Demystifying Systemic Lupus Erythematosus

Signs and symptoms for early recognition

the lupus initiative
Eliminating Health Disparities in Lupus

American College of Rheumatology
Education · Treatment · Research

Welcome.

We are excited to speak with you today about lupus.

Before we get started…

ACCREDITATION STATEMENT

The American College of Rheumatology is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

DESIGNATION STATEMENT

The ACR designates this live activity for a maximum of 1 AMA PRA Category 1 Credit™ Physicians should claim only the credit commensurate with the extent of their participation in the activity.

USE OF PROFESSIONAL JUDGMENT

This activity, including all educational links, is intended to be used as a tool to assess the base knowledge of the learner. The information presented relates to basic principles of diagnosis and therapy, and is meant in no way to substitute for an individual patient assessment based upon the healthcare provider's examination of the patient and consideration of laboratory data and other factors unique to the patient.

DRUGS AND DOSES

When prescribing medications, the physician is advised to check the product information sheet accompanying each drug to verify conditions of use and to identify any changes in drug dosage schedule of contraindications.

ACR DISCLOSURE STATEMENT

The American College of Rheumatology is an independent, professional organization that does not endorse specific procedures or products of any pharmaceutical/biotech concern.

SUPPORT

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FACULTY REPORTED DISCLOSURES

[To be filled in]

Pre/post assessment and follow-up

This assessment is voluntary and used solely to rate the quality of this seminar.

No individual data will be shared as a part of this project. We will use your unique identifier only to match the assessments for analysis. Final data will be reported in aggregate form.

1

PRE-ASSESSMENT
(BEFORE SEMINAR)

- 10 multiple choice or true/false questions and 1 efficacy question
- Additional demographic questions

2

POST-ASSESSMENT
(AFTER SEMINAR)

- Repeat pre-assessment
- Additional qualitative questions

3

FOLLOW UP ASSESSMENT
(4–6 WEEKS AFTER SEMINAR)

- Repeat pre-assessment
- Option for comment
- Requires an email address (completed on the attendee sheet)

Thank you.

We appreciate your time in taking our pre-seminar assessment. Create a unique assessment identifier by by completing your: initials, first three letters of last name, birth year (YYYY) and state.

Please write legibly so we can match and use the data.

Learning objectives

After this presentation, you should:

Recognize the signs and symptoms of lupus.

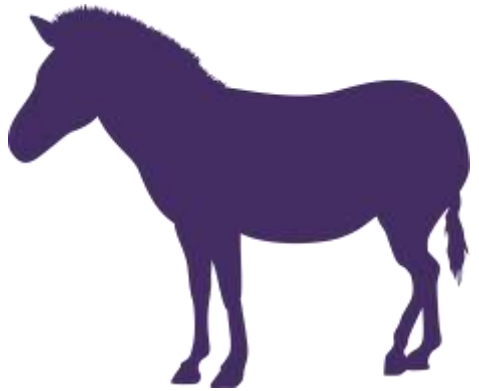
Know how to effectively refer a suspected lupus case to a rheumatologist.

Know how to initiate a work-up for lupus.

Have increased knowledge about lupus epidemiology, health disparities and disease characteristics.

We've all heard the expression,

when you hear hoof beats think horses, not zebras.



In many cases, lupus is a zebra.

With a worldwide prevalence of 140 out of 100,000, lupus is likely not the reason the woman in your office has a fever and fatigue.[1]

But when the person you are treating is a woman of color in her childbearing years, that unexplained, prolonged fever has a greater likelihood of being one indicator of lupus.

Lupus affects up to 1 in 250 young, African American women in the United States, and it is also more prevalent among Hispanic / Latina, Asian and Native American women.

Lupus has a prevalence of 86.6 cases per 100,000 in Hispanics / Latinos and 142.7 per 100,000 in Hispanic / Latino women.[2]

When the person you are treating is a person of color in her childbearing years, lupus is not a zebra. It's a horse.

Video Placeholder

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Furthermore, lupus impacts African American and Hispanic / Latino women at a younger age and more severely than white women.

When the person you are treating is a woman of color in her childbearing years, lupus is not a zebra. It's a horse.

A lupus diagnosis can take as long as two or more years and include visits to three or more health care providers.

Why is the diagnosis of lupus so challenging?

LUPUS IS:

- the great masquerader
- can mimic other conditions like viral syndromes, malignancies, allergic reactions and stress.
- sometimes associated with depression or fibromyalgia

SYMPTOMS MAY BE VAGUE, INCLUDING:

- fatigue
- achiness
- stiffness
- low-grade fever
- swollen lymph nodes
- rashes

SYMPTOMS MAY:

- develop slowly
- come on suddenly

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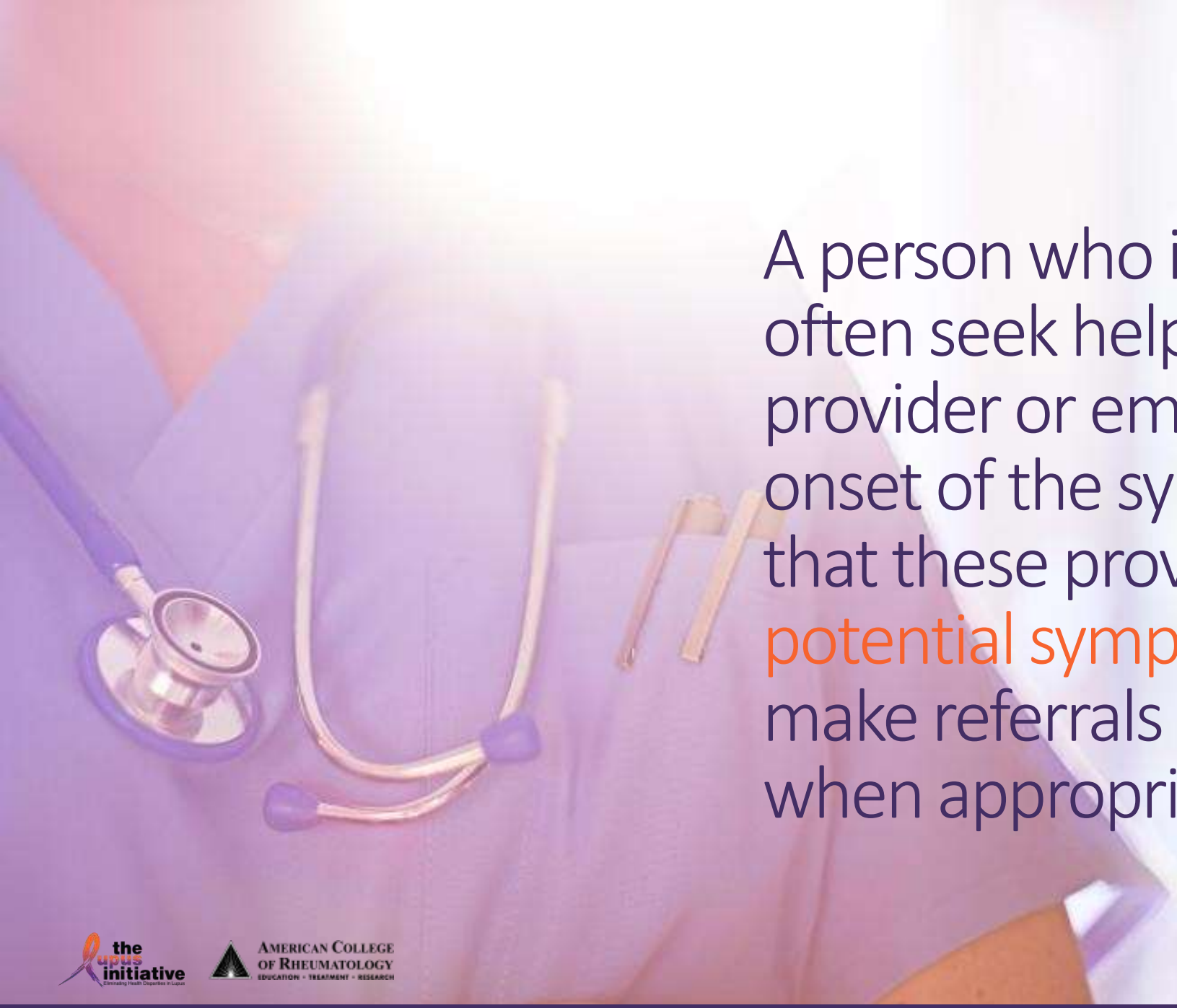
This delay in diagnosis can be devastating for a person with lupus.

THIS COULD LEAD TO:

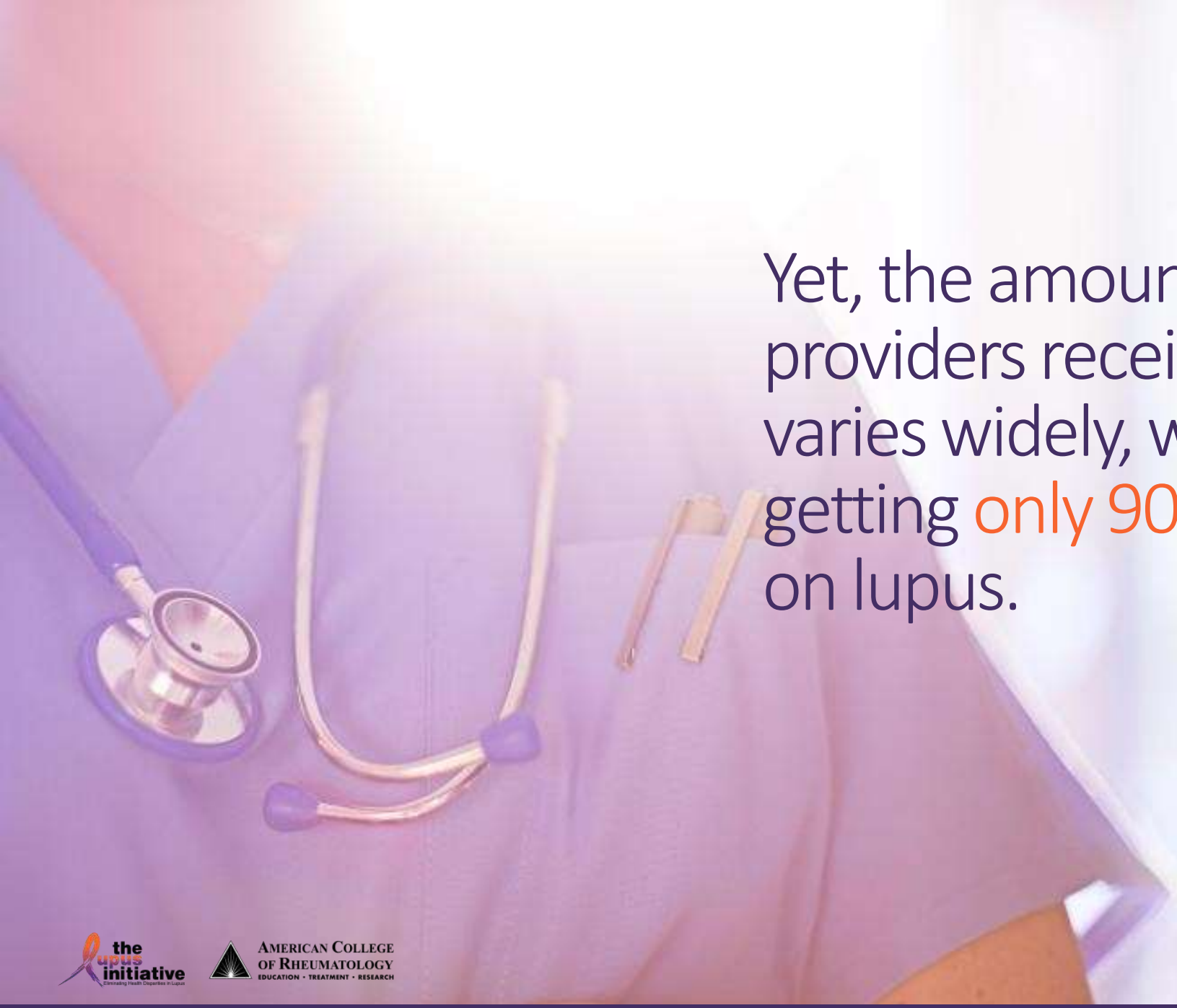
- organ failure
- a five-fold increased risk of death

With an early diagnosis, the chances of a person with lupus living a full life with a manageable, chronic disease are increased.[3]

Specific racial and ethnic minorities with lupus have mortality rates at least three times as high as white individuals, often because they are poor and do not have access to primary-care doctors and specialists who can diagnose and treat them.[4]



A person who is feeling sick will often seek help from a primary care provider or emergency room at the onset of the symptoms. It is crucial that these providers recognize potential symptoms of lupus and make referrals to rheumatologists when appropriate.



Yet, the amount of training these providers receive in medical school varies widely, with some students getting only 90 minutes of education on lupus.

It is our mission to educate primary care providers about lupus, so people with lupus can get the correct referral, diagnosis and treatment they need.

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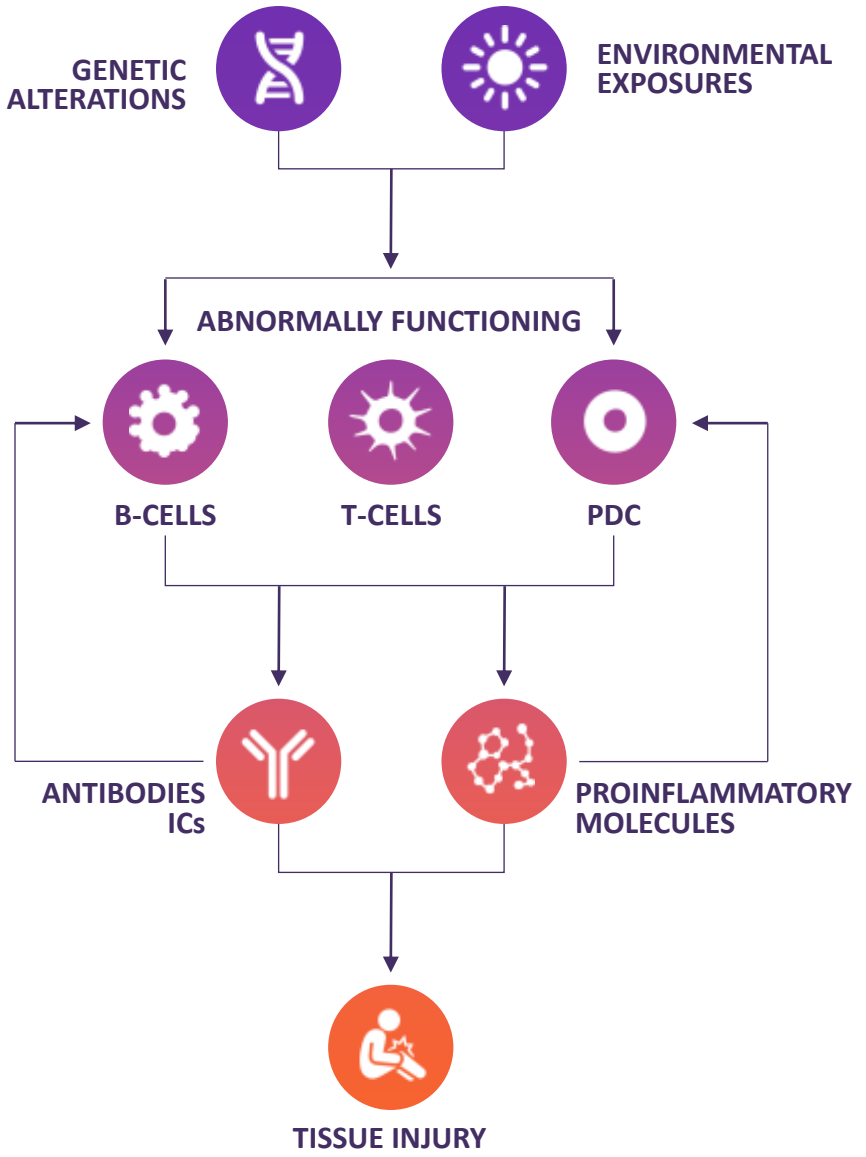
Let’s review some of the symptoms of and challenges related to the diagnosis of lupus.

About systemic lupus erythematosus (SLE)

- Lupus is an inflammatory, multi-system, autoimmune disease of unknown etiology with clinical manifestations that can change frequently and unexpectedly and suggestive laboratory manifestations.
- Lupus can be mild, severe and anything in between.
- The diversity of clinical symptoms is great, and all organ systems are vulnerable.
- Lupus is characterized by periods of flare and remission and can culminate in irreversible, end-organ damage.

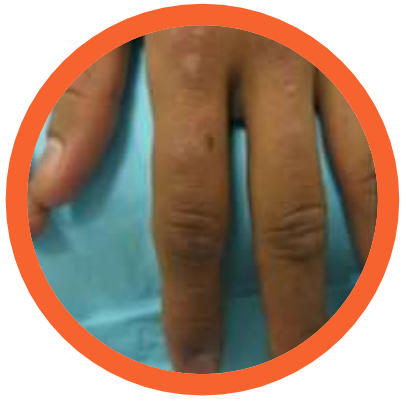
Pathogenesis of lupus

- Autoimmunity is an altered immune homeostasis that leads to autoreactivity, immunodeficiency and malignancy.
- Immune dysregulation leading to autoreactivity and autoantibodies in lupus occurs in different phases and likely represents the untoward effects of environmental triggers on the genetically susceptible host.



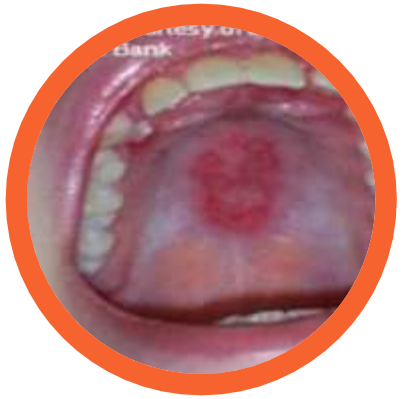
Let’s take a look at some of the symptoms of lupus.

When looking for skin conditions, keep in mind that skin conditions look different on diverse skin tones.



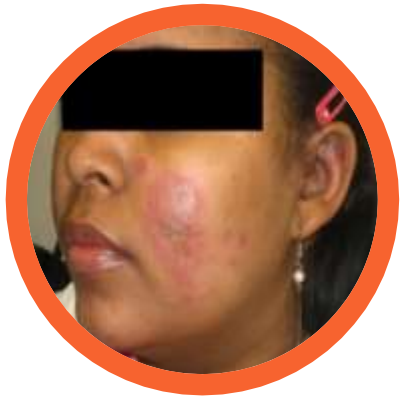
Synovitis

Malar rash

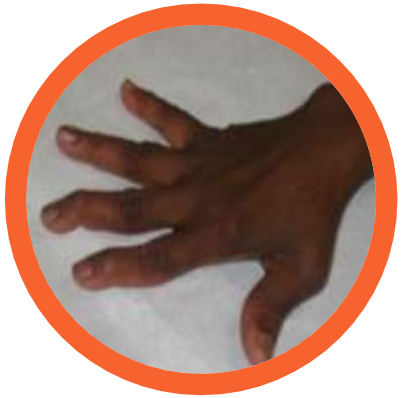


Painless oral ulcer

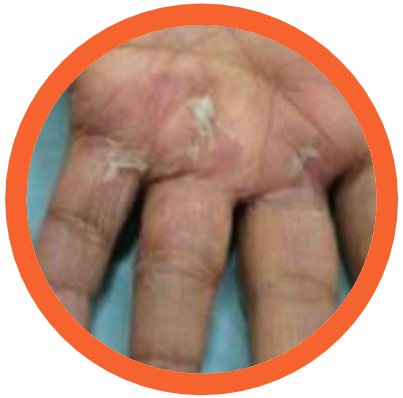
Raynaud's Phenomenon



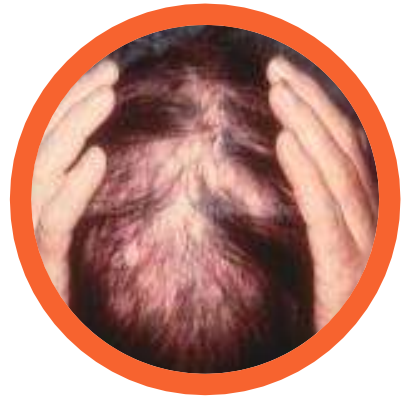
Discoid rash



Jaccoud's arthropathy



Vasculitis



Alopecia

Here are some lupus symptoms that make diagnosis difficult, because they can be indicators of so many conditions.

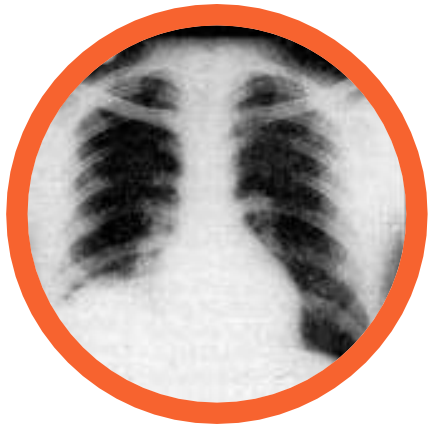
Achiness, headache

Fatigue

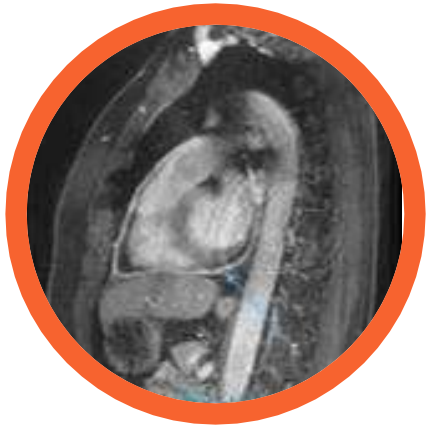
Memory thief / brain fog

Depression

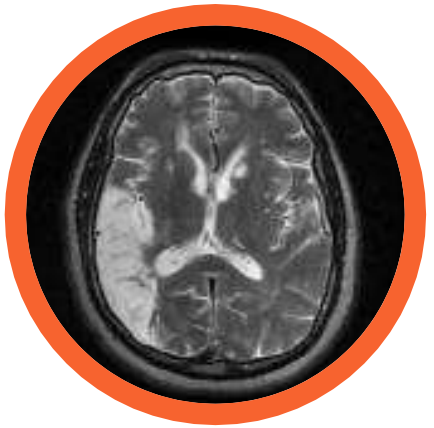
Here are some illustrations of organs impacted by lupus.



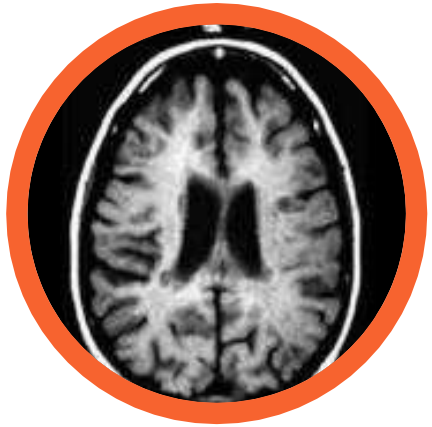
Serositis



Pericardial effusion

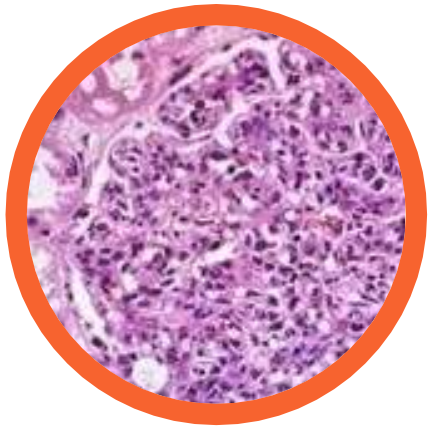


Cerebral infarct



Brain atrophy

Spherocytes



Glomerulonephritis

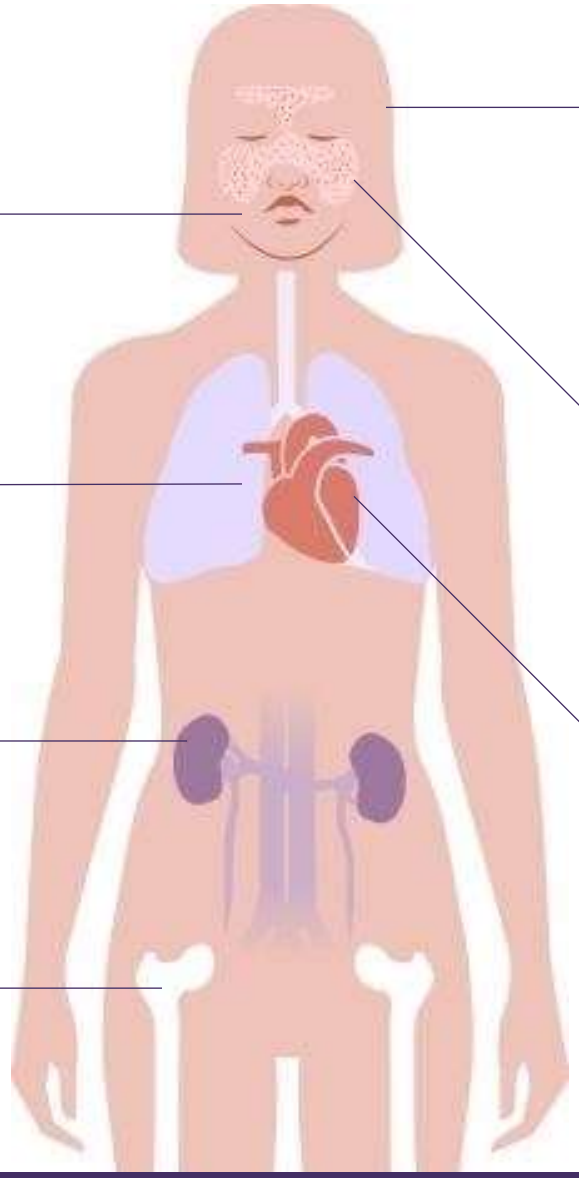
When to suspect lupus[5]

MOUTH
- Oral ulcers

LUNGS / HEART
- Serositis

KIDNEYS
- Proteinuria
- Hematuria

MUSCLE & JOINTS
- Arthritis
- Myositis



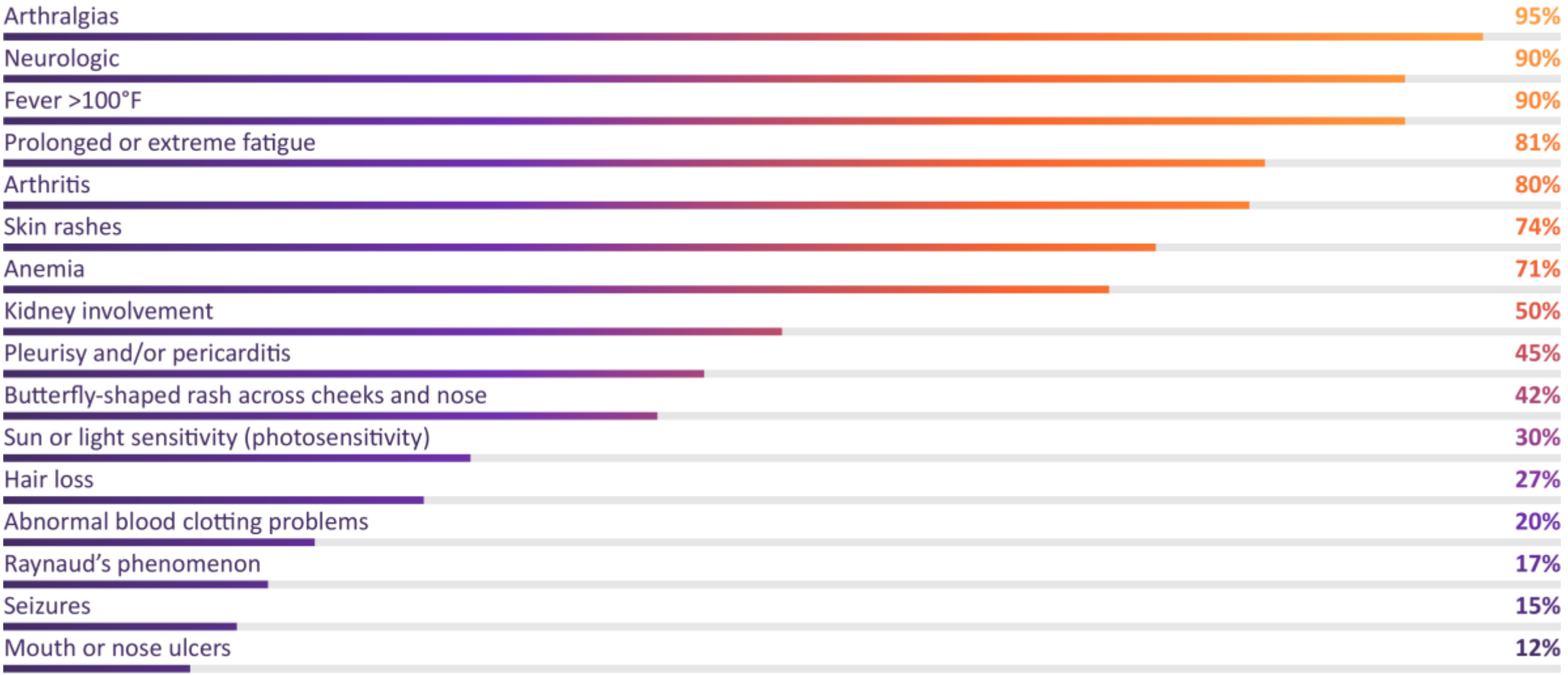
BRAIN
- Seizures
- Psychosis

SKIN
- Malar rash
- Discoid lesions
- Photosensitivity

BLOOD
- Low blood count

IMMUNOLOGIC
- Immunologic disorder
- Antinuclear antibodies (ANA)

Signs and symptoms



IVANA

Mostly external symptoms

Michelle and Ivana are sisters, but they have different symptoms, with Ivana's being more external and Michelle's more internal.

MICHELLE

Mostly internal symptoms

Video Placeholder

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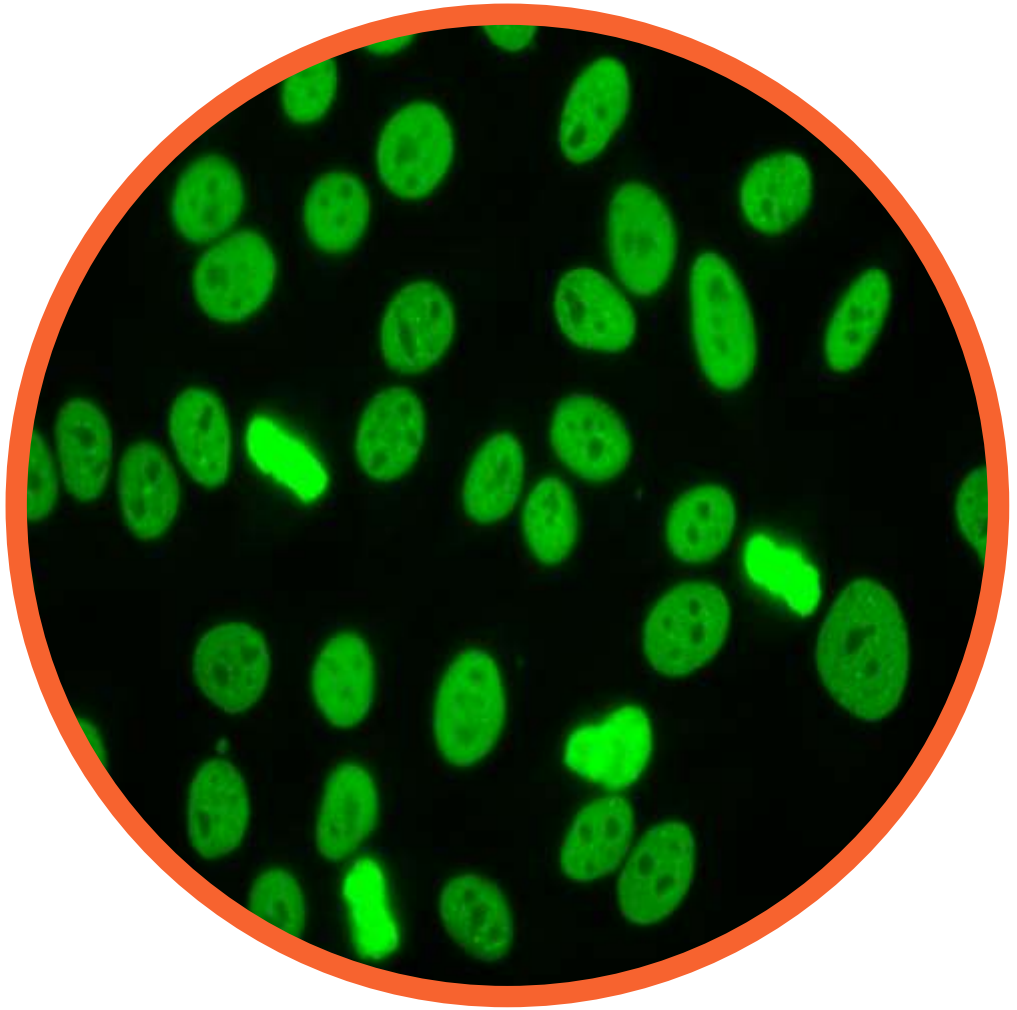
Unfortunately, there is no gold-standard diagnostic test for lupus.

The most common screen is for ANA—antinuclear antibodies.

The vast majority of women with lupus test positive for ANA, but a positive ANA test does not mean the person has lupus.

ANA could also indicate scleroderma, Hashimoto's thyroiditis, idiopathic pulmonary fibrosis and other chronic conditions.



What do most lupus patients have in common? antinuclear antibodies (ANA).

- Autoantibodies against various components of the cell nucleus.
- Present in many autoimmune disorders as well as some healthy subjects.
- Sensitive (not specific for SLE)
- Because of low specificity, ANA usefulness increases if the pretest probability for lupus is high; i.e., the patient has symptoms and signs that can be attributed to SLE.
- Because of the high sensitivity of the ANA, a patient with negative ANA is unlikely to have lupus even when her/his clinical presentation is suggestive of lupus.

If you suspect lupus, you can order these tests:

CBC WITH DIFFERENTIAL, UA, RENAL FUNCTION PANEL

- Urine protein/creatinine ratio if any proteinuria.

ANTINUCLEAR ANTIBODY (ANA)

- Positive in vast majority of patients with SLE.
- Beware false positives!
- Higher titer more likely to be clinically significant.
- If ANA is positive, consider additional autoantibodies.
- Anti-dsDNA and/or anti-Sm – more specific but less sensitive.

COMPLEMENTS: C3, C4

- Often but not always low in active disease.
- Acute phase reactants: elevated in other causes of inflammation (infection).

Autoantibodies in lupus

ANTIBODIES	LUPUS SPECIFICITY	LUPUS SENSITIVITY	CLINICAL ASSOCIATIONS
ANA	● ○ ○ Low	● ● ● High	
Anti-dsDNA	● ● ● High	● ● ○ Intermediate	Nephritis
Anti-Sm	● ● ● High	● ○ ○ Low	
Anti-RNP	● ○ ○ Low		Arthritis, myositis, lung disease
Anti-SSA	● ○ ○ Low		Dry eyes/mouth, subacute cutaneous lupus erythematosus (SCLE), neonatal lupus, photosensitivity
Anti-SSB	● ○ ○ Low		Same as above
Antiphospholipid	● ● ○ Intermediate	● ● ○ Intermediate[5]	Clotting diathesis

So how do you determine whether to order an ANA?

If autoimmune rheumatic disease is likely, the ANA can be helpful for diagnosis and classification.

If autoimmune rheumatic disease is unlikely, do not order an ANA. A positive ANA may cause anxiety, unnecessary investigations and potential confusion for both patients and providers.

Labs to consider in patients with non-specific symptoms and low probability of lupus

LOOK FOR EVIDENCE OF KIDNEY DISEASE

- Urinalysis, urine protein / creatinine ratio.
- Can be done conveniently on random 'spot' urine.

LOOK FOR (HEMOLYTIC) ANEMIA, THROMBO-CYTOPENIA, LYMPHOPENIA, NEUTROPENIA

- CBC with differential white count.

LOOK FOR RENAL FUNCTION, ACIDOSIS, LIVER DISEASE, MUSCLE INFLAMMATION

- Often but not always low in active disease.
- Acute phase reactants: elevated in other causes of inflammation (infection).

THYROTROPIN HORMONE (TSH)

- Fatigue, various symptoms in hypothyroidism and hyperthyroidism.

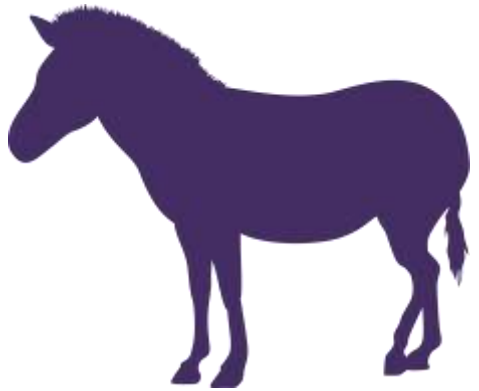
LOOK FOR EFFECTS OF LUPUS

- Not just autoimmunity.

ASK ABOUT THROMBOSIS OR POSSIBLE ANTIPHOSPHOLIPID SYNDROME

When the person you are treating has symptoms of lupus and a positive ANA test, it's important to refer to a rheumatologist.

When the person you are treating is a woman of color in her childbearing years, lupus is not a zebra. It's a horse.



Epidemiology of lupus

Prevalence 2–140/100,000 worldwide but as high as 207/100,000

Incidence 1–10/100,000

African American, Hispanic / Latino, Asian and Native American women have the highest prevalence.[6]

Affects mainly women in their reproductive years.[6]

People with lower incomes are less likely to receive recommended care and are two to three times more likely to die.[6]

African American women have a higher risk of poverty in the United States.[7]

Lupus affects up to 1 in 250 African American women in the United States.[7]

African American and Hispanic / Latino women are more likely to develop lupus than men.[7]

Women are nine times more likely to develop lupus as white women.[7]

African American and Hispanic / Latino women with lupus have mortality rates at least three times as high as white women with lupus.[7]

African American and Hispanic / Latino women are more likely to develop lupus at a younger age and to have more severe symptoms at onset.[7]

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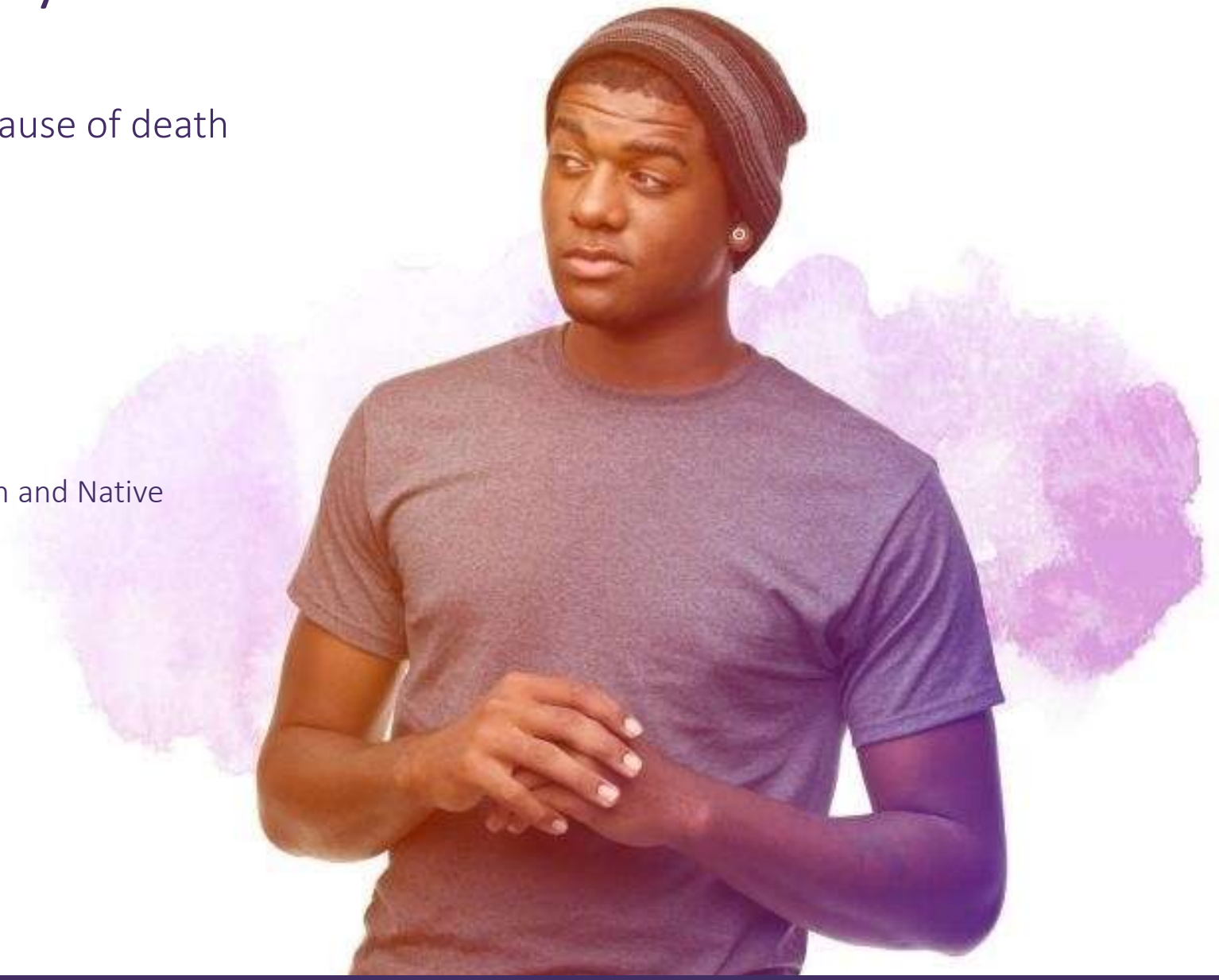
Lupus and mortality

Cardiovascular disease is the major cause of death in people with longstanding lupus.[8]

Factors contributing to increased mortality:

- Active lupus and infection
- High disease severity at diagnosis
- Younger age at diagnosis
- African American and Hispanic / Latino, Asian and Native American ethnicity
- Male gender
- Low socioeconomic status
- Poor adherence to treatment protocol
- Inadequate support system
- Limited education



Importance of early referral

- Mortality is higher in people with lupus compared to the general population.
- Five-year survival rate in 1953 was 50 percent. Today the survival rate is 90 percent because of better detection and treatment.
- Currently 80 to 90 percent of people with lupus survive 10 years after diagnosis, but that drops to 60 percent with advanced stages of organ deterioration.
- The leading causes of mortality are preventable with appropriate therapies.[9]

Let’s look at a case study.

A 23-year-old Hispanic / Latino woman with no past medical history presented in the emergency department with these symptoms:

- Eight-week history of joint pain and swelling in hands, knees and ankles
- Fever
- Myalgias
- Pleuritic chest pain
- Weight loss
- Facial rash that worsened with sun exposure

She initially went to a local clinic and was treated for cellulitis with oral Keflex.

Two days before, she went to another emergency department. She had a temperature of 103°F and anemia. She was told it was a “viral syndrome” and discharged.

EXAM

- T 37.9°C
- BP 130/90
- Painless ulceration on the palate
- Malar rash
- Diffuse lymphadenopathy
- Synovitis of the MCP/PIP joints

LABS

Accumulated from various providers over time

- WBC 2.5x10 (9)/L
- Total protein 9 g/dl
- Albumin 3 g/dL
- Hgb 11g/dL
- Hct 32%
- BUN 11 mg/dL
- Cr .06 mg/dL
- UA: 100 mg/dL protein
- RBC 20 – 40/hpf
- WBC 0-1/hpf
- ANA+
- Anti-dsDNA+
- Sm+

Should this person be referred to a rheumatologist?

Should this person be referred to a rheumatologist?

Yes.

What features in this case are concerning for lupus?

Let’s look at another case study.

A woman from western Africa recently diagnosed with anemia, presumed but not confirmed to have iron-deficiency, visited her doctor with these symptoms:

- swelling of feet and hands
- non-specific rash on her face and arms
- swelling in joints
- enlarged lymph nodes
- generalized body aches
- sweating

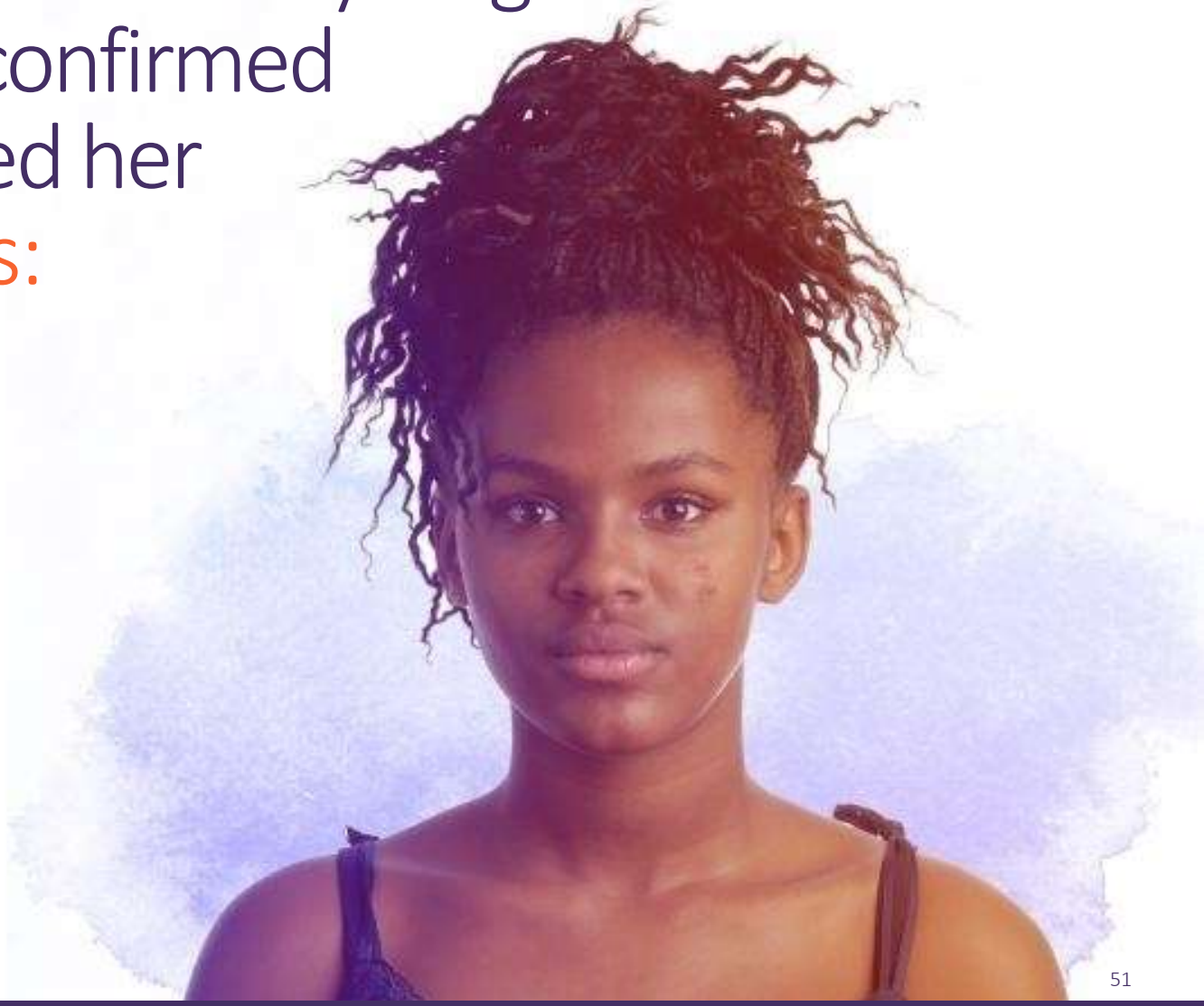


CHART REVIEW REVEALS:

- Positive ANA of 1:1280
- 4.2 WBC with normal differential
- Hb/Hct is 9.6/30.4 MCV 77.3
- Plt 307

Should this person be referred to a rheumatologist?

Should this person be referred to a rheumatologist?

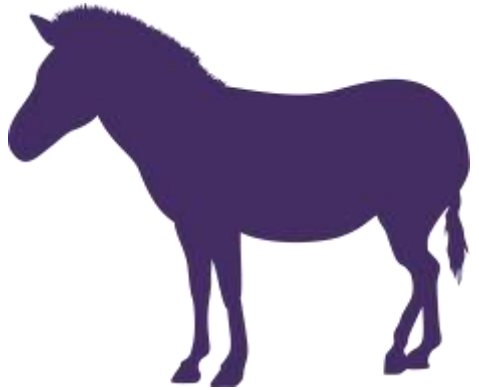
Yes.

What features in this case are concerning for lupus?

Attribution of symptoms to lupus is challenging and often requires

- First a certain level of suspicion (horses, not zebras) and
- Then a careful exam as well as history

As these patients often are frustrated and have seen other health care providers about their lupus symptoms.



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In summary

- Early symptoms can be non-specific and be easily mistaken for other illnesses or syndromes.
- Symptoms may be transient or prolonged and independent of one another.
- Consider lupus if the person you are treating presents with vague complaints from the signs and symptoms list.
- Also consider lupus if the person has a family history of autoimmune disease.
- Do an initial screening, including: CBC, BMP, LFTs, ESR, CRP, ANA, UA
- Refer to a rheumatologist for assessment and diagnosis.

Working together toward diagnosis

Building trust is critical.

People from different cultural and socioeconomic backgrounds experience illness and treatment differently.

Physicians from different cultural and socioeconomic backgrounds perceive the people they are treating and their symptoms differently.

Through education, we can eliminate disparities in the time it takes African American and Hispanic / Latino women to get diagnosed with lupus.

When the person you are treating is a woman of color in her childbearing years, lupus is not a zebra. It's a horse.

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Referrals

Text *Program Director/Fellow, please (1) delete this note and (2) insert the details for how and where to refer patients with suspected or diagnosed lupus.*

Resources and Information

Ongoing care for people with lupus is a team effort, and it is a matter of life and death.

For presentations, videos, interactive case studies and CE/CME courses, visit The Lupus Initiative at http://thelupusinitiative.org/providers/.

We appreciate your participation in a post assessment and a four- to six-week follow-up assessment.

Thank you.

Notes

1. Helmick CG, Felson DT, Lawrence RC et al. Arthritis Rheum. 2008: 58(1): 15–25; Chakravarty EF, Bush TM, Manzi S., Clarke AE, Ward MM. Arthritis Rheum. 2007; 56(6)2092–2094; Fessel WJ. Rheum Dis Clin North Am. 1988; 14(1): 15–23.

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3. Abu-Shakra M, Urowitz MB, Gladman DD, Gough J. Mortality studies in systemic lupus erythematosus. Results from a single center. II. Predictor variables for mortality. J Rheumatol. 1995;22(7):1265–1270

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