Demystifying **Systemic Lupus Erythematosus:** Signs and Symptoms for Early Recognition

Teaching Fellows in Lupus Project

Lupus Research Institute

American College of Rheumatology
EDUCATION • TREATMENT • RESEARCH

the lupus initiative
Eliminating Health Disparities in Lupus

Introduction: Why are we here?

- Lupus can take 4-6 years and 3 providers before diagnosis*
- During that time, organ damage can develop leading to 5 fold increased risk of death
- Patients go to primary care providers or emergency rooms at onset of illness, so detection of lupus by these providers is critical to early diagnosis
- These providers may have received only 90 minutes of training on lupus in medical school*

* Survey data of health professionals

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.

How you can help: Teaching Fellows Project

- **Problem:** Education about lupus is important for all providers, but there is a shortage of peer educators
- **Solution:** Recruit fellows/junior faculty in Rheumatology to serve as lupus educators for practicing physicians
- **What you can do:** Participate in the voluntary pre and post assessment and follow up so we can evaluate the project
- **Benefits to you:** Increased self efficacy in lupus detection, access to CMEs from the ACR
- **Our goal:** To bring this project to Rheumatology Fellowship Programs nationally to expand quality education on lupus to improve detection, increase appropriate referral, and decrease diagnosis time

Pre/Post Assessment and Follow Up

Voluntary, Used solely to rate the quality of this seminar
De-identified: Linked by numeric identifier

- **Pre- assessment (before seminar)**
  - 10 multiple choice or true/false questions and 1 efficacy question
  - About 3 minutes to complete
- **Post- assessment (after seminar)**
  - Repeat pre assessment
  - Additional qualitative and demographics questions
  - About 5 minutes to complete
- **Follow up assessment (4-6 weeks after seminar)**
  - Repeat pre assessment
  - Option for comment
  - Requires an email address
- Access to CME modules available from ACR for completion
- Answers available after session

Thank you

We appreciate your time in taking our pre seminar assessment

Presentation Goals

- To improve recognition of lupus and increase appropriate referral for diagnosis by:
- Increasing lupus knowledge in:
  - Epidemiology
  - Health Disparities
  - Genetics, Pathogenesis, ANA and other Autoantibodies
  - Disease characteristics: activity, severity, mortality
- Reviewing the classification criteria
- Discussing real case presentations of patients with lupus

Patient Voices

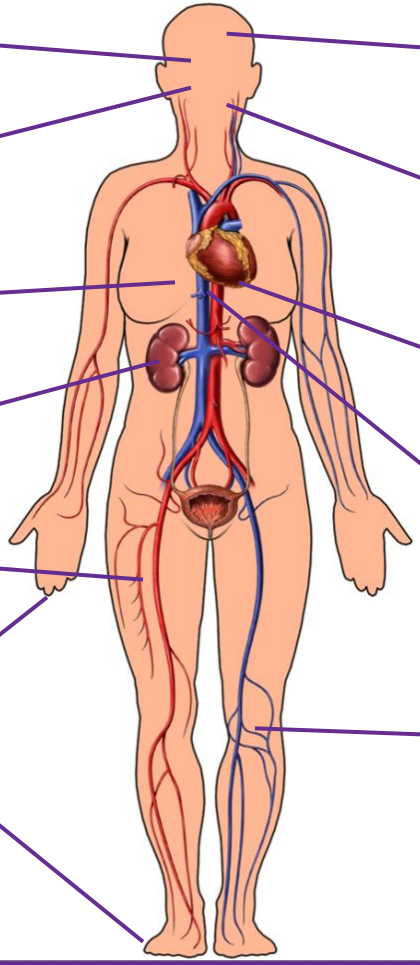
Systemic Lupus Erythematosus (SLE)

- An inflammatory, multisystem, autoimmune disease of unknown etiology with protean clinical and laboratory manifestations and a variable course and prognosis
- Lupus can be a mild disease, a severe and life-threatening illness, or anything in between
- The diversity of clinical symptoms in SLE is great, and all organ systems are vulnerable
- Disease is characterized by periods of flare and remission (or low level activity) and can culminate in irreversible end-organ damage

Why is diagnosis so hard?

- The Great Masquerader: can mimic viral syndromes, malignancies, allergic reactions, stress, etc.
- May be associated with depression and/ or fibromyalgia.
- Initial symptoms might be non-specific: fatigue, achiness, stiffness, low grade fevers, swollen lymph nodes, rashes.
- Symptoms may develop slowly or suddenly.
- There is no gold standard diagnostic test for lupus
- Wide variety of symptoms and organ involvement may be present.

Examples of Organs Involved, Signs, and Symptoms



- Eyes
- Skin
- Pleurisy
- Kidney disease
- Muscle
- Raynaud's & vasculitis
- Central nervous system
- Oral & nasal ulcers
- Pericarditis
- Blood disorders
- Joints & arthritis

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Why is early referral important?

- Mortality is higher in lupus patients compared to the general population
- 5-year survival rate in 1953 was 50%, increased to 90% with better detection and treatment
- Currently 80 to 90% of lupus patients survive 10 years after diagnosis, but that drops to 60% with advanced stages of organ threatening disease
- Leading causes of mortality are preventable
- Appropriate therapeutic management, compliance with treatment and improved treatment of long-term consequences can prevent excess and premature deaths. **This starts with clinical suspicion of the diagnosis and early recognition.**

American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus. Guidelines for referral and management of systemic lupus erythematosus in adults. Arth Rheum 1999;42:1785--96

Mortality

- **Cardiovascular disease is the major cause of mortality in patients with longstanding lupus**
- Factors contributing to increased mortality*
  - Active lupus & infection (early stages of disease)
  - High disease severity at diagnosis
  - Younger age at diagnosis
  - Ethnicity: Black, Hispanic, Asian, and Native American populations
  - Male gender
  - Low socioeconomic status
  - Poor patient adherence*
  - Inadequate patient support system*
  - Limited patient education*

*Indicates opportunity for improvement.

Bernatsky S, Boivin JF, Joseph L, et al. *Arthritis Rheum.* 2006;54:2550-2557.

Epidemiology

- **Prevalence:** 2–140/100,000 worldwide but as high as 207/100,000
- **Incidence:** 1–10/100,000 worldwide
- **Health Disparities and At-Risk Populations:**
  - Women in their reproductive years
  - Women are 9 times more likely to develop lupus than men
  - Non-Caucasians have the highest prevalence:
    - Affects up to 1/250 Black women in US
    - 2-3 times higher risk than white women
- **Cost:** Direct costs associated with treatment (e.g., $100 billion in healthcare cost associated with autoimmune diseases) and indirect cost related to lost productivity and wages

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.

Other Health Disparities in Lupus

- Specific racial/ethnic minorities are more likely to develop lupus at a younger age and to have more severe symptoms at onset
- Specific racial/ethnic minorities with lupus have mortality rates at least 3 times as high as White individuals
- Low income individuals less likely to receive recommended care
- Poverty associated with poor outcomes

Duran S, Apte M, Alarcón GS. *J Natl Med Assoc.* 2007;99(10):1196-1198; Ward MM, Pyun E, Studenski S. *Arthritis Rheum*. 1995;38(2):274-283; Alarcón GS, McGwin G Jr, Bastian HM, et al. *Arthritis Rheum*. 2001;45(2):191-202.

McCarty DJ, Manzi S, Medsger TA Jr, Ramsey-Goldman R, LaPorte RE, Kwoh CK. *Arthritis Rheum*. 1995;38(9):1260-1270; Cooper GS, Parks CG, Treadwell EL, et al. *Lupus*. 2002;11(3):161-167.

CDC. *MMWR Morb Mortal Wkly Rep.* 2002;51:371-374.

Disease Activity and Severity

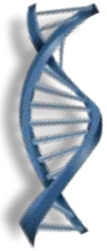
- Predictors of flare (in some but not all cases)
  - New evidence of complement consumption
  - Rising anti-dsDNA titers
  - Increased ESR
  - New lymphopenia
- Severity characterized by:
  - Abrupt onset of symptoms
  - Increased renal, neurologic, hematologic, and serosal involvement
  - Rapid accrual of damage (irreversible organ injury)
  - Associated with race, younger age, male gender, poverty

SLE

Initiation

Amplification

Perpetuation



Genetic alterations

Environmental Exposures & Behavior

Abnormally functioning
B-cells
T-cells
pDC

Autoantibodies
ICs

Proinflammatory
molecules

TISSUE INJURY

Antigen
Hormones (estrogen)
Infections
Toxins
Medications
Sun exposure
Vitamin D deficiency
Smoking
Stress
Toxins

Pathogenesis of Lupus- Important Concepts

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

Lupus Intangibles

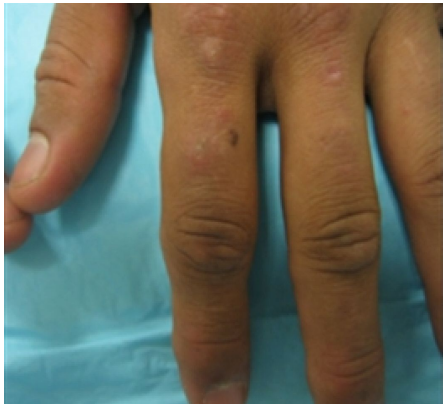
Achiness, Headache

Fatigue

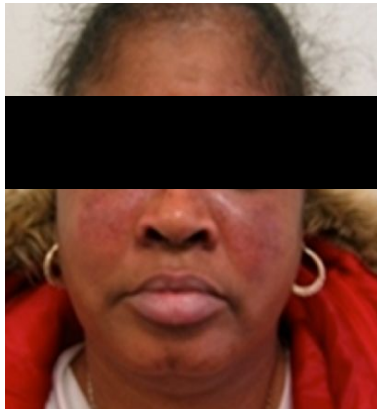
Memory thief
“brain fog”

Depression

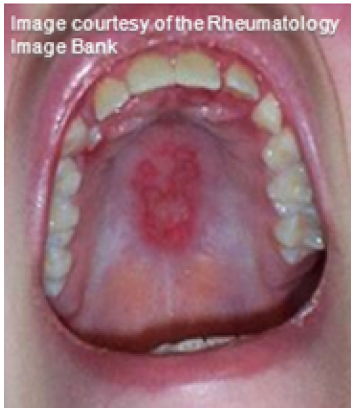
Lupus on the Outside



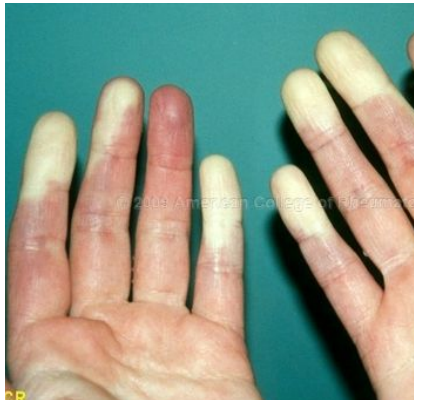
Synovitis



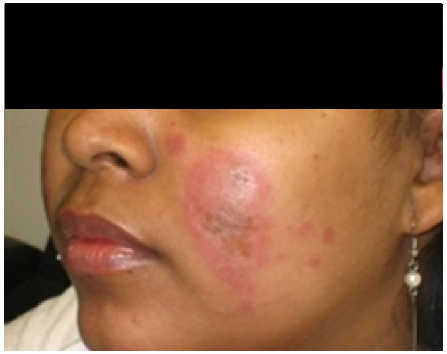
Malar rash



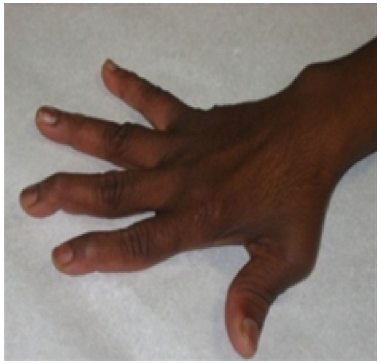
Painless oral ulcer



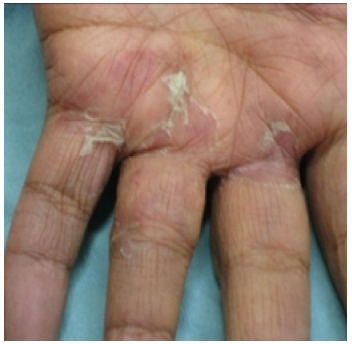
Raynaud's Phenomenon



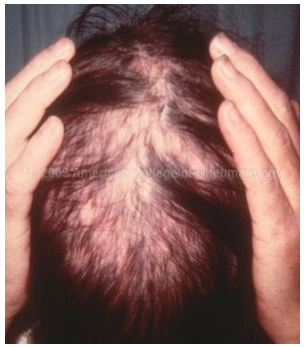
Discoid rash



Jaccoud's arthropathy

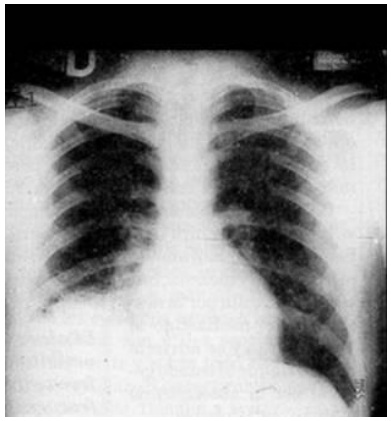


Vasculitis

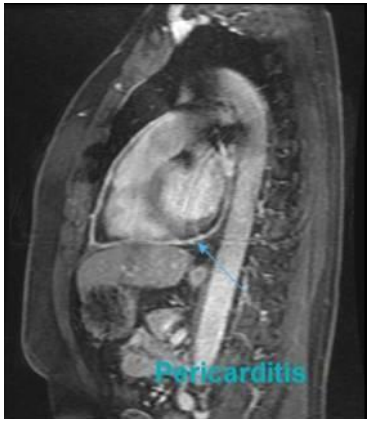


Alopecia

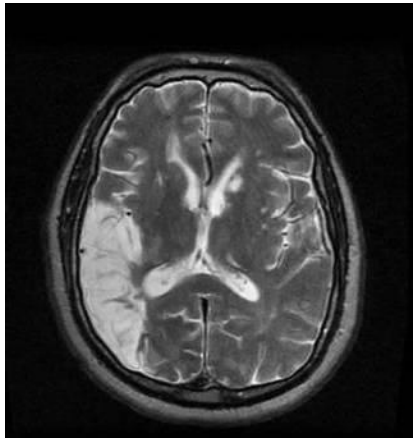
Lupus on the Inside



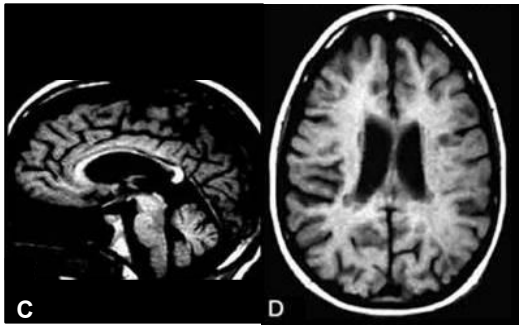
Serositis



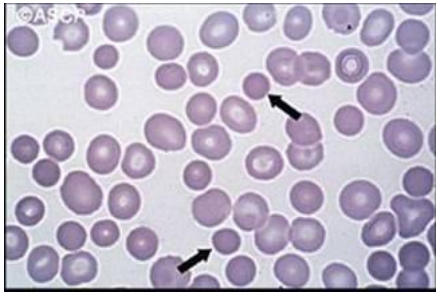
Pericardial effusion



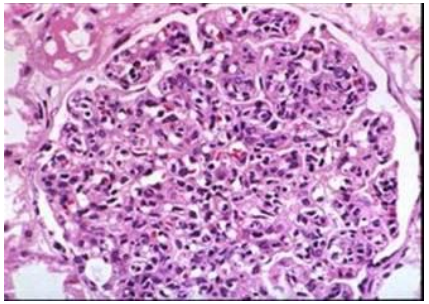
Cerebral infarct



Brain atrophy



Spherocytes



Glomerulonephritis

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; ie, 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

Incidence of Positive ANA

- Non- lupus subjects 3%−4%
- SLE 95%−99%
- Scleroderma 95%
- Hashimoto's thyroiditis 50%
- Idiopathic pulmonary fibrosis 50%
- Incidence increases with age, chronic infections, and other chronic conditions
- **Interpret the ANA in context of clinical complaints**
  ANA+ does not = SLE

Autoantibodies in SLE

Antibodies	Lupus Specificity	Clinical Associations
ANA	Low	Nonspecific
Anti-dsDNA	High	Nephritis
Anti-Sm	High	Nonspecific
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	Clotting diathesis

When to suspect SLE:

ACR (Revised) Criteria for Classification
4/11= 95% Specificity; 85% Sensitivity

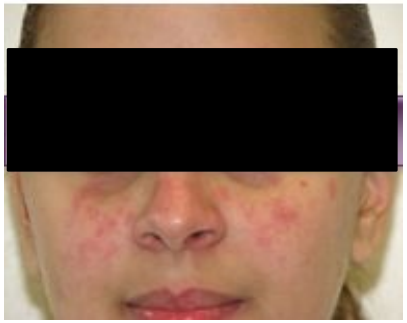
1. Serositis
2. Oral ulcers
3. Arthritis
4. Photosensitivity
5. Blood cells
6. Renal involvement
7. Antinuclear antibodies (ANA)
8. Immunologic disorder
9. Neurologic disorder
10. Malar rash
11. Discoid rash

Tan EM, Cohen AS, Fries JF, et al. *Arthritis Rheum.* 1982;25:1271-1277. Hochberg MC. *Arthritis Rheum.* 1997;40:1725. [Letter].

Signs and Symptoms

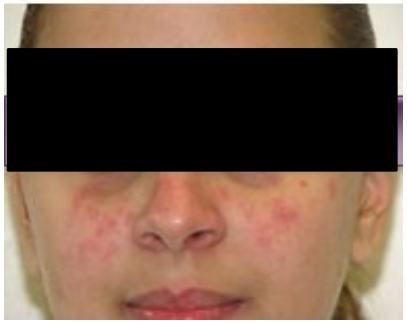
Symptom Occurrence (ever)	
Neurologic	90%*
Arthralgias	95%
Fever >100 F (38 Degrees C)	90%
Arthritis	80%
Prolonged or extreme fatigue	81%
Skin rashes	74%
Anemia	71%
Kidney involvement	50%
Pleurisy and/or pericarditis	45%
Butterfly-shaped rash across cheeks and nose	42%
Sun or light sensitivity (photosensitivity)	30%
Hair loss	27%
Abnormal blood clotting problems	20%
Raynaud's phenomenon	17%
Siezures	15%
Mouth or nose ulcers	12%

Case Presentation A



- **History:** A 23-year-old Hispanic female with no past medical history presented to the emergency department (ED) with an 8-week history of joint pain and swelling in the hands, knees, and ankles; fever; myalgias; pleuritic chest pain; weight loss; and a facial rash that worsened with sun exposure. She had been seen initially at a local clinic and treated for “cellulitis” with oral Keflex. Two days prior, she was seen in another ED, found to have a temperature of 103 °F, proteinuria, and anemia; she was told it was a “viral syndrome” and discharged home.

Case Presentation A (cont.)



- **Exam:** T 37.9 °C, BP 130/90, painless ulceration on the palate, malar rash, diffuse lymphadenopathy, and synovitis of the MCP/PIP joints
- **Labs:** 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+

Case Presentation B - What features are concerning for lupus?

- 23 year old woman from Western Africa with recently diagnosed anemia (presumed but not confirmed to be iron-deficiency anemia) presents with swelling of feet and hands and a non-specific rash on her face and arms. She reported swelling in the joints, enlarged lymph nodes, generalized body aches and 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

Lupus Detection—In Summary

- **Early symptoms can be**
  - Non-specific, easily confused with other illnesses or syndromes
  - Transient or prolonged, independent of one another
- **Consider lupus if your patient presents with**
  - Vague complaints from the signs and symptoms list
  - Family history of autoimmune disease
- **Do an initial screening**
  - CBC, BMP, LFT's, ESR, CRP, ANA, UA
- **Make a referral for assessment and diagnosis by a Rheumatologist**

Final Thoughts

- **Patient engagement and trust building is critical**
  - Patients from different cultural/socioeconomic backgrounds experience illness and treatment differently
  - Physicians from different cultural/socioeconomic backgrounds perceive patients and symptoms differently
- **What you can do to reduce health disparities**
  - Discuss lupus prevalence and disparities with colleagues
  - Pursue continuing education about causes of disparities and cross-cultural communication
  - Learn about and refer patients to community resources

Resources and Information

Ongoing care of lupus patients is a team effort

For presentations, videos, interactive case studies and CE/CME courses that can help, visit the Lupus Initiative at www.tlitools.org

We appreciate your participation in the post assessment and 4-6 week follow up assessment

Thank you!

This project is part of the American College of Rheumatology's Lupus Initiative (www.tlitools.org) and is administered by the Lupus Research Institute (lupusresearchinstitute.org/).

This project is supported by Grant Number 1 CPIMP141065-01-00 from the U.S. Department of Health and Human Services office of Minority Health.

Questions about the Project?

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