys and other organs over weeks to months.

6. The immune system is 'reset,' with fewer autoreactive (self-attacking) cells.

SAFETY WATCH

Infertility: can damage ovaries or testes, leading to permanent infertility, especially with cumulative doses. Women may want to consider egg preservation before treatment; men may consider sperm banking. · Bladder damage (hemorrhagic cystitis): the metabolite acrolein can irritate and damage the bladder lining, causing blood in the urine. Drink lots of fluids, urinate frequently, and mesna (a protective medicine) is often given with IV cyclophosphamide to protect the bladder. · Infections: severe suppression of white blood cells increases risk of serious bacterial, viral, and fungal infections. Preventive (Prophylactic) antibiotics (like trimethoprim-sulfamethoxazole to prevent Pneumocystis pneumonia) are often given. · Low blood counts: bone marrow suppression can cause low white cells (infection risk), low red cells (anemia), and low platelets (bleeding risk). Regular blood tests are essential. · Nausea and vomiting: common; anti-nausea medicines are given with treatment. · Hair loss: temporary; hair usually grows back after treatment ends. · Increased cancer risk: long-term or high cumulative doses raise the risk of bladder cancer, leukemia, and lymphoma. · Birth defects and pregnancy loss: MUST NOT be used during pregnancy. Effective contraception is required. · Heart damage (cardiomyopathy): rare but possible, especially with high doses.

Azathioprine · Immunosuppressant (purine analog antimetabolite)

Azathioprine slows down the multiplication of B cells and T cells by interfering with the building blocks they need to copy their DNA. It is converted in the body into a fake DNA building block that gets incorporated into new DNA strands, causing errors and stopping cell division. It is used as maintenance therapy to keep lupus quiet after initial treatment, particularly for kidney disease, and for people who cannot tolerate mycophenolate.

1. Azathioprine is absorbed and converted in the liver to 6-mercaptopurine (6-MP), the active form.
2. 6-MP is further converted to thioguanine nucleotides.
3. These fake nucleotides get incorporated into the DNA of dividing B and T cells.
4. The fake building blocks cause errors, DNA strand breaks, and cell death when the cells try to divide.
5. Over weeks to months, the number of active immune cells drops, reducing the immune attack on organs and lowering the chance of lupus flares.

SAFETY WATCH

Bone marrow suppression: can lower white blood cells (infection risk), red blood cells (anemia), and platelets (bleeding risk). Regular blood counts are essential, especially in the first few months. · Infections: increased risk due to immune suppression. · TPMT enzyme deficiency: about 1 in 300 people lack the enzyme thiopurine methyltransferase (TPMT), which breaks down azathioprine. Without it, toxic levels build up and cause severe, life-threatening bone marrow suppression. Many doctors test TPMT levels before starting azathioprine; people with low or absent TPMT should not take this drug or need much lower doses. · Liver inflammation (hepatotoxicity): can raise liver enzymes; regular monitoring is needed. · Nausea and vomiting: common, especially at the start. · Increased cancer risk: long-term use slightly raises the risk of skin cancer and lymphoma. Use sun protection. · Pancreatitis: rare but serious inflammation of the pancreas; stop the drug if severe abdominal pain occurs. · Birth defects: some risk in pregnancy, but azathioprine is sometimes used carefully in pregnancy when lupus control is critical, under close specialist supervision. Always discuss with a doctor.

Voclosporin · Calcineurin inhibitor immunosuppressant

Voclosporin blocks the activation of T cells, the immune cells that orchestrate the attack on kidneys and other organs in lupus. It works by inhibiting calcineurin, an enzyme inside T cells that turns on genes needed for the cells to spring into action and release inflammatory signals. By keeping T cells quiet, voclosporin reduces kidney inflammation. It is approved specifically as an add-on to mycophenolate and low-dose steroids for active lupus nephritis (kidney inflammation from lupus).

1. Voclosporin enters T cells and binds to a protein called cyclophilin.
2. The voclosporin-cyclophilin complex blocks calcineurin, an enzyme that normally removes phosphate groups from NFAT.
3. Without calcineurin, NFAT cannot enter the nucleus and turn on genes for interleukin-2 (IL-2) and other cytokines that activate and multiply T cells.
4. T cells stay quiet and do not release the inflammatory signals that drive kidney inflammation.
5. Over weeks to months, inflammation in the kidney glomeruli (tiny filters) decreases, protein leakage into the urine drops, and kidney function stabilizes or improves.

SAFETY WATCH

Kidney function changes: can reduce kidney filtration (GFR) in the short term; kidney function is monitored closely, and the dose is adjusted based on function. · High blood pressure: can raise blood pressure; regular monitoring and treatment are needed. · Infections: increases infection risk by suppressing T-cell immunity. · Low magnesium and high potassium: can affect electrolyte levels; regular blood tests are needed. · Tremor and headache: neurologic side effects can occur. · Gum swelling (gingival hyperplasia) and excess hair growth: less common than with cyclosporine but can happen. · Drug interactions: many medicines interact with voclosporin through the liver enzyme CYP3A4. Tell your doctor about all medicines, supplements, and grapefruit juice (which increases voclosporin levels).

Belimumab · Monoclonal antibody (B-cell activation inhibitor)

Belimumab targets B cells, the immune cells that make autoantibodies (self-attacking antibodies) in lupus. It works by blocking a protein called BLyS (B-lymphocyte stimulator), which B cells need to survive and mature. Without BLyS, excess B cells die off, reducing the number of cells making harmful antibodies. Belimumab is used for active lupus that is not controlled with standard medicines, and it is approved as an add-on for lupus nephritis (kidney inflammation).

1. Belimumab is a monoclonal antibody given by IV infusion or subcutaneous injection.
2. It binds to soluble BLyS in the blood and tissues, preventing BLyS from attaching to receptors on B cells.
3. Without BLyS signaling, B cells—especially the autoreactive B cells that make anti-DNA and other autoantibodies—lose their survival signal.
4. These B cells undergo apoptosis (programmed cell death) and their numbers drop over weeks to months.
5. Fewer B cells mean fewer autoantibodies, less immune complex formation, and reduced inflammation in skin, joints, and kidneys.

SAFETY WATCH

Infections: increased risk of respiratory and urinary tract infections; serious infections are possible. · Infusion reactions (for IV form): nausea, headache, rash, or rarely allergic reactions during or shortly after infusion. · Depression and suicidal thoughts: rare reports; tell your doctor if mood changes occur. · Progressive multifocal leukoencephalopathy (PML): extremely rare brain infection; report any new neurologic symptoms. · Hypersensitivity reactions: rare severe allergic reactions can happen. · Do not use live vaccines while on belimumab.

Rituximab · Monoclonal antibody (anti-CD20 B-cell depleting agent)

Rituximab wipes out B cells, the immune cells that make autoantibodies in lupus. It works by binding to a marker called CD20 on the surface of B cells, tagging them for destruction by the immune system and causing them to die. This resets the B-cell population, reducing harmful antibody production. Rituximab is used off-label (not FDA-approved for lupus, but widely used) for severe or refractory (stubborn) lupus, especially kidney disease that does not respond to standard treatment.

1. Rituximab is given by IV infusion.
2. It binds to CD20 on the surface of B cells.
3. This triggers three killing mechanisms: antibody-dependent cellular cytotoxicity (immune cells attack the tagged B cell), complement-dependent cytotoxicity (proteins in the blood punch holes in the B cell), and direct signaling that causes the cell to die.
4. B cells are depleted within days to weeks; levels stay low for months.
5. Without B cells, production of new autoantibodies drops, and immune complex-driven inflammation in kidneys and other organs decreases.
6. Over 6 to 12 months, B cells gradually return, but often with a less autoreactive (self-attacking) profile.

SAFETY WATCH

Infusion reactions: fever, chills, rash, low blood pressure, or difficulty breathing during or shortly after infusion. Premedication with acetaminophen, antihistamines, and sometimes steroids reduces this risk. · Infections: significantly increased risk, especially respiratory infections, urinary tract infections, and reactivation of hepatitis B virus. Screening for hepatitis B is required before starting rituximab. · Progressive multifocal leukoencephalopathy (PML): rare but serious brain infection caused by JC virus reactivation; report any new neurologic symptoms (confusion, weakness, vision changes). · Low immunoglobulin levels: long-term B-cell depletion can drop antibody levels, increasing infection risk. · Tumor lysis syndrome: rare, mostly in people with high disease burden. · Heart problems: rare severe heart reactions during infusion. · Do not give live vaccines during or for months after rituximab.

Anifrolumab · Monoclonal antibody (type I interferon receptor blocker)

Anifrolumab blocks interferon, a powerful inflammatory signal that is overactive in many people with lupus. Interferons are proteins that normally fight viruses, but in lupus, the immune system mistakenly makes too much interferon, which drives inflammation in skin, joints, and organs. Anifrolumab binds to the interferon receptor on cells, preventing interferon

from delivering its inflammatory message. It is used for moderate to severe lupus that is not controlled with standard treatment.

1. Anifrolumab is given by IV infusion every 4 weeks.
2. It binds to the type I interferon receptor on the surface of immune cells, skin cells, blood vessel cells, and other tissues.
3. By blocking the receptor, anifrolumab prevents all type I interferons from binding and sending inflammatory signals into the cell.
4. Cells stop producing interferon-stimulated genes (ISGs), which drive inflammation, immune cell activation, and tissue damage.
5. Over weeks to months, skin rashes improve, joint pain decreases, and overall disease activity drops in people with high interferon signatures.

SAFETY WATCH

Infections: especially respiratory infections (bronchitis, pneumonia) and herpes zoster (shingles). Consider the shingles vaccine before starting treatment. · Infusion reactions: rare; premedication is not always needed but may be given. · Interference with vaccine response: because interferons help fight viruses, blocking them may reduce the body's response to vaccines. Avoid live vaccines. · Increased risk of serious infections and tuberculosis reactivation: screening for TB is recommended before starting. · Hypersensitivity reactions: rare severe allergic reactions.

Methotrexate · Disease-modifying antirheumatic drug (DMARD) and antimetabolite

Methotrexate calms inflammation in the joints and skin by interfering with folate (a B vitamin) metabolism inside immune cells. It blocks an enzyme called dihydrofolate reductase, which cells need to make DNA and proteins. At the low doses used for lupus, methotrexate reduces the activity of T cells and other inflammatory cells, lowering cytokine production and tissue inflammation. It is used mainly for joint pain (arthritis) and skin rashes in lupus.

1. Methotrexate is taken by mouth (pills) or injection once a week.
2. It enters cells and is converted to methotrexate polyglutamates, which stay inside cells longer.
3. It blocks dihydrofolate reductase, slowing DNA and protein synthesis in rapidly dividing immune cells.
4. It also increases adenosine release, a molecule that dampens inflammation.
5. Over weeks to months, T-cell activity drops, cytokine production (like TNF-alpha and IL-1) decreases, and joint and skin inflammation improves.

SAFETY WATCH

Liver damage (hepatotoxicity): can raise liver enzymes and, with long-term use, cause scarring (fibrosis or cirrhosis). Regular liver enzyme monitoring is essential. Limit alcohol. · Bone marrow suppression: can lower white blood cells (infection risk), red blood cells (anemia), and platelets (bleeding risk). Regular blood counts are needed. · Lung inflammation (pneumonitis): rare but serious; report new cough, shortness of breath, or fever. · Mouth sores and nausea: common; taking folic acid (1 mg daily or 5 mg weekly) on non-methotrexate days helps. · Infections: immune suppression increases infection risk. · Birth defects (teratogenic): **MUST NOT** be used during pregnancy—causes severe birth defects and miscarriage. Effective contraception is required for women and men. Stop methotrexate at least 3 months before trying to conceive. · Kidney function: dose must be reduced or avoided in people with kidney disease, as methotrexate is cleared by the kidneys.

Warfarin · Vitamin K antagonist anticoagulant (blood thinner)

Warfarin prevents blood clots by blocking vitamin K, which the liver needs to make clotting factors (proteins that help blood clot). People with lupus and antiphospholipid syndrome (APS) have antibodies that make their blood clot too easily, leading to strokes, a clot in a deep leg vein (deep vein thrombosis), pulmonary embolism (a clot lodging in a lung artery), or pregnancy loss. Warfarin thins the blood just enough to prevent clots without causing too much bleeding. The dose is carefully adjusted using a blood test called INR (international normalized ratio), with a target usually between 2 and 3 (or 3 to 4 for arterial clots like strokes).

1. Warfarin is taken by mouth (pill) daily.
2. It enters the liver and blocks the enzyme vitamin K epoxide reductase.
3. Without this enzyme, vitamin K cannot be recycled, and levels of active vitamin K drop.
4. The liver cannot fully activate clotting factors II, VII, IX, and X (proteins needed to form clots).
5. Clotting factors decline over days, and the blood's ability to clot is reduced to a safe, controlled level, measured by the INR.
6. Clots are less likely to form in veins, arteries, or the placenta during pregnancy.

SAFETY WATCH

Bleeding: the biggest risk. Can range from easy bruising and nosebleeds to life-threatening bleeding in the brain, gut, or elsewhere. Report unusual bruising, blood in urine or stool, severe headache, or prolonged bleeding. · INR monitoring: requires regular blood tests (often weekly at first, then monthly once stable) to keep INR in the target range—too low means clot risk, too high means bleeding risk. · Drug and food interactions: many medicines (antibiotics, antifungals, NSAIDs, amiodarone, many others) and foods (vitamin K-rich foods like kale, spinach, broccoli) affect warfarin levels. Keep vitamin K intake consistent, not zero. · Pregnancy: warfarin causes severe birth defects (especially in the first trimester) and bleeding in the fetus. Women with APS planning pregnancy usually switch to heparin or low-molecular-weight heparin. Discuss with a specialist before conception. · Skin tissue death (necrosis): rare, can happen in the first few days of treatment, especially in people with protein C or S deficiency. · Purple toe syndrome: rare, painful purple discoloration of toes due to small cholesterol clots.

NSAIDs (e.g., ibuprofen, naproxen) · Nonsteroidal anti-inflammatory drugs

NSAIDs reduce pain, swelling, and fever by blocking enzymes called COX-1 and COX-2, which make prostaglandins (chemicals that cause inflammation and sensitize pain nerves). In lupus, NSAIDs are used for mild joint pain, muscle aches, and serositis (inflammation of the lining around the heart or lungs). They do NOT treat the underlying immune problem and should be used cautiously because people with lupus, especially those with kidney involvement, are at higher risk of kidney damage and stomach ulcers from NSAIDs.

1. NSAIDs are absorbed in the stomach and enter the bloodstream.
2. They block COX-1 and COX-2 enzymes at sites of inflammation.
3. With less prostaglandin production, blood vessels dilate less, swelling decreases, pain nerve sensitization drops, and fever-regulating centers in the brain cool down.
4. Pain, stiffness, and inflammation improve within hours.

SAFETY WATCH

Kidney damage: especially risky in lupus, where kidneys may already be inflamed (lupus nephritis). NSAIDs reduce blood flow to the kidneys and can worsen kidney function or cause acute kidney injury. Use the lowest dose for the shortest time, and avoid if kidney disease is present. · Stomach ulcers and bleeding: NSAIDs irritate the stomach lining and can cause ulcers, bleeding, or perforation. Taking with food or adding a proton pump inhibitor (PPI) reduces risk. · Cardiovascular risk: long-term use can raise blood pressure and increase heart attack and stroke risk, especially with COX-2 selective NSAIDs like celecoxib. · Aseptic meningitis: rare in lupus but reported; stop NSAIDs if severe headache and neck stiffness occur. · Liver enzyme elevation: monitor liver function with long-term use. · Bleeding risk: NSAIDs affect platelet function and increase bleeding, especially if combined with blood thinners like warfarin.

Red flags

- 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)

Nursing priorities

1. Check urine dipstick for protein and blood, and monitor daily weights — 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 — 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 — Lupus nephritis causes high blood pressure (hypertension) (high blood pressure) which damages kidneys further; corticosteroids also raise blood pressure and increase cardiovascular risk
4. Check complete blood count daily for low white cells, platelets, or hemoglobin — Lupus causes cytopenias (low blood counts) from autoantibodies attacking blood cells; a low platelet count (thrombocytopenia) (low platelets) below 50,000 risks serious bleeding; a low white blood cell count (leukopenia) (low white cells) increases infection risk
5. Ensure hydroxychloroquine is given daily and teach the patient it prevents flares — Hydroxychloroquine reduces lupus activity by 50 percent, prevents organ damage, and improves survival; it takes 3 to 6 months to work so patients must stay on it even when feeling well
6. Teach sun protection with SPF 50 sunscreen, hats, and long sleeves every day — Ultraviolet light triggers lupus flares by activating the immune system and causing cell death that releases autoantigens (self proteins that trigger autoantibodies)
7. Monitor for signs of serositis including sharp chest pain, friction rub on lung sounds, or muffled heart sounds — Serositis (inflammation of lung or heart linings) causes pericarditis or pleuritis which can progress to tamponade (fluid compressing the heart) or large pleural effusions (fluid around lungs) needing drainage
8. Screen for depression and teach that brain fog and mood changes are part of lupus — Lupus causes neuropsychiatric symptoms in 40 percent of patients from inflammation, autoantibodies crossing into the brain, or corticosteroid side effects; untreated depression worsens medication adherence

Sources

- EULAR/ACR 2019 Classification Criteria for SLE
- American College of Rheumatology (ACR) SLE Guidelines
- Lupus Foundation of America
- UpToDate Clinical Overview (peer-reviewed synthesis)

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