Lupus 101

Jennifer L. Rogers, MD
Assistant Professor of Medicine
Rheumatology
University of North Carolina at Chapel Hill
Co-director UNC Rheumatology Lupus Clinic

October 25, 2014

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Overview

- Definition
- Pathophysiology
- Epidemiology
- Clinical Presentation
- Diagnosis
- Clinic Visits
- Treatment
- Living with Lupus

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Lupus

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Systemic Lupus Erythematosus

- Lupus or SLE
- Chronic multisystem autoimmune disease
- Autoantibodies
- Immune system dysregulation
- Wide spectrum of clinical presentations and manifestations

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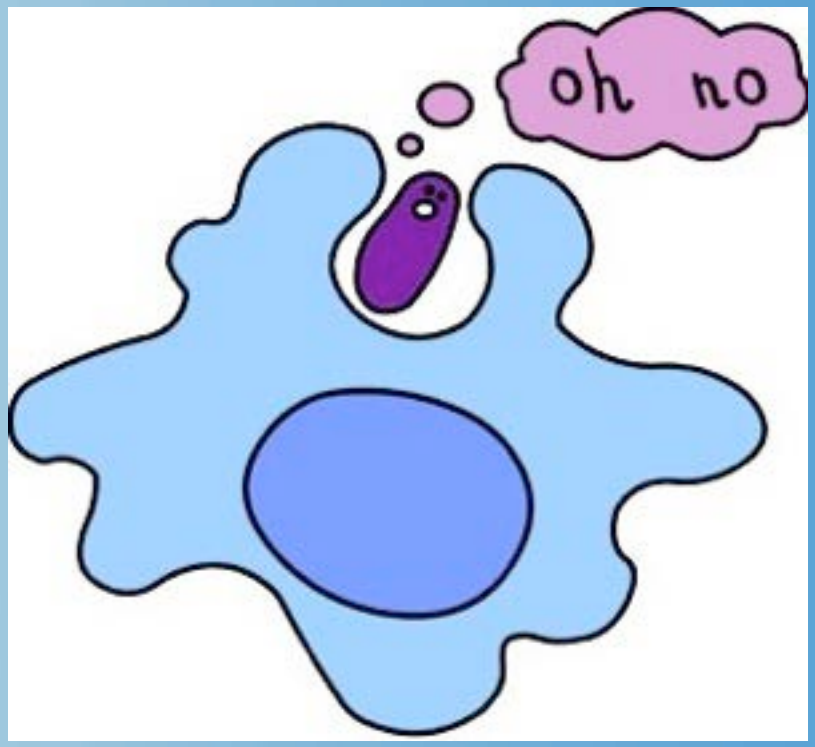
Immune System



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Phagocytosis of a bacterium by an immune cell by Zazzle.

Pathogenesis

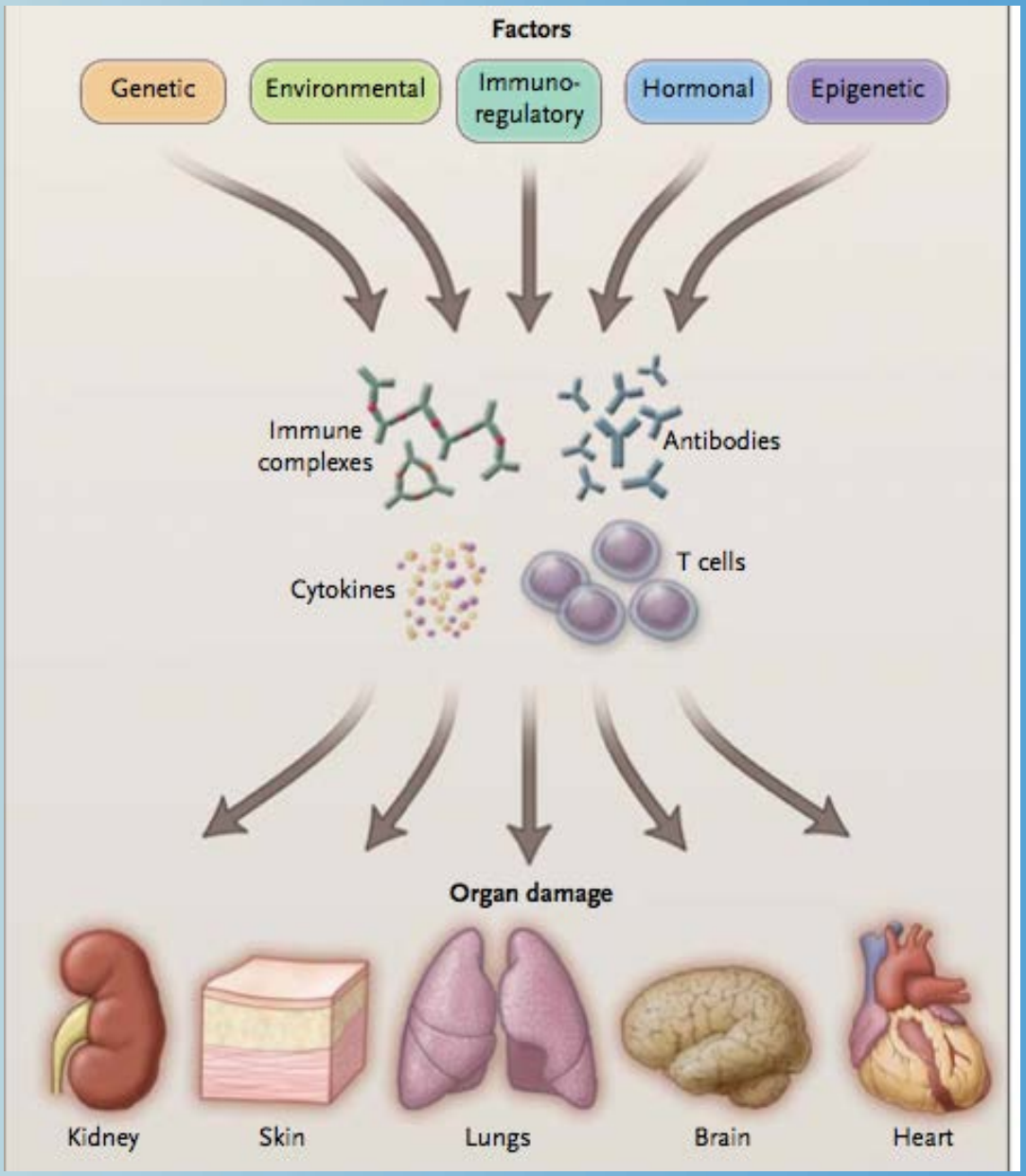
-Complex pathogenesis due genetic, epigentic and environnmental factors

-Autoreactive and inflammatory T and B cells

-Autoantibody production

-Immune complex formation and tissue deposition

-Secretion of inflammatory cytokines



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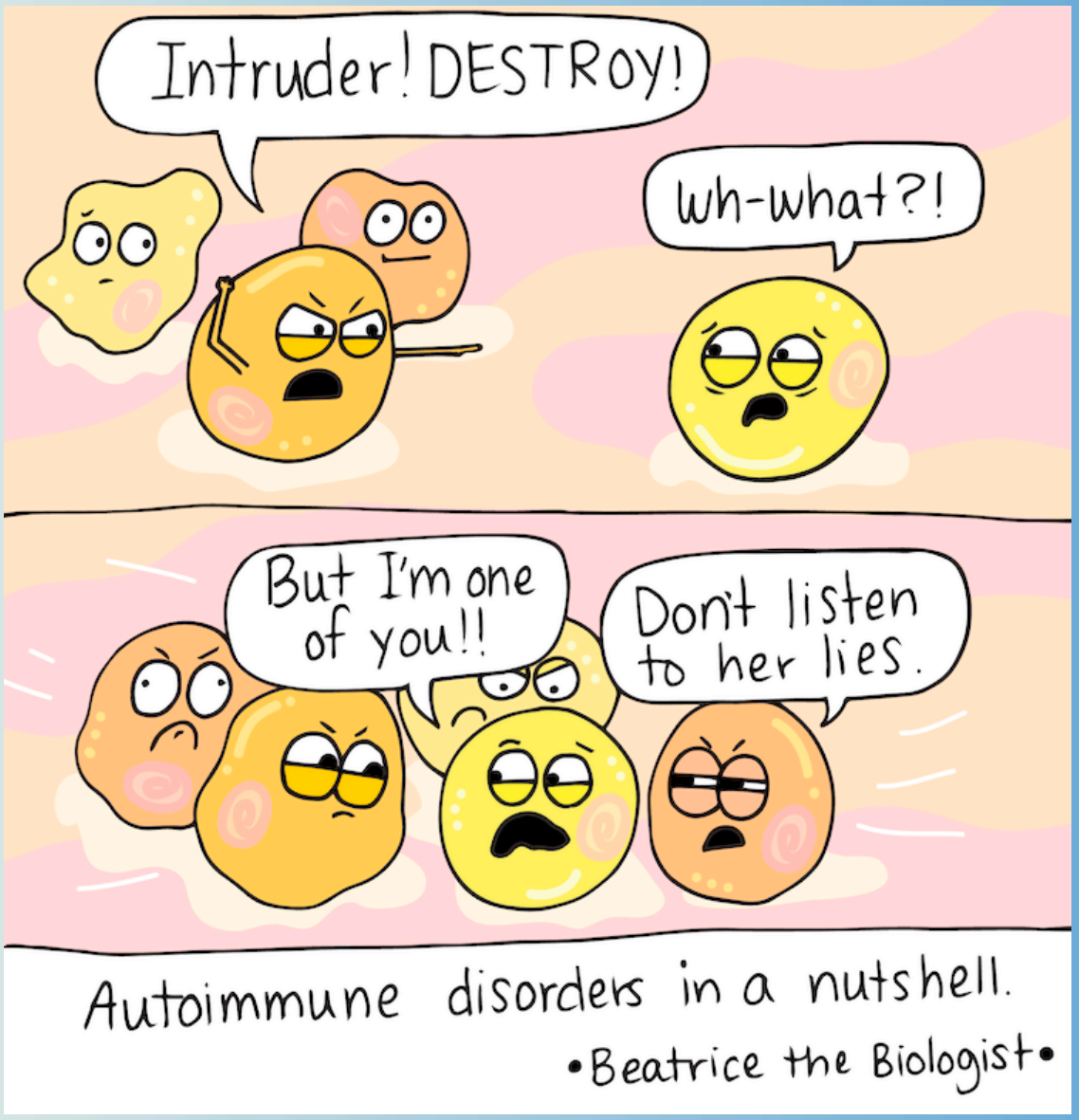
Tsokos. NEJM. 2011



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www.beatricebiologist.com

Environmental Factors

- Sunlight
- Cigarette smoke
- Infection
- Vitamin D deficiency
- Medications
- Pesticides

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Munoz. Autoimmunity Rev 2010

Genetic Factors

- Predisposition to SLE is most often due to combined effect of multiple genes
- Genes + Environment = SLE
- 10-fold increase in monozygotic twins
- 5-29 fold increased risk for individuals with 1^{st}-3^{rd} degree relative
- Rare cases due to single gene defect (C1q, C4, TREX1, DNASE1L3)

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Epidemiology

- Incidence and prevalence are increasing
- Varies between populations
- Higher rates in African, Asian and Hispanic Americans
- United States: 5 per 100,000 per year

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Tassiulas. Kelly's Textbook of Rheumatology. 2009

Epidemiology

- Female predominance 9:1 (F:M)
- Pediatric and older adults 2:1 (F:M)

- Majority (65%) present between ages: 16-55yrs
- 20% pediatric patients before 16yrs
- 15% Older patients after 55yrs

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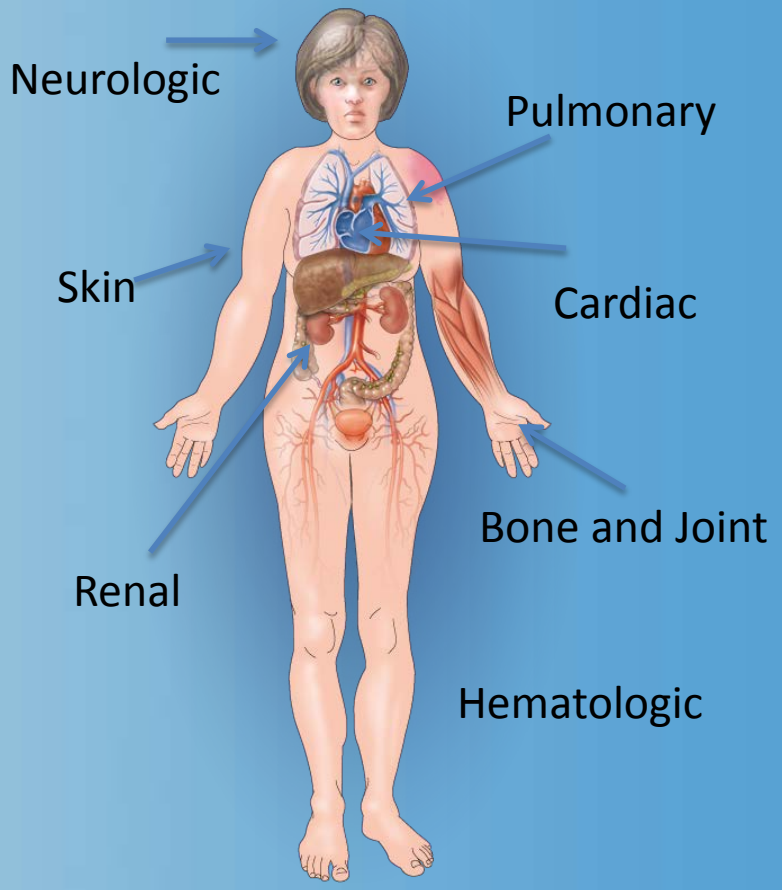
Clinical Presentation

Most commonly affects skin, joints, kidneys, and blood

Can vary from mild, serious, to life threatening



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Initial Manifestations

- Skin 73%
- Arthritis, arthralgias 62-67%
- Fatigue 50%
- Renal 16-38%
- Fever 36%
- Weight loss 21%
- Pulmonary 2-12%
- Cardiac 15%
- GI 18%
- Lymphadenopathy 7-16%
- Central Nervous System 12-21%

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Von Feldt JM, Postgrad Med 1995; 97:79.

Symptoms Over Time

- Fatigue 74-100%
- Arthritis, arthralgias 83-95%
- Skin 80-91%
- Renal 34-73%
- Fever 40-80%
- Weight loss 44-60%
- Hematologic >50%
- Pulmonary 24-98%
- Cardiac 20-46%
- GI 38-44%
- Lymphadenopathy 21-50%
- Central Nervous System 25-75%
- Mucous Membranes 25-60%

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Von Feldt JM, Postgrad Med 1995; 97:79.

General Systems

- Fatigue, fever, malaise are common
- Due to SLE or due to complications of the disease or therapy
- Fatigue is very common

  -strong correlation with depression

  -frequently independent of serologic or clinical lupus

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Cutaneous Lupus

- Acute cutaneous lupus
- Subacute cutaneous lupus
- Chronic cutaneous lupus
  - Discoid lupus erythematosus
  - Lupus profundus/panniculitis
  - Chilblain lupus erythematosus

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Malar Rash

Lupus Foundation

Acute Cutaneous Lupus

- Includes malar rash
- Localized or generalized
- Fluctuates with disease activity
- Photosensitive
- Last days to weeks
- Heals without scarring

ACR Image Bank

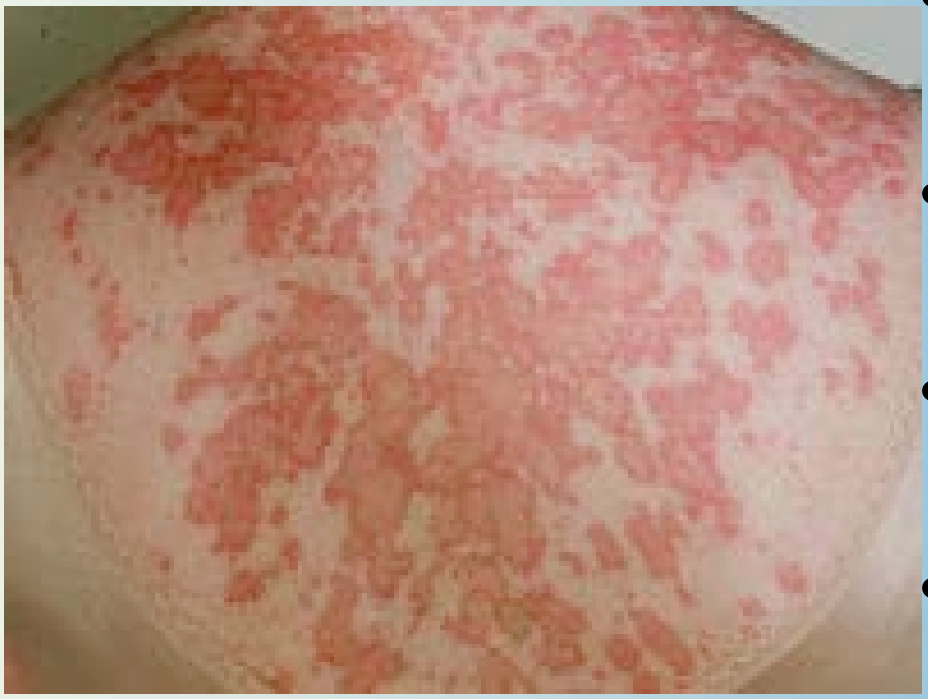
Similar Rashes

Polymorphic light eruption

Seborrheic Dermatitis

Rosacea

Subacute Cutaneous Lupus



- Symmetric distribution on sun-exposed skin
- 50% of SCLE patients will have SLE
- 10% of SLE patients will have SCLE lesions
- Involve shoulders, arms, torso but spares the face

ACR Image Bank

Chronic Cutaneous Lupus

- Discoid lupus most common
- 25% SLE patients have DLE
- 5-10% DLE patients develop SLE
- Heal with depressed scar, atrophy and dyspigmentation

ACR Image Bank

Alopecia

- Common
- Reversible due to "Lupus hairs"
- Irreversible due to scarring discoid lesions

Dvorkina. Rheumatology 6th ed. Hochberg. 2015

Mucous Ulcers

- 24-45% SLE ulcers in mouth or nors
- Often painless in the mouth
- Nasal ulcers more often associated with disease activity

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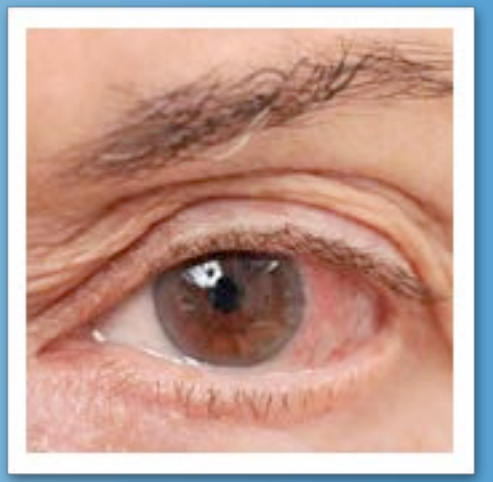
Dvorkina. Rheumatology 6th ed. Hochberg. 2015

Sjogren's Syndrome



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Arthritis

- Joint pain earliest and most common initial symptom
- 53-95% SLE, arthritis affects hands, wrist and knees
- Pain and stiffness often non-deforming
- Rare Jacoud's arthropathy

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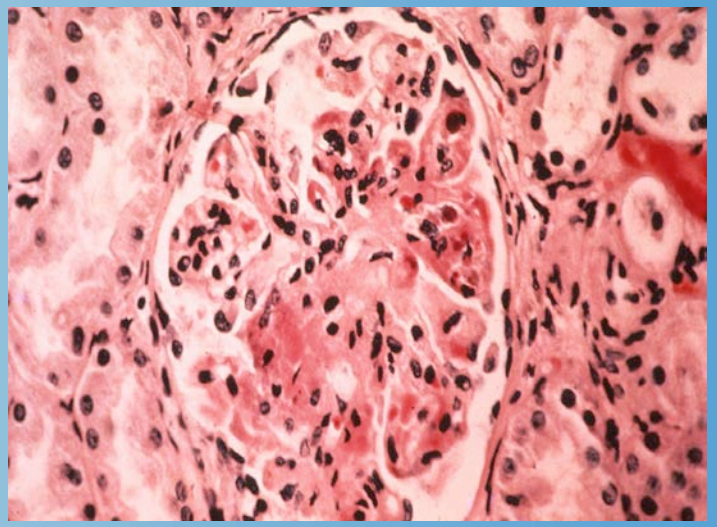
Muscle Symptoms

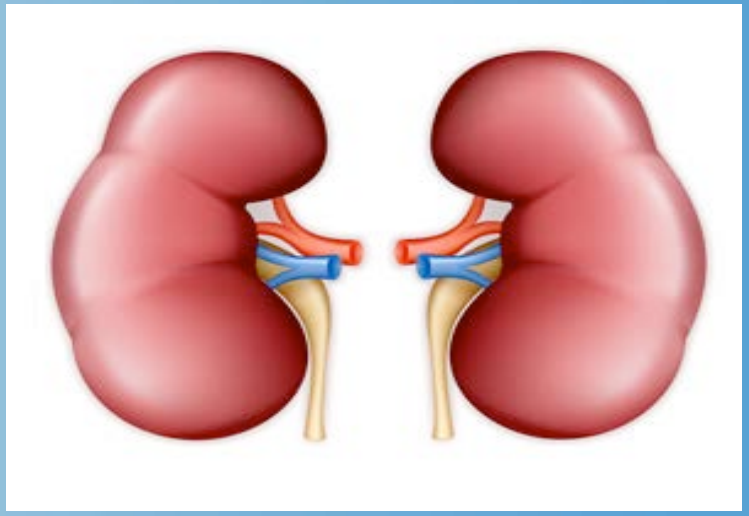
- General and diffuse Muscle pain or weakness is common
- Fibromyalgia 22%
- Steroid myopathy
- Inflammatory myositis rare 5-10%

Tassiulas. Kelly's Textbook of Rheumatology. 2009

Kidney

- 40-70% of SLE
- Often within first 2 years
- One of the more serious SLE manifestations
- 80% 15 year survival





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Nephritis

- Indication for Renal biopsy:
- Hematuria with active urinary sediment
- Elevated urine protein >0.5-1g/day
- Worsening renal function

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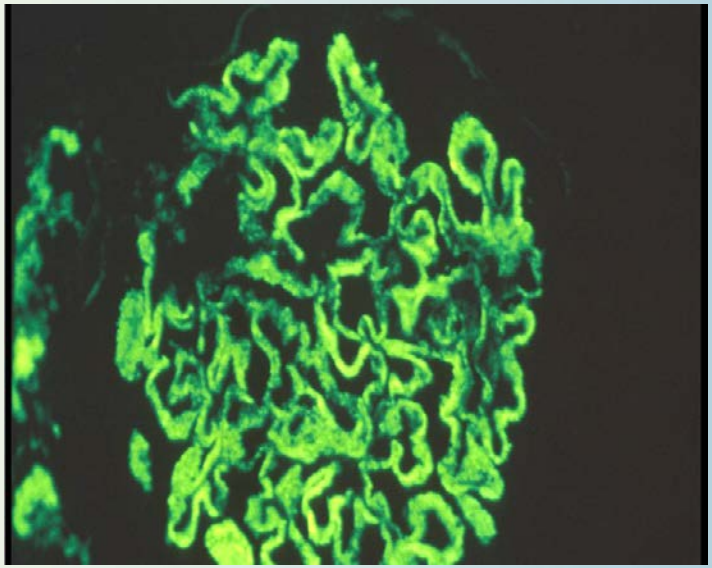
Renal Disease



- 27-66% recurrent renal flares
- 10% progress to chronic renal disease or end stage disease
- Candidate for renal transplant

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Raynaud's Syndrome

50% SLE Patients

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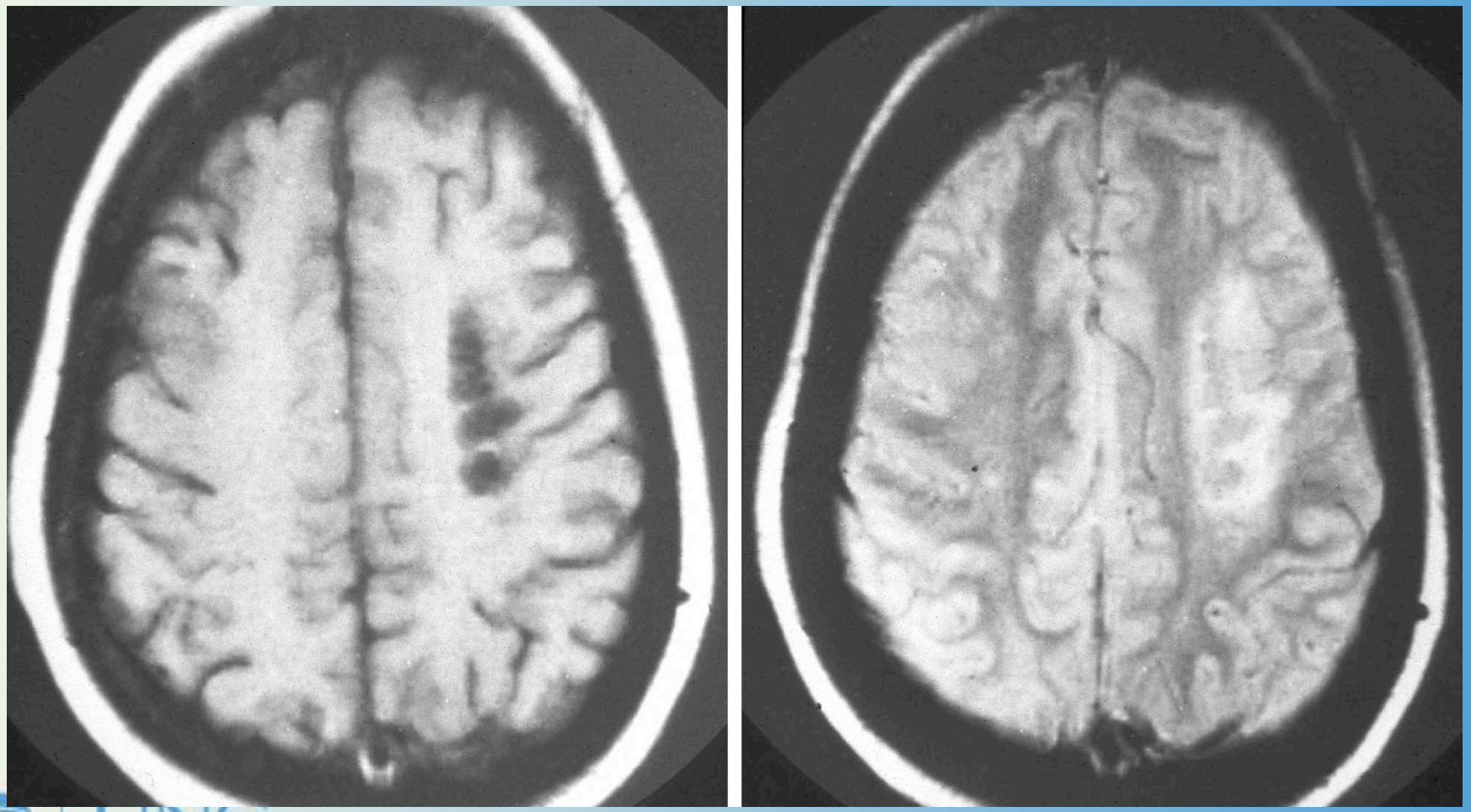
Nervous System



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Nervous System

- Central or Peripheral nervous system 14-75%
- Often present within 1st year
- 19 neuropsychiatric manifestations:
  - Meningitis, vasculitis, stroke, seizure, movement disorder, cognitive dysfunction, psychosis, peripheral neuropathy

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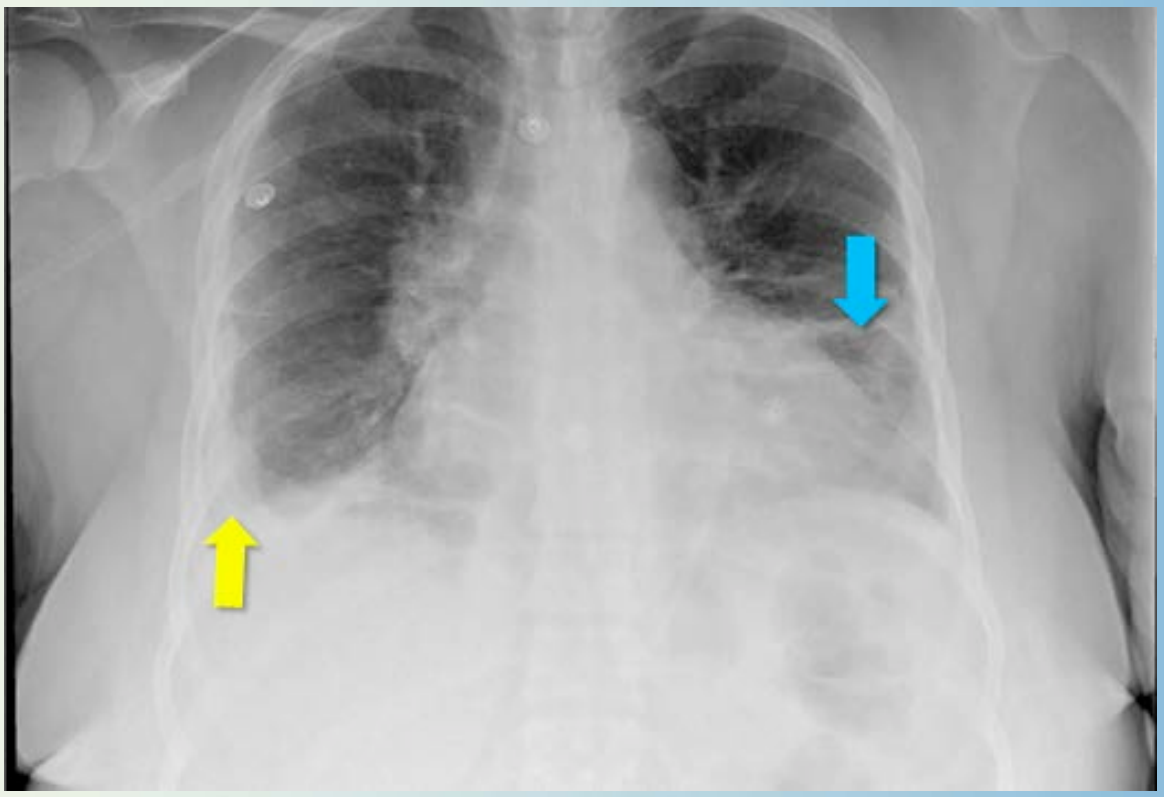
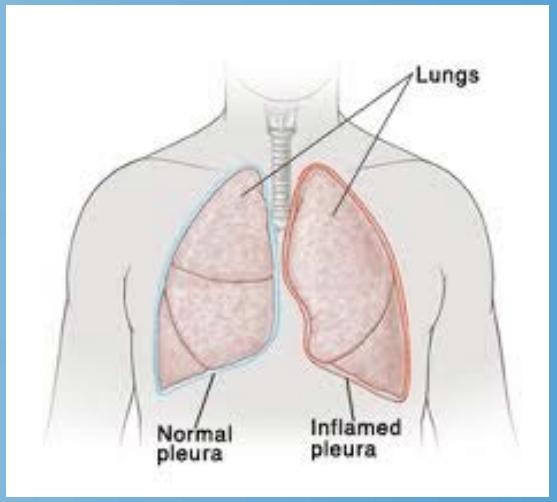
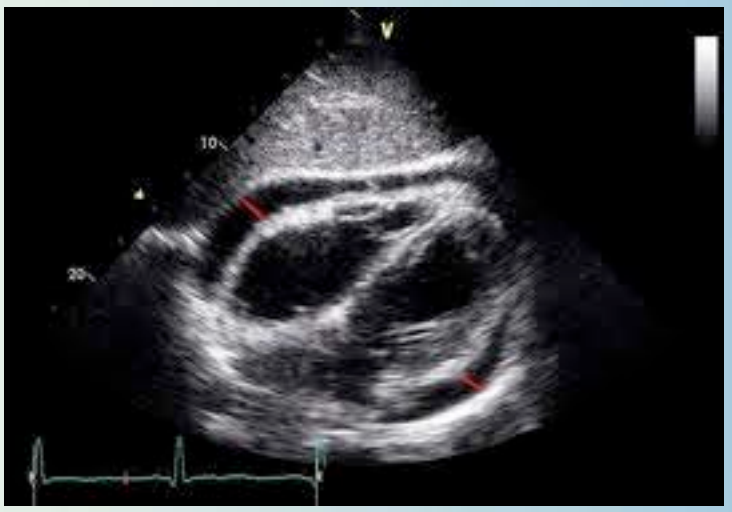
Pulmonary

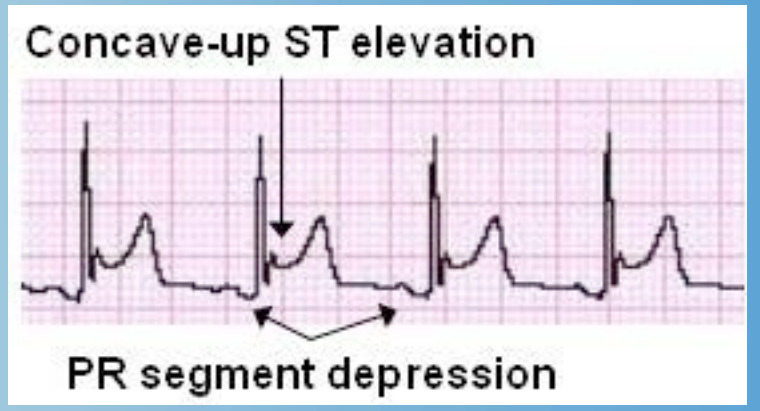




Pleuritis is most common lung symptom in Lupus; 45-60%

Cardiac





Pericarditis is most common; affect 25%
Asymptomatic pericardial effusion
Valvular heart disease

Cardiovascular Disease

- Increased atherosclerosis and risk of heart disease due to inflammation
- Woman age 35-44 with SLE have significantly increased risk of heart attack compared to healthy age matched women

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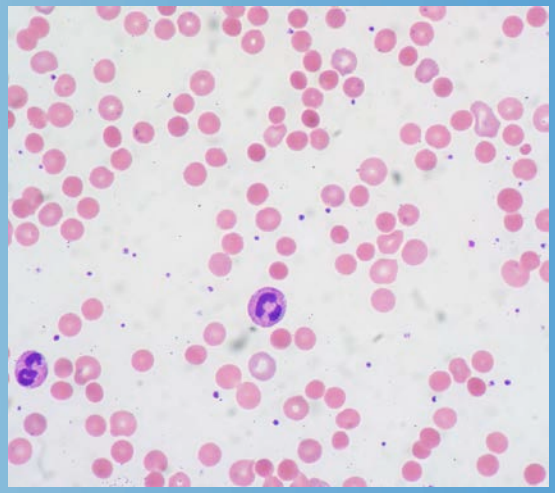
Lisnevskaia et al. Lancet. 2014

Hematologic

- Anemia very common due to several causes
- Hemolytic anemia 10%
- Low white blood cell (leukopenia)
- Low platelets (thrombocytopenia)



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Lupus Diagnosis

- Diagnosis can be challenging
- Clinical diagnosis
- Lupus serologies (antibodies)
- Laboratory and imaging studies
- 1997 ACR Criteria with 4 or more items
- 2012 SLICC criteria

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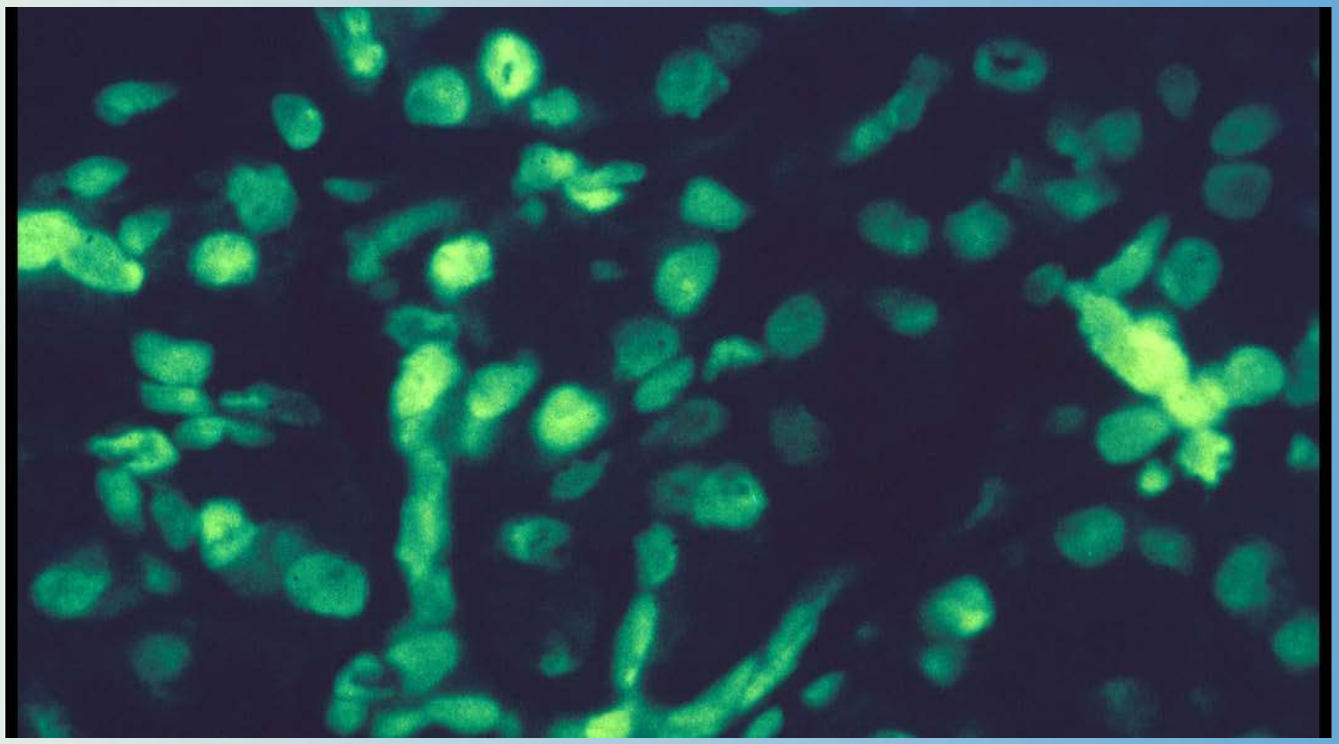
Anti-nuclear Antibody

ANA



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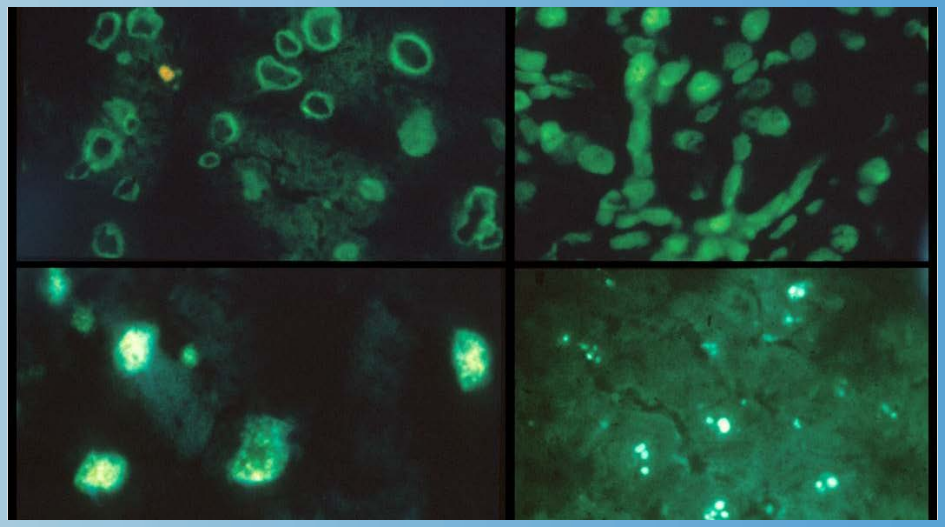
ANA

- ANA sensitive but not specific test
- 95-100% SLE are ANA+
- 5-30% healthy population have low titer +ANA
- Do not follow titer over time

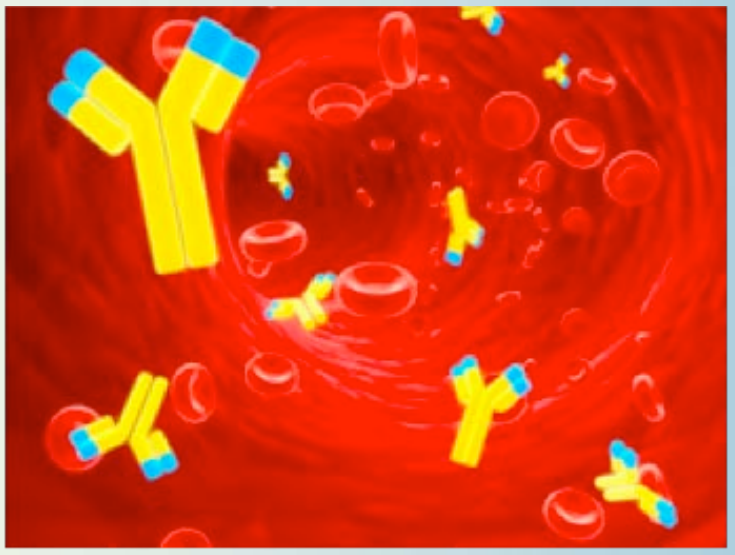
Lupus Specific Antibodies

- Smith (Sm): specific for SLE, 10-30%
- dsDNA (double stranded DNA)

95% specific, 70% of SLE, can correlate with disease activity (kidney) in some patients



Other Laboratory Tests



- Ro/SSA: Sjogren's, Neonatal lupus, congenital heart block
- La/SSB
- RNP
- Complement C3, C4
- Antiphospholipid antibodies: LA, ACA, B2GP1

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Clinic Visits

- All lupus patients should have rheumatology
- Often nephrology and dermatology
- Full history and physical
- Clinic visits every 3-4 months
- Blood work and urinalysis at every visit
- Monitor for disease activity and side effects
- Treatment

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Treatment

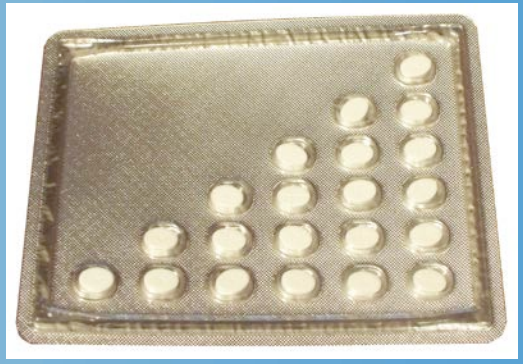
- Treatment depends upon type and severity of lupus symptoms
- Topical steroid cream
- Anti-inflammatory (NSAIDs)
- Anti-malarial medication
- Immune suppressing medication

Plaquenil

- Hydroxychloroquine
- Mainstay of treatment
- Anti-malarial medication
- Does not suppress the immune system
- Skin and joint disease
- Few side effects except nausea, GI upset
- Risk of retinal damage, dilated eye exam

Steroids

- Used often initial immune suppressing medication
- Quick onset of action
- Dose depends on severity (oral, injection, IV)
- Taper, do not abruptly discontinue
- Several potential side effects if used in high doses over long periods of time



Immunosuppressants

- Azathioprine (Imuran)
- Methotrexate (MTX)
- Mycophenolate Mofetil (Cellcept)
- Cyclophosphamide (Cytoxan)

Benlysta® (belimumab)

- First FDA Approved medication SLE in 40 years
- Good for skin, joint, fatigue SLE
- Clinical trials excluded serious renal or CNS Lupus
- Given as IV infusion once a month
- On-going trials for renal disease and auto-injector forms

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Clinical Trials

- Several new biologic medications
- Epratuzumab (CD22 monoclonal antibody)
- Sifalimumab and rontalizumab (type 1 interferon receptor antibody)
- PF-04236921: IL-6 antibody
- SM-101: FcRIIB agonist
- Anti-Blys therapy

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Koutsokeras, Healy. Nature Review Drug Discovery. 2014

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Pregnancy

- Fertility not affected
- SLE flare occurs at higher rate during pregnancy and post-partum
- Recommend stable SLE for 6 months before conception
- High risk Obstetrics clinic
- Continue Plaquenil

Vaccines

- Annual Influenza vaccine
- Pneumococcal vaccine

- No live vaccines while on immune suppressing medications (Shingles/zoster)

Nutrition

- No specific lupus diet
- Ensure adequate vitamin D
- Healthy balanced died
- Alternative therapies: omega 3 fatty acids, tumeric show promise

Exercise

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Tobacco Cessation

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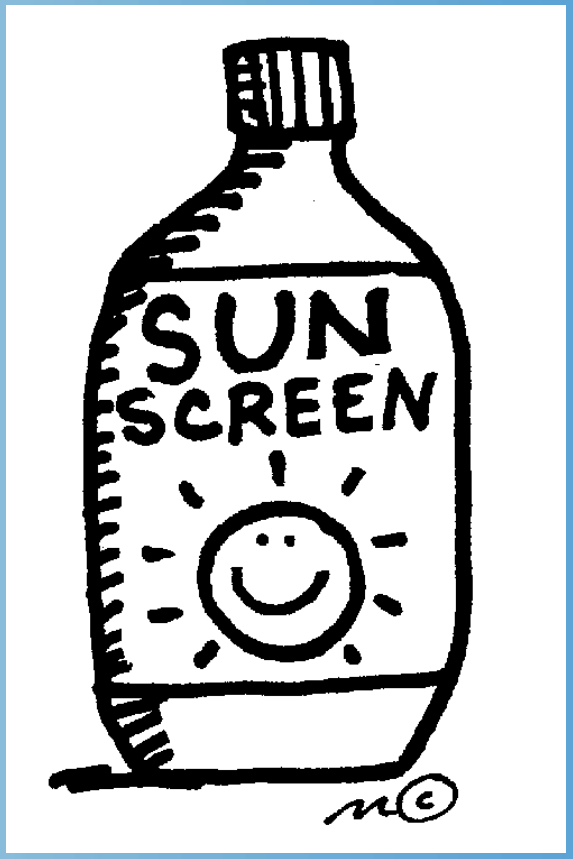
Sun Protection



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Summary

- SLE is a chronic autoimmune disease
- Autoantibodies and immune dysregulation
- Wide variety of clinical presentation including skin, kidney, heart, nervous system
- Clinical and serological heterogeneity makes SLE a challenge for diagnosis
- Several treatment options
- Live with Lupus

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Thank you

UNC Rheumatology Lupus Clinic

UNC Rheumatology Clinical Trials

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