


# Demystifying Systemic Lupus Erythematosus


**Signs and symptoms for early recognition**  
**Satellite Conference and Live Webcast**  
**Thursday May 31, 2018**  
**12:00-1:00pm Central Time**

Produced by the Alabama Department of Public Health  
 Video Communications and Distance Learning Division




# Faculty

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**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.



## Before we get started...


**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.



## Before we get started...

**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.



## Before we get started...

### SUPPORT

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### FACULTY REPORTED DISCLOSURES

No disclosures



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## 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.



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## Pre/post assessment and follow-up

①

### PRE-ASSESSMENT (BEFORE SEMINAR)

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



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## Pre/post assessment and follow-up

②

### POST-ASSESSMENT (AFTER SEMINAR)

- Repeat pre-assessment
- Additional qualitative questions



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## Pre/post assessment and follow-up

③

### FOLLOW UP ASSESSMENT (4-7 WEEKS AFTER SEMINAR)

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



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## Thank you!

We appreciate your time in taking our pre-seminar assessment. Create a unique assessment identifier 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.



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## Learning objectives

After this presentation, you should:

- Recognize the signs and symptoms of lupus.
- Know when 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.<sup>1</sup>



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 / Latino, Asian and Native American women.


•Lupus has a prevalence of 87.7 cases per 100,000 in Hispanics / Latinos and 142.7 per 100,000 in Hispanic / Latino women.<sup>2</sup>



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




Meet  
Ivana and  
Michelle.



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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.**



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




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### 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




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### Why is the diagnosis of lupus so challenging?

**SYMPTOMS MAY BE VAGUE, INCLUDING:**

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




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### Why is the diagnosis of lupus so challenging?


**SYMPTOMS MAY:**

- develop slowly
- come on suddenly




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Ivana describes the difficulty in being accurately diagnosed.



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




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**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.<sup>3</sup>




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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.<sup>4</sup>




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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.




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



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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.



Michelle describes her experience in being diagnosed.




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.



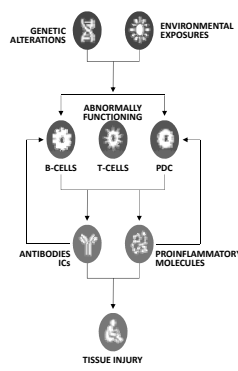
### About Systemic Lupus Erythematosus (SLE)

- 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-stage organ damage.




### Pathogenesis of lupus

- Autoimmunity is an altered immune homeostasis that leads to autoreactivity, immunodeficiency and malignancy.



```

    graph TD
      GA[GENETIC ALTERATIONS] --> AF[ABNORMALLY FUNCTIONING]
      EE[ENVIRONMENTAL EXPOSURES] --> AF
      AF --> BC[B-CELLS]
      AF --> TC[T-CELLS]
      AF --> PDC[PDC]
      BC --> AI[ANTIBODIES/ICs]
      TC --> PM[PROINFLAMMATORY MOLECULES]
      PDC --> PM
      AI --> TI[TISSUE INJURY]
      PM --> TI
  
```



## Pathogenesis of lupus

- 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.

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

24

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

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

25

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

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Here are some illustrations of organs impacted by lupus

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### When to suspect lupus<sup>5</sup>

- BRAIN**
  - Seizures
  - Psychosis
- SKIN**
  - Malar rash
  - Discoid lesions
  - Photosensitivity
- BLOOD**
  - Low blood count
- IMMUNOLOGIC**
  - Immunologic disorder
  - Antinuclear antibodies (ANA)
- MOUTH**
  - Oral ulcers
- LUNGS / HEART**
  - Serositis
- KIDNEYS**
  - Proteinuria
  - Hematuria
- MUSCLE & JOINTS**
  - Arthritis
  - Myositis


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### Signs and symptoms


Arthritis	95%
Neurologic	90%
Fever > 38.3°C	90%
Prolonged or extreme fatigue	82%
Raynaud's	80%
Skin rashes	74%
Anemia	72%
Kidney involvement	50%
Photosensitivity or pericarditis	45%
Butterfly-shaped rash across cheeks and nose	42%
Sun or light sensitivity (photosensitivity)	38%
Hair loss	33%
Abnormal blood clotting problems	28%
Raynaud's phenomenon	17%
Sarcopenia	15%
Mouth or nose ulcers	12%

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



**IVANA**  
Mostly external symptoms



**MICHELLE**  
Mostly internal symptoms

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Ivana and Michelle describe the differences in their respective symptoms.

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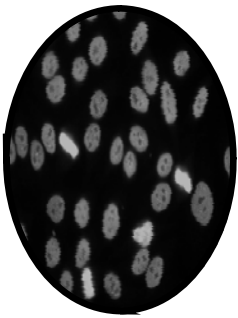
Unfortunately, there is no gold-standard diagnostic test for lupus.

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### 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.



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### What do most lupus patients have in common? Antinuclear Antibodies (ANA).

- Autoantibodies against various components of the cell nucleus.
- Present in other autoimmune illnesses, several infections, malignancies and in healthy people, as well.
- Sensitive (not specific for SLE)



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### What do most lupus patients have in common? Antinuclear Antibodies (ANA).

- 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.



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### If you suspect lupus, you can order these tests:



#### CBC WITH DIFFERENTIAL, UA, RENAL FUNCTION PANEL

- Urine protein/creatinine ratio if any proteinuria.



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### If you suspect lupus, you can order these tests:



#### 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.



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### If you suspect lupus, you can order these tests:



#### COMPLEMENTS: C3, C4

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



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### Autoantibodies in lupus

ANTIBODIES	LUPUS SPECIFICITY	LUPUS SENSITIVITY	CLINICAL ASSOCIATIONS
ANA	●○○ Low	●●● High	Nonspecific
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 (SCLC)
Anti-SSB	●○○ Low		neonatal lupus, same as above photosensitivity
Antiphospholipid	●●○ Intermediate	●●○ Intermediate <sup>5</sup>	Clotting diathesis



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## 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.



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## 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.



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



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

- CBC with differential white count.



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



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).



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



THYROTROPIN HORMONE (TSH)

- Fatigue, various symptoms in hypothyroidism and hyperthyroidism.



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



LOOK FOR EFFECTS OF LUPUS

- Not just autoimmunity.



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



ASK ABOUT THROMBOSIS OR POSSIBLE ANTIPHOSPHOLIPID SYNDROME



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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.



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### Epidemiology of lupus

Prevalence 2–140/100,000 worldwide but as high as 207/100,000  
Incidence 1–10/100,000

Women are nine times more likely to develop lupus than men.<sup>7</sup>

Affects mainly women in their reproductive years.<sup>7</sup>



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### Epidemiology of lupus

African American, Hispanic / Latino, Asian and Native American women have the highest prevalence.<sup>7</sup>

Lupus affects up to 1 in 250 African American women in the United States.<sup>8</sup>



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### Epidemiology of lupus

People with lower incomes are less likely to receive recommended care, and poverty is associated with poor outcomes.<sup>8</sup>

African American women have two to three times higher risk than white women.<sup>7</sup>



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### Epidemiology of lupus

African American and Hispanic / Latino women are more likely to develop lupus at a younger age and to have more severe symptoms at onset.<sup>8</sup>

African American and Hispanic / Latino women with lupus have mortality rates at least three times as high as white women with lupus.<sup>8</sup>



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There are significant disparities in the diagnosis and treatment of lupus.



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## Lupus and mortality

Cardiovascular disease is the major cause of death in people with longstanding lupus.<sup>9</sup>

Factors contributing to increased mortality:

- Active lupus and infection
- High disease severity at diagnosis
- Younger age at diagnosis



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## Lupus and mortality

- 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



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## 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.



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## Importance of early referral

- Currently 80 to 90 percent of people with lupus survive 10 years after diagnosis, but that drops to 70 percent with advanced stages of organ deterioration.
- The leading causes of mortality are preventable with appropriate therapies.<sup>10</sup>



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Let's look at a case study.



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**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



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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
- BPPainless ulceration on the palate
- 130/90
- Malar rash
- Diffuse lymphadenopathy
- Synovitis of the MCP/PIP joints



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#### 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 .07 mg/dL

- UA: 100 mg/dL protein
- RBC 20 – 40/hpf
- WBC 0-1/hpf
- ANA+
- Anti-dsDNA+
- Sm+




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Should this person be referred to a rheumatologist?



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Should this person be referred to a rheumatologist?

Yes.



43

What features in this case are concerning for lupus?



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Let's look at another case study.




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



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



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**CHART REVIEW REVEALS:**

- Positive ANA of 1:1280
- 4.2 WBC with normal differential
- Hb/Hct is 9.7/30.4 MCV 77.3
- Plt 307



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Should this person be referred to a rheumatologist?



53


Should this person be referred to a rheumatologist?

Yes.



54

What features in this case are concerning for lupus?





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**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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Ivana on the importance of listening.




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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.**




## A call to action.



## Referral to Rheumatology Process

***UAB Rheumatology***

- call the Rheumatology Scheduling Office at (205) 996-7438; fax 205-801-7510




## 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://tlitools.org/lectures>.

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



# Thank you.





## Notes

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