SYSTEMIC LUPUS ERYTHEMATOUS

MAYA'S JOURNEY

WHAT IS LUPUS?

Lupus is a chronic autoimmune disease where the immune system attacks the body's own tissues, causing inflammation in multiple organs. [1]

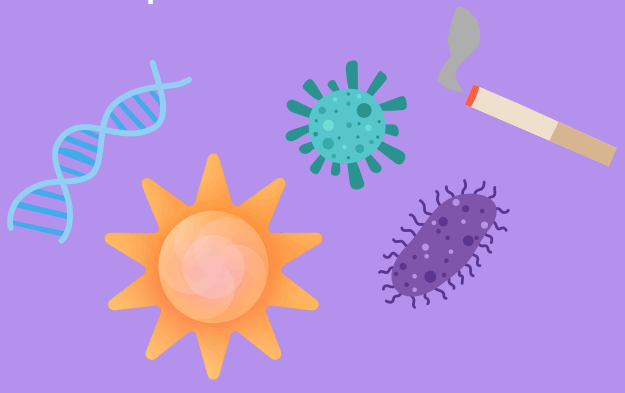
WHO IS AFFECTED?

Lupus affects mostly women (90%) [1], especially during child-bearing years.

It can affect anyone, but it tends to be more common and more severe in people of African, Asian, Hispanic, and Indigenous backgrounds.[2]

WHAT CAUSES LUPUS?

The exact cause of lupus is unknown, but it is believed to result from a combination of genetics, hormones, and environmental triggers such as infections or sun exposure. [1]

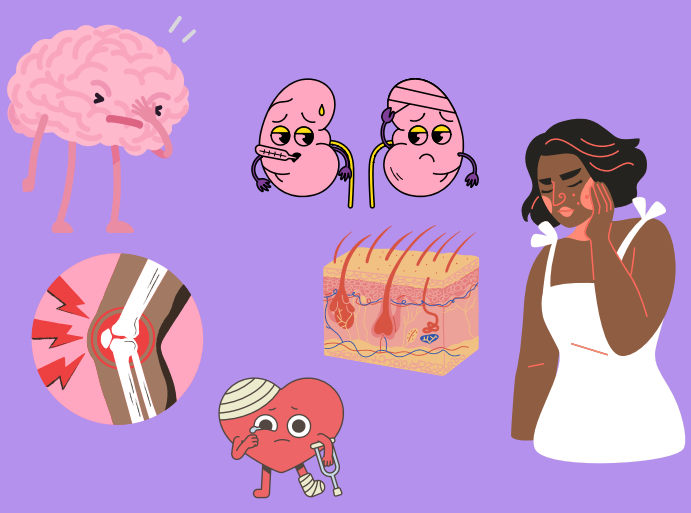


GENERAL SYMPTOMS

Symptoms may be mild or severe, come and go over time, and often resemble other illnesses like arthritis, infections, or fatigue disorders.

Lupus can look very different from person to person, making it difficult to diagnose.

A large hospital study of nearly 1,000 patients found fatigue, joint pain, and skin symptoms were the most common initial features of lupus. [3]



WHAT IS AUTOIMMUNITY?

Autoimmunity occurs when the immune system loses the ability to recognize the body's own cells as "self" and begins attacking them. [7]

INTERACTIVE CASE: MEET MAYA

Hi! My name is **Maya Smith**. I am **24 years old** and a **graduate student**.

For the past **4 months**, I have been experiencing several concerning symptoms.

Symptoms I reported to my doctor[4-6]:

- Severe fatigue
- Joint paint in my hands and knees
- A facial rash that worsens after sun exposure
- Hair thinning
- Sharp chest pain when breathing deeply
- New ankle swelling
- Dark, foamy urine

DIAGNOSING CASE: MEET DR. PAYNE

Hello, I am **Dr. Payne**. I will be your **guide** that will help walk you through this **patient's case**, figure out the **diagnosis**, and get her on the **right treatment path**.

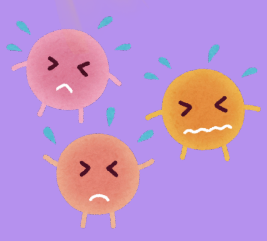
So let me ask you this:
What pattern do you notice?[4-6]

- Are multiple organ systems involved?
- Does this sound localized or systemic?

PATHOPHYSIOLOGY

ENVIRONMENTAL TRIGGER (UV LIGHT)

Increased apoptosis (cell death)



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Failure of immune tolerance

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Autoantibody Production

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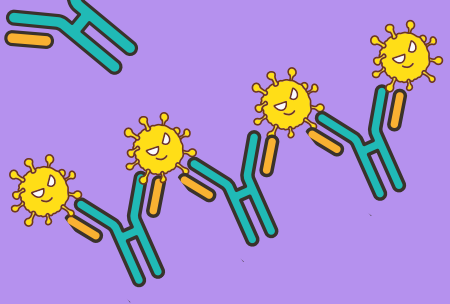
Immune Complexes Form



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C3

C4

Complement Activation

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Inflammation

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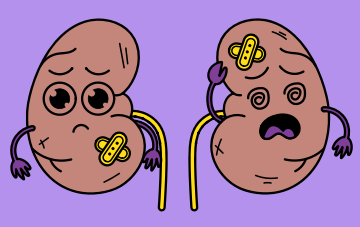
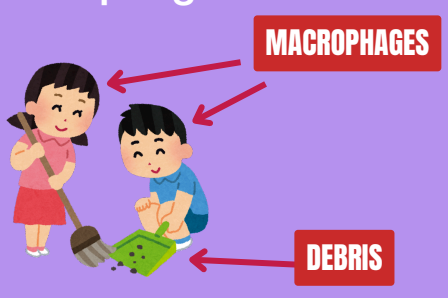
Organ Damage [8]



APOPTOSIS

Normally when cells die:

- Apoptotic debris (DNA, nuclear proteins, histones) are rapidly cleared by macrophages.



In lupus:

- Apoptotic debris are not cleared properly
- Nuclear material remains in circulation
- Immune cells recognize it as foreign
- This becomes a major source of autoantigens[7]

TYPE III HYPERSENSITIVITY - WHAT DOES THIS MEAN?

The immune system makes antibodies that bind to antigens and form clusters called immune complexes.

These complexes travel through the bloodstream and get trapped in tissues where they activate the complement system and cause inflammation which leads to organ damage. [8]

IMMUNE INTOLERANCE - WHAT DOES THIS MEAN?

- The immune system fails to distinguish self from non-self.
- This leads to production of autoantibodies, including:
- Antinuclear antibodies (ANA)
- Anti-double-stranded DNA antibodies
- Anti-Smith antibodies (Maya)[7]

STEP 1: IDENTIFYING THE PATTERN

Based on what you learned about **lupus**, it is[4,6,9]:

- **Systemic**
- **Immune complex-mediated**
- **Multisystem disease**
- Most common in **women of child-bearing age**

Looking at **Maya's symptoms**, ask yourself:

- How many **organ systems** are **involved?**
- Could this reflect **failure of immune tolerance?**
- Does this match an **immune complex disease?**

ORGAN-SPECIFIC EFFECTS

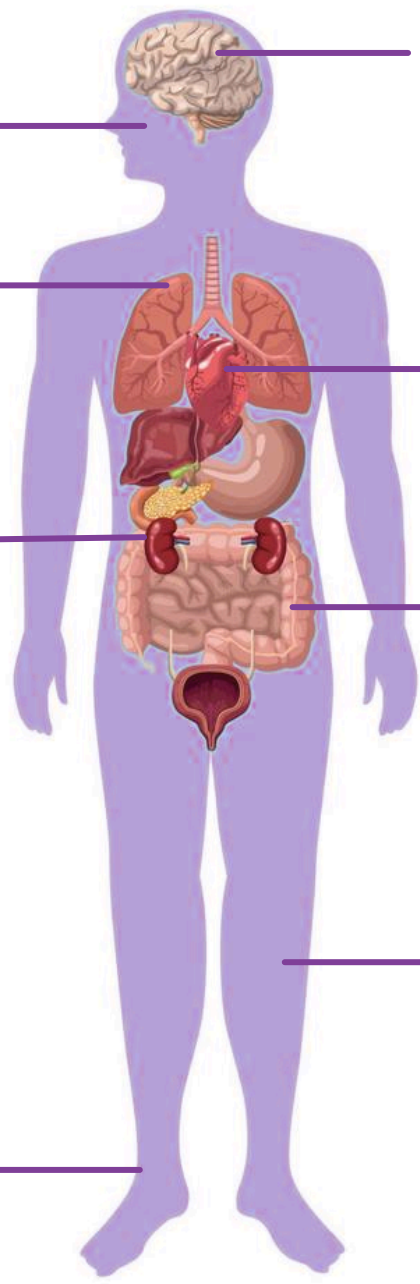
Dermatitis - lupus can cause rashes, especially after sun exposure.

The classic “malar rash” across the cheeks and nose occurs in about 30% of patients.[1]

Brain and Nervous System - Lupus can affect the brain and nerves, leading to headaches, mood changes, memory problems, or seizures.

These symptoms may occur when inflammation or antibodies affect blood vessels and nervous tissue.

Lungs - Inflammation of the lung lining (pleuritis) is the most common pulmonary complication of lupus and can cause sharp chest pain and shortness of breath. In rare cases, lupus can lead to serious lung problems such as pulmonary hypertension or bleeding in the lungs.[1]



Heart - Lupus can cause inflammation of the heart and surrounding tissues, most commonly pericarditis, which produces chest pain that may improve when leaning forward. People with lupus also have an increased risk of atherosclerosis and cardiovascular disease.[1]

Kidneys - Immune complex deposition in the glomeruli, leading to a condition called lupus nephritis. This may cause protein or blood in the urine, swelling, high blood pressure, and in severe cases kidney failure.[1]

Digestive System - Some people with lupus develop mouth ulcers, abdominal pain, nausea, or inflammation of the digestive organs. These symptoms may result from lupus itself, medication side effects, or inflammation of blood vessels supplying the intestines.[1]

Arthritis - Joint pain and stiffness are very common in lupus and are often one of the first symptoms.

Unlike some types of arthritis lupus joint pain usually does not permanently damage the joints.[1]

Ankle Swelling - Swelling in the ankles or legs can occur when lupus affects the kidneys (lupus nephritis). Damage to the kidney’s filtering units allows protein to leak into the urine, leading to fluid buildup in tissues and visible swelling (edema).

Image Source: Vecteezy.com[10]

STEP 2: CONNECTING SYMPTOMS TO THE BODY[4-6]

Symptom	Organ System	Explanation
Malar rash	Skin	UV-triggered apoptosis exposes nuclear antigens
Joint pain	Musculoskeletal	Immune complexes deposit in synovium
Chest pain	Serosal membranes	Immune-mediated pleuritis
Foamy urine	Kidneys	Proteinuria from glomerular inflammation
Fatigue	Systemic	Anemia + chronic inflammation
Ankle swelling	Kidneys	Protein loss → edema

*Multiple organ systems involved ⟶ **Systemic autoimmune disease**

DIFFICULT TO DIAGNOSE[1,2]

Clinical variability
- Symptoms differ widely from person to person.

Relapsing disease
- Symptoms come and go.

Non-specific symptoms
- Lupus mimics other diseases.
- Some common early symptoms include fatigue, fever, and weight changes (not specific)

Multiple organs involved
- Different systems are affected and in different combinations
- Symptoms may come and go depending on what part of the body is affected, and may be mild, moderate or severe

Exact cause of the disease is unknown
- Related to genetic, socioeconomic, sociocultural, demographics, etc.

DIAGNOSTIC TESTS[11]

Test	What it shows
ANA (anti-nuclear antibody)	Autoimmune activity (entry criteria for SLE classification)
Anti-dsDNA	Highly specific
Anti-Smith	Antibodies specifically against Maya’s cells
Low C3/C4	Complement consumption during immune complex activation

STEP 3: WHAT DO THE LAB RESULTS SHOW?[4-6,11]

Blood tests (CBC):
- Leukopenia
- Mild anemia
- Thrombocytopenia

⟶ These changes occur due to **immune-mediated destruction of blood cells.**

Inflammation marker:
- Elevated ESR
- rinalysis:
- Proteinuria (protein in urine)
- Hematuria
- RBC casts ⟶ suggests glomerulonephritis

Autoimmune tests:
- ANA positive (1:640)
- Anti-dsDNA positive
- Anti-Smith positive
- Complement C3 and C4 decreased (low complement)
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Key Point:
- Low complement levels suggest active immune complex disease.

TREATMENT & LIFESTYLE

SLE management aims to[12]:

- Control inflammation and autoimmune activity
- Prevent organ damage
- Minimize long-term steroid toxicity
- Maintain remission and reduce disease flares

Treatment is stepwise, and dependent on disease severity and organ involvement

1. FIRST-LINE BASELINE THERAPY: ANTIMALARIAL DRUGS

Modulate the immune system by:

- Interfering with antigen presentation and toll-like receptor signaling
- Reducing autoantibody production and inflammation
- Maintain remission and reduce disease flares [12]
- Examples: Hydroxychloroquine & Chloroquine

2. GLUCOCORTICOIDS

Used for rapid suppression of inflammation during disease flares. They inhibit multiple inflammatory pathways and cytokine production[12]

Examples:

- Prednisone (inhibit cytokine production)
- Methylprednisolone (Potent Immune suppression)

3. STEROID-SPARING IMMUNOSUPPRESSANTS

Used when disease activity is moderate to severe or when steroid doses cannot be reduced.

Suppress immune cell proliferation or specific immune signaling pathways to reduce autoantibody production and organ damage[12]

Example:

- Azathioprine (Inhibit purine synthesis reducing T and B cell proliferation)

NOTE: NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) MAY AGGRAVATE SLE COMPLICATIONS FURTHER, AND ARE THEREFORE CONTRAINDICATED IN THE TREATMENT OF LUPUS.[13]

LIFESTYLE

Sun protection

- UV can trigger lupus flares.[14]

Prioritize sleep and self-care

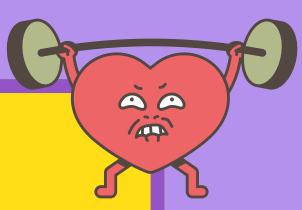
- Stress and a poor quality sleep can worsen lupus symptoms.[14]

Connect with others

- A sense of community is always beneficial, especially when it comes to living with a chronic disease.[14]

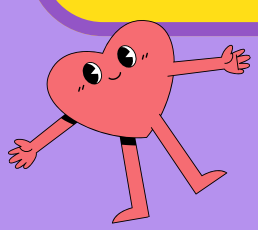
Stop smoking

- Smoking reduces the effectiveness of antimalarial drugs like hydroxychloroquine.[14]



Exercise

- Support cardiovascular health.[14]



Adhere to medications and stay up to date with vaccinations

- Some medications may make people more prone to infections, it is important to protect oneself![14]

STEP 4:
WHAT IS HAPPENING IN MAYA'S BODY?[4,9,15,16]

Step	What Happens in Lupus	What Happens in Maya
UV trigger	Increased apoptosis	Rash worsens after sun
Tolerance failure	Autoreactive T cells survive	Autoimmune response begins
B-cell activation	Autoantibodies produced	Anti-dsDNA positive
Immune complexes	Antigen-antibody clusters form	Circulating DNA complexes
Deposition	Complexes deposit in tissues	Kidney, skin, joints affected
Complement	Activated and consumed	Low C3 and C4
Inflammation	Neutrophils recruited	Tissue damage occurs

STEP 5:
LUPUS NEPHRITIS

Immune complexes deposit in the **glomeruli of the kidneys.**[4-6]

This causes:

- Inflammation
- Increased capillary permeability
- Protein leakage
- Red blood cell leakage

Clinical Signs in Maya:

- Proteinuria (protein in urine)
- Hematuria (blood in urine)
- RBC casts
- Hypertension
- Ankle swelling

Kidney disease is **one of the most serious complications of lupus.**

STEP 6:
MAKING THE DIAGNOSIS

According to **2019 EULAR/ACR criteria**[11]**:**

(Entry Criterion)

- Positive ANA

(Additional Findings in Maya)

- Malar rash
- Joint involvement
- Serositis
- Renal involvement
- Hematologic abnormalities
- Anti-dsDNA antibodies
- Anti-Smith antibodies
- Low complement

Diagnosis:
Systemic Lupus Erythematosus (SLE) with **Lupus Nephritis**

KEY TAKEAWAYS:
WHAT SHOULD YOU REMEMBER?[4-6,9]

- **Lupus is a systemic autoimmune disease**
- **It is driven by immune complex deposition**
- **Complement activation leads to inflammation**
- **Low complement levels indicate active disease**
- **Multiple organ systems may be affected**
- **Kidney involvement is a major complication**

QUIZ YOURSELF

QUESTION 1

Maya's low C3 and C4 levels are best explained by:

A) Decreased liver production of complement proteins
B) Complement consumption due to immune complex activation
C) Genetic absence of complement proteins
D) Infection suppressing complement synthesis

ANSWER 1:
B)

Explanation:
Immune complexes trigger the conventional complement pathway in SLE. The circulation amounts of complement proteins (C3 and C4) decline when they are repeatedly activated and depleted. Particularly in lupus nephritis, low complement levels are a sign of an active immune complex illness.[4,6,15,16]

QUESTION 2

Which step occurs FIRST in the pathogenesis of systemic lupus erythematosus?

A) Immune complex deposition in kidneys
B) Complement activation
C) Failure of immune tolerance
D) Neutrophil recruitment

ANSWER 2:
C)

Explanation:
Immune tolerance breakdown is the first stage of SLE. Regulatory T cells are unable to inhibit or eradicate autoreactive T cells. After being activated by these T cells, B cells create autoantibodies. This initial failure is the cause of all subsequent inflammation.[4,6,9]

QUESTION 3

Why does UV exposure worsen Maya's rash?

A) UV radiation increases bacterial growth on skin
B) UV radiation triggers excessive melanin production
C) UV radiation increases apoptosis, exposing nuclear antigens
D) UV radiation decreases regulatory T cells directly

ANSWER 3:
C)

Explanation:
Skin cell apoptosis is increased by UV exposure. Apoptotic material is improperly removed in lupus. Increased immune complex formation and worsening rash are caused by nuclear material (DNA, histones) that is still in circulation and stimulates autoreactive B cells. [4,6,9]

QUESTION 4

The kidney damage seen in lupus nephritis is primarily due to:

A) Direct antibody attack on kidney cells
B) T-cell–mediated cytotoxicity
C) Immune complex deposition in the glomeruli
D) Reduced blood flow to the kidney

ANSWER 4:
C)

Explanation:
One type of hypersensitive reaction is lupus nephritis. Immune complexes promote inflammation, activate complement, attract neutrophils, and deposit in the glomerular basement membrane. RBC casts, hematuria, and proteinuria are the outcomes. [4-6]

QUESTION 5

The kidney damage seen in lupus nephritis is primarily due to:

A) Direct antibody attack on kidney cells
B) T-cell–mediated cytotoxicity
C) Immune complex deposition in the glomeruli
D) Reduced blood flow to the kidney

ANSWER 5:
C)

Explanation:
Type III hypersensitivity reactions include lupus nephritis. Immune complexes promote inflammation, recruit neutrophils, activate complement, and deposit in the glomerular basement membrane. Hematuria, RBC casts, and proteinuria are the outcomes.[4,5,9]

QUESTION 6

Maya's anemia, leukopenia, and thrombocytopenia are caused by:

A) Bone marrow failure
B) Nutritional deficiency
C) Immune-mediated destruction of blood cells
D) Chronic kidney disease

ANSWER 6:
C)

Explanation:
Red blood cells, white blood cells, and platelets can all be targeted by autoantibodies in lupus. cytopenias, which are a component of the hematologic diagnostic criteria for SLE, result from this immune-mediated damage. [4,6,11]

QUESTION 7

Systemic lupus erythematosus is classified as which type of hypersensitivity reaction?

A) Type I
B) Type II
C) Type III
D) Type IV

ANSWER 7:
C)

Explanation:
Type III hypersensitivity reactions are the main cause of SLE. Antigen-antibody complexes, also known as immune complexes, accumulate in tissues, trigger complement, and result in tissue damage and inflammation. [6,15,16]

QUESTION 8

If Maya stopped her medications and experienced worsening symptoms after stress and sun exposure, this would be called:

A) Remission
B) Flare
C) Relapse infection
D) Drug toxicity

ANSWER 8:
B)

Explanation:
In lupus, a flare is a time of elevated disease activity. UV exposure, stress, infection, and non-adherence to medicine are common triggers. [6,17]

QUESTION 9

Why does complement activation both protect the body and contribute to tissue damage in lupus?
A) Complement only destroys bacteria
B) Complement proteins are toxic in all situations
C) Complement enhances immune defense but causes inflammation when activated against self-antigens
D) Complement prevents immune complex formation

ANSWER 9:
C)

Explanation:
Through opsonization and inflammation, complement typically aids in the removal of infections. However, immune complexes containing self-antigens activate complement in lupus, resulting in tissue damage and persistent inflammation. [15,16]

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