Disclosures

Heather Hansen, MD, rheumatologist at Charles Rheumatology Clinic disclose.

Systemic Lupus Erythematosus (SLE): Labs, Signs, and Symptoms

Lupus is a multisystem disease with myriad symptoms that can take 4-6 years and 3 providers before diagnosis.

To improve recognition of signs and increase referral for diagnosis:

- Early and socioeconomic disparities are wide in SLE and those with SLE.
- Before diagnosis, often damage can develop leading to 5 fold increase in mortality.
- Providers may have received only 90 minutes of training on diagnosis so detection of lupus by these providers is critical to early intervention.
- Patients to primary care providers of emergency rooms at onset.

Introduction: Why are we here?

Lupus in medical school:

- Discuss real case presentations of patients with lupus
- Reviewing all classification criteria
- Demystifying systemic lupus
- Identify patients from rheumatology
- General presentation and review of management

Objectives
Objectives

- Systemic Lupus Erythematosus (SLE)
- An inflammatory, multisystem, autoimmune disease of unknown etiology with protein clinical and laboratory abnormalities involving multiple organ systems, and can mimic several other diseases.

Examples of Organs Involved, Signs, and Symptoms

- Raynaud’s & vasculitis
- Muscle
- Kidney disease
- Peptide
- Oral & nasal ulcers
- Central nervous system
- Eyes

Why is diagnosis so hard?

- Irreversible end-organ damage
- Interchangeable signs and symptoms may be present
- There is no gold standard diagnostic test for lupus
- Symptoms may develop slowly or suddenly

- Initial symptoms might be non-specific: fatigue, arthralgias, stiffness, low-grade fever, swollen lymph nodes, rashes
- May be associated with depression and/or hypomania

- The great mimicader; can mimic viral syndromes, manifestations allergic reactions, stress, etc.

Familiarize providers with common SLE therapies

- With a positive ANA and/or disease activity
- Increase awareness of other disease that may be associated
- Order serological testing
- Understand the significance of a positive ANA and when to identify features consistent with early or undiagnosed lupus

SLE (Systemic Lupus Erythematosus)
Antinuclear Antibodies (ANA)

What do most Lupus patients have in Common?

Antinuclear Antibodies (ANA) are antibodies that bind to the nucleus of cells. They are commonly found in patients with SLE (Systemic Lupus Erythematosus), but can also be present in other autoimmune diseases and healthy individuals.

SLE Prevalence: Central Oregon

The prevalence of SLE in Central Oregon is unknown.

Epidemiology

Prevalence: 2-4/100,000 worldwide. Rate as high as 20/100,000.

Rheumatology (Hoboken, N.J.) 66:—–'

What do most Lupus patients have in common?

Antinuclear Antibodies (ANA)

What do most Lupus patients have in common?

Antinuclear Antibodies (ANA)

What do most Lupus patients have in common?

Antinuclear Antibodies (ANA)
### Incidence of Positive ANA

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<th>Symptom Occurrence (%)</th>
<th>12%</th>
<th>15%</th>
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### When to Suspect SLE

When interpreting the ANA in the context of clinical complaints, ANA+ does not = SLE. Analyze the following conditions:

- Interstitial lung disease
- Infections
- Vasculitis
- Endocarditis
- Malar rash
- Discoid rash
- Photosensitivity
- Neutrophilic dermatitis
- Rheumatoid arthritis
- Arthritis
- Serositis
- Oral ulcers
- Renal involvement
- Skin rashes
- Arthritis
- Photosensitivity
- Oral ulcers
- Renal involvement
- Skin rashes

### Incidence of Positive ANA

- 32 Million persons in US (13.8% > 12 yo)

### Interpretation of Positive ANA

When interpreting positive ANA, consider the following factors:

- *Positive ANA* does not mean SLE.
- Consider clinical correlation with ANA positivity.
- Refer to ACR revised criteria for classification:
  - 4/11 = 95% specificity; 85% sensitivity
  - SLE (Revised) Criteria for Classification
  - 11 Discoid rash
  - Oral ulcer
  - Renal involvement
  - 5 Blood cells
  - Malar rash
  - Photosensitivity
  - 3 Arthritides
  - Neurologic disorder
  - Antinuclear antibodies

### 32 Million People in US

- 13.8% > 12 yo
Testing Algorithm for ANA testing in suspected SLE:

- Very low pre-test probability: do not test
- Reasonable pre-test probability: screen with ANA
- Very low post-test probability: do not test
- High post-test probability: check lupus-specific autoantibodies

Other tests have higher specificity. Used to

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
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<tbody>
<tr>
<td>ANA</td>
<td>95</td>
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<td>Anti-dsDNA</td>
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ANA has high sensitivity, but relatively low specificity. Used to 'rule out' SLE. Other tests have higher specificity. Used to 'rule in' SLE, if reasonable probability.
Many different substances/antigens in a cell nucleus (e.g., DNA, RNA).

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<th>ANA Patterns</th>
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<td>• Peripheral or &quot;nuclear&quot;</td>
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<tr>
<td>• Nuclear</td>
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<td>• Speckled</td>
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<td>• Diffuse</td>
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**Central Oregon ANA Testing Options**

- **St. Charles**: ANA with titer if positive: $63.13
- **ANA reflex panel**: $300.38
- **Smith, RNP, centromere, SSA/SSB, C3, C4, Jo**: $44.33
- **ANA with titer**: $52.37
- **Health services**: ANA with titer and ANA reflex panel both $52.37
- **BMC/Peace**: ANA with titer: $44.33
- **Interpath**: ANA with titer: $44.33
- **ANA with titer and ANA reflex panel**: $52.37
- **ANA reflex panel**: $300.38
- **ANA reflex panel**: $520.38
- **ANA reflex panel**: $300.38

**Peripheral or "n.m."**

Different clinical associations - different patterns observed.
Why is early referral important?

- Mortality is higher in lupus patients compared to the general population.
- Leading causes of mortality are preventable.
- Appropriate therapeutic management, compliance with treatment, and detection and treatment are critical.
- Mortality is higher in lupus patients compared to the general population.

Disparities in Lupus Prevalence

- Women are twice more likely to develop lupus.
- Hispanic, Asian, and Native populations are also more likely.
- Women are 3 times more likely to develop.

Black women are 3 times more likely to develop.

Mortality

- Cardiovascular disease is the major cause of mortality in patients with longstanding lupus.
- Early recognition, this starts with clinical suspicion of the diagnosis.
- Improved treatment of long-term consequences can prevent excess morbidity.
- Mortality is higher in lupus patients compared to the general population.

Disparities in Health Care Delivery

- Inequity of facilities and services
- The United States
- Health disparities are the differences in access to or availability of facilities and services among specific population groups in the United States.

Definition of Health Disparities

- Health disparities refer to differences in access to or availability of facilities and services in health conditions and other adverse health outcomes among specific population groups.

Inequity of Facilities and Services

- Equitable access to health care is the key to reducing health disparities.
- The American College of Rheumatology (ACR) and the American College of Physicians (ACP) recommend early recognition of lupus.

Reducing Health Disparities in Lupus

Pathogenesis of Lupus

Genetically susceptible host represents the interaction of environmental triggers on the immune dysregulation leading to autoaggressivity and autoinflammation. Autoimmunity is an altered immune homeostasis that leads to...

Causes of Autoimmune Disease = Multifactorial

- Genes
- Environment
- Behavior
- Risk

Immune deficiency leading to autoaggressivity and autoinflammation.

Reducing Health Disparities in Lupus

Other Health Disparities in Lupus

Poverty associated with poor outcomes

- Low income individuals less likely to receive recommended care
- Rates at least 3 times as high as white individuals have mortality
- onset
- Speciﬁc racial/ethnic minorities with lupus are more likely to develop...
Lupus on the Inside

Lupus Intangibles

Tissue Injury

Environmental Exposures & Behavior

Intangibles

Genetic Alterations

Autoantibodies

ICs

Proinflammatory Molecules

Environmental Exposures & Behavior

Lupus Initiation

Amplification Perpetuation

Abnormally functioning B-cells T-cells

pDC

Antigen Hormones (estrogen)

Infections

Toxins

Medications

Sun exposure

Vitamin D deficiency

Smoking

Stress

Toxins

Depression

Fatigue

"Brain fog"

Memory loss

Achiness, Headache

Painless oral ulcer

Synovitis

Discoid rash

Alopecia

Vasculitis

Malar rash

Jaccoud's arthropathy

Raynaud's Phenomenon

Cerebral infarct

Serositis

Pericardial effusion

Brain atrophy

Glomerulonephritis

Spherocytes

Cerebral infarct

Serositis

Pericardial effusion

Brain atrophy

Synovitis

Painless oral ulcer

Discoid rash

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Vasculitis

Malar rash

Jaccoud's arthropathy

Raynaud's Phenomenon

Cerebral infarct

Serositis

Pericardial effusion

Brain atrophy

Glomerulonephritis

Spherocytes
### Drug Induced Lupus

**Definite** —
- Increased anti-nuclear antibodies
- Symmetrical joint swelling and pain
- Pleuritis
- Pericarditis
- Hemolytic anemia
-Renal involvement
-Neutropenia

**Probable** —
- Hemolytic anemia
- Renal involvement
- Neutropenia

**Possible** —
- Arthritis
- Gastrointestinal symptoms
- Hemolytic anemia
- Neutropenia

**Drug Induced Lupus Erythematosus**

**Cutaenous Lupus Erythematosus**

**Systemic Lupus Erythematosus**

---

**Which Lupus is it?**

**Drug Induced Lupus**

**Definite** —
- Increased anti-nuclear antibodies
- Symmetrical joint swelling and pain
- Pleuritis
- Pericarditis
- Hemolytic anemia
- Renal involvement
- Neutropenia

**Probable** —
- Hemolytic anemia
- Renal involvement
- Neutropenia

**Possible** —
- Arthritis
- Gastrointestinal symptoms
- Hemolytic anemia
- Neutropenia

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**Monitors of Lupus Activity – Target Organ**

- CBC
- Serum creatinine
- Measure and more concerning:
  - Spot protein/creatinine ratio is equally good
  - 24-hour urine protein is traditional measure
  - Urine protein quantitation

**Disease Activity and Severity**

- Associated with race, younger age, male gender, property
- Acute or chronic (reversible organ injury)
  - Involvement
  - Increased immunologic, hemolytic, and serosal
    - Initial onset of symptoms
    - New symptom
    - Increased ESR
    - Anti-dsDNA titers
    - New evidence of complement consumption
    - Predictors of flare (in some but not all cases)
Neonatal Lupus

Malar Rash

Systemic Lupus Erythematosus:
Jaccoud Arthropathy

Current Therapy for SLE

• Aspirin (1948)
• Belimumab (2011)
• Hydroxychloroquine (1955)
• Methotrexate
• Mycophenolate mofetil
• Methotrexate
• Cyclophosphamide
• Corticosteroids (1955)

(FDA approved dates in parentheses)
Immunosuppressive drugs confer an increased risk for:

- Infection
- Cancer
- Infertility
- Common side effects of corticosteroids
- Infections
- Cushingoid appearance
- Osteoporosis
- Osteonecrosis
- Diabetes
- Mood Disturbances
- Hypertension
- Lipid Abnormalities
- Increased risk for:
  - Light Photomembranes
  - Hypertension
  - Infection
  - Cancer

New Therapeutic Strategies—

Targeted ImmunoTherapy

Stem cell transplant

B-cell directed

Immune Largely therapy

Current Therapy—Limitations

Quiz 1

1. Which of the following is not considered part of the current criteria for classification of systemic lupus erythematosus:
   a. discoid rash
   b. rosacea
   c. serositis
   d. oral ulcers

Quiz 2

2. Which of the following ANA results is most likely clinically significant?
   a. 1:160, speckled in an 85 y.o male with no other symptoms
   b. 1:1280, homogenous in a 20 y.o female with joint pain
   c. 1:160, speckled in a 85 y.o male with no other symptoms
   d. 1:40, homogenous in a 35 y.o female with low back pain

*2014 FDA approved for lupus
Case Presentation 1 (cont.)

History:
Answer: The history notes are not provided.

Exam:
Answer: The exam notes are not provided.

Case Presentation 2

Exam:
Answer: The exam notes are not provided.

Case Presentation 1 (cont.)

History:
Answer: The history notes are not provided.

Exam:
Answer: The exam notes are not provided.
Lupus

Hydroxychloroquine is a mainstay for treating those with lupus.

• A positive ANA is not in and of itself diagnostic of lupus.

providers.

Ineffective therapies and potential complications for both patients and

• If autoimmune thrombotic disease is unlikely, do not order an

helpful for diagnosis and classification.

• If autoimmune thrombotic disease is likely, the ANA can be

organ systems are vulnerable.

The diversity of clinical symptoms in SLE is great, and all

Lessons for Practice

Lupus Detection—In Summary

• CBC, BMP, LFTs, ESR, CRP, ANA, UA

Do an initial screening

Family history of autoimmune disease

• Family history of autoimmune disease, complaints from the signs and symptoms list

Consider lupus if your patient presents with

• Transient or prolonged, independent of one another

symptoms

• Non-specific, easily confused with other illnesses or

Early symptoms can be

Immunochemistry staining IgG, IgM, IgA, C3 and C4

Renal biopsy: Disease nephritis class IV with full house

B’ s DNA highly in line

• ANCA may be present in cases of granulomatous.

• ANCA may be present in cases of granulomatous

• Neutrophilic, case of additional labs ordered:

to confirm diagnosis post biopsy

Labs received Monday following Friday visit

Creatinine: 3.1 ± 5.1

WC 11.2 H/H 10.4/3.1, Platelets 89K

Case 2 (cont’d)
Final Thoughts

- Patient engagement and trust building is critical
- Uncertain diagnosis
- Confusing lab results
- Uncomfortable with treatment
- Patient not responding
- Side effects
- Uncertain minority health
- What you can do to reduce health disparities
- Discuss lungs prevalent and disparities with colleagues
- Provide continuing education about causes of disparities and cross
- Cultural competence
- Learn about and refer patients to community resources

When to Refer