How Lupus Affects the Skin

Lupus Education Day

Chris Richardson MD, PhD

October 2018
Outline

1. Defining lupus
2. Lupus-specific skin disease
3. Lupus-associated skin disease
4. Treatment

* Pictures from VisualDx.com unless otherwise noted.
Defining Lupus
Systemic Lupus Erythematosus (SLE)
Systemic Lupus Erythematosus (SLE)

**Some Common Symptoms of Lupus**

- **Central Nervous System**: Headache, dizziness, depression, memory disturbances, vision problems, seizures, stroke, or changes in behavior.
- **Lungs**: Pleuritis, inflammation, or pneumonia.
- **Joints**: Painful, swollen joints.
- **Blood**: Anemia, decreased white cells, increased risk of blood clots.
- **Kidneys**: Inflammation.

**Heart**
- Chest pains, Heart murmurs.

*It’s recommended to review any information from searching the Internet with a health care professional—the primary resource to meet individual medical needs.*

**May is Lupus Awareness Month**

Help DHPE LEAP, Lupus Education and Awareness Program to decrease the diagnosis time frame of lupus by learning the signs and symptoms.

**Top Five Symptoms**

- 97% Fatigue or Tiredness
- 92% Painful Swollen Joints
- 87% Problems with Sleep
- 79% Other than Joint Pain
- 78% Skin Rash

**DID YOU KNOW?**

- Women of color are diagnosed with lupus two to three times more than white women.
- Nearly three-quarters (77%) of those with lupus experience depression and/or anxiety as a result of their lupus.

Learn more about the DHPE LEAP Program at www.bit.ly/lupus. This program and its site is supported by the National Health Education Program on Lupus of the National Office of Minority Health, U.S. Department of Health and Human Services.
Many People Only Have Lupus in the Skin

Figure 2. Incidence of cutaneous lupus erythematosus (CLE) vs systemic lupus erythematosus (SLE) in Olmsted County, Minnesota, from 1965 through 1992 (SLE data from Uramoto et al).
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How Lupus Affects the Skin

Table 1  The Gilliam classification of skin lesions associated with LE

<table>
<thead>
<tr>
<th>I. LE-specific skin disease (Cutaneous LE [CLE])¹</th>
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<tbody>
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<td>A. Acute Cutaneous LE [ACLE]</td>
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II. LE-nonspecific skin disease
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      (a) Leukocytoclastic
         1 > Palpable purpura
         2 > Urticarial vasculitis
      (b) Periarteritis nodosa-like cutaneous lesions
   (2) Vasculopathy
      (a) Dego’s disease-like lesions
      (b) Secondary atrophy blanche (livedoid vasculitis, livedo vasculitis)
   (3) Periungual telangiectasia
   (4) Livedo reticularis
   (5) Thrombophlebitis
   (6) Raynaud’s phenomenon
   (7) Erythromelalgia
B. Nonscarring alopecia
   (1) ‘Lupus hair’
   (2) Telogen effluvium
   (3) Alopecia aerata
C. Sclerodactyly
D. Rheumatoid nodules
E. Calcinosis cutis
F. LE-nonspecific bullous lesions
G. Urticaria
H. Papulo-nodular mucinosis
I. Cutis laxa/anetoderma
J. Acanthosis nigricans (secondary to Type B Insulin resistance)
K. Erythema multiforme (Rowell’s syndrome)
L. Leg ulcers
M. Lichen planus
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Lupus (1997) 6, 84-95
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Cutaneous Lupus Erythematosus (CLE)

Types of cutaneous lupus erythematosus

- Acute cutaneous lupus ("acute skin lupus")
  - "Butterfly rash" (redness across cheeks and nose)

- Subacute cutaneous lupus ("subacute lupus")
  - Red, raised, scaly nonscarring rash on sun-exposed areas

- Chronic cutaneous lupus ("discoid lupus")
  - Red to purple rash with discoloration and scarring
  - Scarring and hair loss
  - Typical location (bowl of ear)
Relationships Among Types of Lupus

SLE: Systemic
ACLE: Acute Cutaneous
NLE: Neonatal
SCLE: Subacute Cutaneous
DLE: Discoid
LET: Tumid
LEH: Hypertrophic
LEP: Panniculitis
Lupus-specific Skin Disease
Acute Cutaneous Lupus (ACLE)

Always associated with active systemic lupus.
Subacute Cutaneous Lupus (SCLE)

Sometimes associated with systemic lupus or Sjogren’s syndrome.
Discoid Lupus (DLE)

The most common & most scarring.
Tumid Lupus (LET)

Rarely associated with systemic lupus.
Lupus panniculitis & Lupus profundus
Lupus-associated Skin Disease
Raynaud’s Phenomenon
Vasculitis

Can cause pain, fatigue, and fever

Normal artery and blood flow

Inflamed artery and decreased blood flow
Hair Loss (Alopecia)
Treatment
Sun Protection

“Help, I think the sun is trying to kill me!”

What is Photosensitivity?
1. Do you feel like the sun is your enemy?
2. Have you noticed that you have flares or feel less fantastic during warmer sunnier months or with increased sun exposure?
3. Do you get rashes or irritated skin after exposure to the sun?
4. Are you sensitive to fluorescent lighting?
5. Have you been diagnosed with lupus?

Read more: www.mollysfund.org/lupus-and-photosensitivity-when-the-sun-is-your-enemy

LUPUS IN COLOR
SLIP SLOP SLAP SEEK SLIDE

TIPS FOR SUN PROTECTION AS YOU BATTLE LUPUS
BE SUN SMART WITH LUPUS

If you are photosensitive, the best rule is to avoid midday and tropical sun entirely. Unfortunately, that’s not always the most practical advice, especially if your job or family situation requires that you spend time outside or near UV rays. People with lupus should not stay in the sun for extended periods and should make every effort to avoid UV rays outside, which are at their peak between 10 a.m. and 4 p.m.

#LupusInColor
Smoking
Topicals
Topicals & Intralesionals
FDA Approved Medications for Systemic Lupus

1948 – Aspirin
1955 – Prednisone
1955 – Hydroxychloroquine*
2011 – Belimumab (Benlysta)

*Approved for DLE & SLE.
Therapeutic Ladder

Mild/Limited: sun protection, smoking cessation, topical tacrolimus, topical steroids, intralesional steroids, vitamin D

Moderate:
- antimalarials
  - hydroxychloroquine (Plaquinil)
  - chloroquine
  - quinacrine

Severe/Unresponsive:
- prednisone
- methotrexate, mycophenolate, azathioprine
- thalidomide, lenalidomide
- belimumab, ustekinumab, rituximab, JAK inhibitors, apremilast
Future Therapies

### Table 1: Pipeline of drugs being evaluated in phase III clinical trials for SLE

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Overview of current phase III</th>
<th>Overview of phase III development in SLE</th>
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<tbody>
<tr>
<td>Abatacept</td>
<td>T-cell costimulation modulator (lystoxic T lymphocyte-associated antigen 4-lyg, soltron) Efficacy and safety of abatacept in lupus nephritis on a background of MMF and GCs. Trial is ongoing.</td>
<td>In a 52-week phase III trial involving patients with lupus nephritis, there was no difference between treatment groups and placebo in time to confirmed complete response (primary endpoint), although biological activity was observed. Treatment was well tolerated.</td>
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<tr>
<td>Anifrolumab</td>
<td>Fully human, IgG1 monoclonal antibody that binds to and neutralizes receptors of all type I IFNs. Two currently ongoing trials are evaluating the efficacy and safety of anifrolumab either at one or two different dosing regimens for patients with moderate-to-severe SLE. A third trial evaluating the long-term safety and tolerability of anifrolumab for patients with moderate-to-severe SLE is enrolling patients who completed one of the above phase III trials.</td>
<td>In a phase IIb trial for patients with moderate-to-severe SLE who did not have active and severe lupus nephritis or neuropsychiatric SLE, a significantly greater percentage of patients receiving anifrolumab 300 mg every 4 weeks achieved an SR(6) response at week 24 with sustained reduction of GCS compared with placebo (primary endpoint).</td>
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<tr>
<td>Atacicept</td>
<td>TAC-Fc fusion protein that blocks BAFF and APRIL. Trial has been completed and results are published.</td>
<td>In a phase II trial, atacicept did not improve flare rate (primary endpoint) or time to first flare (main secondary endpoint) during a 52-week trial compared with placebo. However, a post hoc analysis indicated that patients with large baseline BAFF and APRIL concentrations may benefit more with this agent. More recently, results from a 24-week phase IIb trial showed no significant improvement in SR(6) with atacicept treatment versus placebo (primary endpoint). However, patients with high disease activity did demonstrate significant improvements with atacicept versus placebo in SR(6) response and incidence of flares.</td>
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<tr>
<td>Lupuzor</td>
<td>21-mer peptide derived from small nuclear riboprotein U1-70K, which is phosphorylated at Ser143. Efficacy and safety of Lupuzor plus standard of care for patients with SLE. Trial is ongoing.</td>
<td>In a phase IIb trial, a significantly greater percentage of patients achieved SR(6) response at week 12 with Lupuzor given once every 4 weeks compared with placebo (primary endpoint). Treatment was well tolerated in general.</td>
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</tr>
<tr>
<td>Rituximab</td>
<td>Anti-CD20 monoclonal antibody (B cell). Evaluation of rituximab plus MMF for flare prevention and steroid-sparing benefit for patients with lupus nephritis (RITUX&amp;MMF). Trial is ongoing.</td>
<td>Although previous phase II trial did not meet their primary endpoint, additional clinical studies in combination with different drugs and under various conditions are being explored.</td>
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<tr>
<td>Vicosporin</td>
<td>Immunosuppressant, calcium ion inhibitor. Efficacy and safety of vicosporin in patients with active lupus nephritis. Trial is currently recruiting patients.</td>
<td>In a completed phase IIb trial, at 48-weeks of treatment, 40% of patients with lupus nephritis achieved complete remission with the lower dosage vicosporin regimen (23.7 mg twice per week) compared with 24% in the control arm (P=0.001).</td>
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<tr>
<td>APRIL, a proliferation-inducing ligand; BAFF, B cell-activating factor; GCS, glucocorticosteroid; IFN, interferon; MMF, mycophenolate mofetil; SR, SLE Responder Index (SR) with ≥5-point reductions; SR(6), SR with ≥6-point reductions; SR(9), SR with ≥9-point reductions; SR(12), SR with ≥12-point reductions; SR(18), SR with ≥18-point reductions; SR(24), SR with ≥24-point reductions</td>
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### Lupus Science & Medicine

### Table 2: Pipeline of drugs being evaluated in phase II clinical trials for SLE

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<tr>
<td>Abaligoitin (LT-2)</td>
<td>Evaluate efficacy, safety and pharmacokinetics of LT-2 in moderate-to-severe SLE. LT-2 is currently recruiting patients.</td>
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<tr>
<td>Baricitinib (LY203014)</td>
<td>JAK inhibitor Evaluate the safety and efficacy of baricitinib for patients with SLE. Trial is ongoing.</td>
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<tr>
<td>BMS0599</td>
<td>Anti-BC01 monoclonal antibody Efficacy of BMS0599 in reducing skin disease activity for patients with SLE and cutaneous lupus erythematosus with or without systemic manifestations. Trial is currently recruiting patients.</td>
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<tr>
<td>BMS0564</td>
<td>Anti-CD4 monoclonal antibody Dosage finding, efficacy and safety of BMS0564 for patients with active lupus nephritis. Trial is currently recruiting patients.</td>
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<tr>
<td>Borrellobi Pro tease inhibitor Change in disease-specific antibody titre with borrellobi. Trial is currently recruiting patients.</td>
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<tr>
<td>BT096</td>
<td>Anti-IL-10 monoclonal antibody Efficacy and safety of BT096 for patients with SLE. Trial is ongoing.</td>
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<tr>
<td>Cenenerum (ACT-39441)</td>
<td>Sphingosine-1-phosphate receptor agonist Biological activity, safety, tolerability and pharmacokinetics of ACT-39441 for patients with SLE. Trial has been completed, no results posted.</td>
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<tr>
<td>Depotizumab pegol</td>
<td>Anti-CD40L</td>
<td>Efficacy and safety of depotizumab pegol for patients with moderate-to-severe SLE. Trial is currently recruiting patients.</td>
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<td>Ecrolazine</td>
<td>Peptide based on complementary-determining region 1 of a human anti- DNA monoclonal antibody</td>
<td>In a 26-week phase II trial, no significant difference was observed between ecrolazine-treated and placebo-treated patients in reduction in SLEDAI-2K and adjusted mean SLEDAI, although positive trends were noted for other endpoints. Trial is completed, results are published.</td>
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<td>Filgrastim</td>
<td>GM-CSF</td>
<td>Efficacy of filgrastim for female patients with moderate-to-severe active cutaneous lupus erythematosus. Trial is currently recruiting patients. Efficacy and safety of filgrastim in adults with lupus membranous nephropathy. Trial has not begun recruiting.</td>
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<tr>
<td>GS-9675</td>
<td>SYK inhibitor Efficacy of GS-9675 for female patients with moderate-to-severe active cutaneous lupus erythematosus. Trial is currently recruiting patients. Efficacy and safety of GS-9675 in adults with lupus membranous nephropathy. Trial has not begun recruiting.</td>
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<td>Iberdomide (CC-200)</td>
<td>Ubiquitin ligase modulator Efficacy, safety, tolerability, pharmacodynamics and pharmacokinetics of CC-200 for patients with SLE. A pilot study is ongoing, with a phase II trial currently recruiting patients.</td>
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<td>IFN-α-knockout</td>
<td>Anti-IFN-α vaccine Efficacy, neutralisation of the IFN gene signature and safety of IFN-α-knockout for patients with SLE. Trial is currently recruiting patients.</td>
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<tr>
<td>Igrunatim</td>
<td>Antiinflammatory, NF-kB inhibitor Efficacy and safety of igrunatim for patients with active diffuse lupus nephritis and refractory lupus nephritis. Studies have not yet started recruiting.</td>
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<td>Neferin AV-1 protease inhibitor Effect of neferin in reducing anti-dsDNA antibodies. Trial is currently recruiting patients.</td>
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<td>Olumizumab Anti-CD20 monoclonal antibody Efficacy and safety of olumizumab plus MMF/MMP compared with MMF/MMP-treated placebo for patients with proliferative lupus nephritis. Trial is currently recruiting patients.</td>
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<tr>
<td>OMS321</td>
<td>Anti-MASSP-2 monoclonal antibody Safety and tolerability of OMS321 for patients with lupus nephritis. Trial is currently recruiting patients.</td>
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<td>Rapamycin (sirolimus)</td>
<td>Immunosuppressant</td>
<td>Two studies have taken place. One was a prospective study evaluating decrease in disease activity and GCS reduction for patients with SLE. The second study evaluated efficacy and safety for patients with lupus-like and lupus-related membranous nephropathy. Trials are completed, and no results are available.</td>
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<td>RC18</td>
<td>TACI-antibody fusion protein Efficacy and safety of RC18 for patients with moderate-to-severe SLE. Trial is currently recruiting patients.</td>
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<tr>
<td>RSLU-132</td>
<td>RNSF-BC fusion protein Effect of RSLU-132 on cutaneous manifestations for patients with SLE. Trial is currently recruiting patients.</td>
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Continued
Research Opportunities

Research opportunities:

• Surveys
• Blood draw
• Skin biopsy
• Clinical trials

No obligation!
Questions?