Systemic Lupus Erythematosus – presentation and diagnosis in children and adolescents

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SLE

- Multisystem, episodic, chronic fluctuating autoimmune disease
- Extensive inflammation of blood vessels and connective tissues, with variable clinical manifestations, morbidity and course
- Causes multiple organ involvement and damage
- Requires multiple medications with unpleasant short-/long-term side-effects
- SLE-associated responsibilities significantly disrupt lifestyle

Systemic Lupus Erythematosus – presentation and diagnosis in children and adolescents

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Disclosures

- Site PI An Observational Registry of Abatacept in Patients with Juvenile Idiopathic Arthritis- BMS
- Site – PI A 5-Year Prospective Observational Registry to Assess Adverse Events of Interest and Effectiveness in Adults with Active, Autoantibody-Positive Systemic Lupus Erythematosus Treated with or without BENLYSTA™ (belimumab)- GSK

Childhood onset SLE (cSLE)

- Incidence: 0.5 -0.6 case per 100,000 persons (Klein-Gitelman Nov 2015 (Medscape)
- Prevalence 4-250 cases per 100,000 persons
- Onset of disease before 18 years old is seen in approximately 15% of SLE patients
- More in females (male:female ratio 1:4.5)
- Uncommon in <8 yr olds
Ethnic differences in cSLE

Greater prevalence in Native Americans, Asian Americans, Latin Americans and African Americans.
African American children may represent up to 60% patients younger than 20 years with lupus.
Asians have the highest prevalence of SLE and SLE nephritis and have most severe disease (Hiraki et al, Levy et al)
(Hiraki et al, Pluchinotta et al, M Klein Gitelman)

Associations of gender and ethnic origin with longterm outcome in childhood-onset systemic lupus erythematosus (SLE)

Cohort from Vancouver
n=51 (13 males; 38 females); Follow up=7 years
No African-Americans/Hispanics
3-year survival 100%; 10-year survival 86%
Median SDI =2 (0-9)

SDI scores, mortality and need for intensive immunosuppressive therapy were not influenced by either gender or ethnic origin
Miettunen et al, J Rheumatol 2004

Most affected groups were ALA and Mestizo

Ethnic variations in cSLE

Children of European/White ethnicity/race have a lower incidence and prevalence of
- SLE
- lupus nephritis
- have milder disease
- may sustain less damage than other ethnicities/races
(Review by Silverman et al; Levy et al, Watson et al, Hiraki et al, Hersh et al)

Ethnic differences in pediatric SLE

Non-Caucasians were younger at diagnosis (12.6 vs 14.6 yrs; p = 0.007)
Non-Caucasians had more renal disease (62% vs 45%; p = 0.01)
Blacks increased prevalence of CNS disease vs. Asians (p = 0.108).

*Hiraki et al 2009
*Asians and S. Americans seemed to have a younger age of onset (Moorthy et al, 2012)
Dancing while playing chess, 
*By Moorthy LN*

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**Childhood onset versus adult onset SLE**

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**Frequency of nephritis declines with increasing age of onset**

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**New damage in each organ system at years 1, 3 and 5 after diagnosis (n=57)**

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**Percentage of patients with damage in the particular organ system**

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**Childhood–onset SLE versus adult onset SLE**

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**Table 1: Cumulative Incidence of Common SLE Manifestations**

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>cSLE (%)</th>
<th>AIL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional – fever</td>
<td>21-50</td>
<td>43-57</td>
</tr>
<tr>
<td>Malar rash</td>
<td>65-72</td>
<td>95-47</td>
</tr>
<tr>
<td>Oral or nasal ulcers</td>
<td>14-49</td>
<td>14-42</td>
</tr>
<tr>
<td>照片中未出现的</td>
<td>35-50</td>
<td>41-56</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>60-95</td>
<td>63-93</td>
</tr>
<tr>
<td>Arthritis</td>
<td>50-80</td>
<td>31-45</td>
</tr>
<tr>
<td>Renal disease</td>
<td>6-39</td>
<td>9-22</td>
</tr>
<tr>
<td>Neuro-psychiatric test</td>
<td>11-14</td>
<td>6-12</td>
</tr>
<tr>
<td>Anemia</td>
<td>5-10</td>
<td>4-12</td>
</tr>
<tr>
<td>Serositis</td>
<td>29-38</td>
<td>17-28</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>14-28</td>
<td>11-22</td>
</tr>
<tr>
<td>Thrombocytoopenia</td>
<td>15-32</td>
<td>16-38</td>
</tr>
</tbody>
</table>

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• 39 patients completed the entire 5-year follow up period 
  *Bandeira et al, Lupus 2006*

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**Significant and early damage**

- Increased exposure to steroids, Longer disease duration
- Higher frequency of organ involvement cSLE (1-4)

**Cataracts, avascular necrosis, fractures, osteoporosis, low BMD (longer disease vs. steroids), premature atherosclerosis, persistent cognitive dysfunction in cSLE (1-2)**

**Incurable, potentially devastating disease during a vulnerable period of psychosocial development in cSLE**

- Increased and unique psychosocial stressors

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*Similar data from our cohort also, Moorthy et al, PRYSM 2011*
Young adults with SLE: SMR 20 times higher than general population (vs. 2-5 fold in adults)

Accumulate disease damage more quickly

More aggressive course → increased exposure to immunosuppressive medications over a longer disease duration

More likely to meet ACR criteria for renal disease and have ESRD

(58% vs. 24% and 21% vs. 8% (p<0.0001))


Mean age at death 33 (childhood-onset; n=98) versus 52 years (n=859)

Childhood-onset SLE

Education

ESRD

Male sex

Cardiovascular disease

Medicare or Medicaid insurance

(Hersh 2010)

Impaired apoptosis

SLE- Pathogenesis

Candidate genes

Pathway 1

Pathway 2

Pathway 3
The girl with fevers and weight loss

11 year old girl is feeling very tired and has a malar rash that is worsening. It is maculopapular erythematous with brownish plaques. She also has some photosensitivity and alopecia. For the last 2 months she has had intermittent fevers, fatigue, weight loss, and irritability

- CBC and diff, CMP, UA NL
- ESR 50 mm/hr
- ANA positive
- Anti-DS-DNA ab+, Anti-Smith ab +ve;
- -ve anti-Ro, La and RNP ab

Systemic lupus erythematosus: ACR classification criteria --4/11

- Malar rash
- Discoid rash
- Photosensitivity
- Naso-oral ulcers
- Arthritis
- Pleuritis/Pericarditis
- Proteinuria (>500 mg/d) or evidence of nephritis in urinalysis
- Hemolytic anemia, thrombocytopenia, leukopenia, or lymphopenia
- Seizure or psychosis
- Positive ANA finding
- Positive anti–double-stranded DNA, anti-Smith, or antiphospholipid antibody/lupus anticoagulant

Systemic lupus erythematosus: 1982 classification criteria

Common Clinical Features of cSLE

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Prevalence of Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional and generalized symptoms</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>37–100%</td>
</tr>
<tr>
<td>Lupopenidaphy</td>
<td>13–45%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>21–37%</td>
</tr>
<tr>
<td>Mucosatunans</td>
<td>60–90%</td>
</tr>
<tr>
<td>Musclesdalbral</td>
<td>60–90%</td>
</tr>
<tr>
<td>Nephritis</td>
<td>48–78%</td>
</tr>
<tr>
<td>Nerophyspulictrie disease (NPSLE)</td>
<td>15–95%</td>
</tr>
<tr>
<td>Gastrointenial</td>
<td>24–40%</td>
</tr>
<tr>
<td>Hemorholigc</td>
<td>50–100%</td>
</tr>
<tr>
<td>Cardiovoulser</td>
<td>25–0%</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>18–81%</td>
</tr>
</tbody>
</table>

- Review by Levy et al

Clinical presentation and diagnosis

Constitutional symptoms in SLE

- Fever
- Fatigue
- Wt Loss
- Alopecia
- Arthralgias
- Diffuse generalized inflammation
- Lymphadenopathy
- Hepatosplenomegaly

Clinical Characteristics of Patients Who Have SLE

<table>
<thead>
<tr>
<th>Organ System Involved</th>
<th>At Diagnosis (%)</th>
<th>Within 1 Year After Diagnosis (%)</th>
<th>Ever (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse lymphadenopathy</td>
<td>48 (19)</td>
<td>60 (20)</td>
<td>63 (20)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Backward phenomenon</td>
<td>35 (14)</td>
<td>69 (24)</td>
<td>48 (18)</td>
</tr>
<tr>
<td>Rheumatoid arthritis/pneaupneus</td>
<td>5 (2)</td>
<td>2 (1)</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Hepatosplomegaly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>128 (55)</td>
<td>136 (53)</td>
<td>142 (50)</td>
</tr>
<tr>
<td>Nod*</td>
<td>104 (45)</td>
<td>106 (39)</td>
<td>106 (41)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>74 (29)</td>
<td>79 (28)</td>
<td>82 (32)</td>
</tr>
<tr>
<td>Arteritis</td>
<td>51 (20)</td>
<td>77 (28)</td>
<td>77 (28)</td>
</tr>
</tbody>
</table>

- Dry eyes and mouth (Sjogrens)
- Stomach, liver, pancreas
- Thyroid, diabetes
- Irregular or absent periods
Mucocutaneous manifestations - Malar rash

- Acute cutaneous lupus erythematosus (ACLE) - facial rash or generalized eruption (disseminated ACLE)
- Localized ACLE (Butterfly rash) usually after UV light exposure, mistaken for a sunburn
  - Malar rash-fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds

Mucocutaneous manifestations

Subacute cutaneous lupus erythematosus (SCLE) - erythematous scaly papules or annular plaques over neck, upper trunk and arms

Chronic cutaneous lupus including the following:

- Classic discoid rash
  - Localized (above the neck)
  - Generalized (above and below the neck)
- Hypertrophic (verrucous) lupus
- Lupus panniculitis (profundus)
- Mucosal lupus
- Lupus erythematosus tumidus
- Chilblains lupus
- Discoid lupus/lichen planus overlap

**Discoid** – inflammatory plaques evolving into atrophic disfiguring scars

Acute cutaneous lupus including the following:

- Lupus malar rash
- Bullous lupus
- Toxic epidermal necrolysis variant of SLE
- Maculopapular lupus rash
- Photosensitive lupus rash (in the absence of dermatomyositis)
- OR subacute cutaneous lupus (nonindurated psoriaform and/or annular polycyclic lesions that resolve without scarrring, although occasionally with postinflammatory dyspigmentation or telangiectasias

**BC:** Initial management of discoid lupus and subacute cutaneous lupus - UpToDate updated May 2015

**BC:** Systemic Lupus International Collaborating Clinics

*See notes for criteria details

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- Bullous lupus
- Toxic epidermal necrolysis variant of SLE
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Mucocutaneous manifestations

LE panniculitis (Lupus profundus)

Vascular lesions

- Periungual erythema
- Raynauds
- Telangiectasias
- Livedo reticularis
- Chilblain LE
- Urticaria or purpuric vasculitis

ORAL-NASAL ULCERS

- Ulcers in the absence of other causes such as vasculitis, Behçet disease, herpesviruses, inflammatory bowel disease, reactive arthritis, or acidic foods
  - Palate
  - Buccal
  - Tongue
  - Nasal

ALOPECIA

- Nonscarring alopecia (diffuse thinning or hair fragility with visible broken hairs) in the absence of other causes such as alopecia areata, drugs, iron deficiency, or androgenic alopecia

MSKS manifestations

- Synovitis involving 2 or more joints, characterized by swelling or effusion or tenderness in 2 or more joints and at least 30 minutes of morning stiffness (SLICC criteria)
- Commonly children with SLE have arthralgias and arthritis
- Osteopenia (38% LS spine DEXA)
- Osteoporosis (20%) (SLE in children, reviewed in UpToData, 3/2016)

Musculoskeletal manifestations

- Nonerosive synovitis in SLE. Note the inflammatory exudate of occasional neutrophils and numerous lymphocytes immediately beneath the surface layer of synoviocytes.
- Avascular necrosis of bone is a frequent complication, occurring in about 25% of children with SLE over time.
A 13 year old Asian boy presented with malar rash, fevers and cutaneous vasculitis. He had mild renal involvement (class 2)
- Given steroids and mycophenolate
- He started limping
- He had avascular necrosis of both his knees

“Walking is the best possible exercise. Habituate yourself to walk very far.” - Jefferson

Serositis
- Serositis in the absence of other causes such as infection, uremia, and Dressler pericarditis
  - Typical pleurisy for more than 1 day
  - OR pleural effusions
  - OR pleural rub
  - Typical pericardial pain (pain with recumbency improved by sitting forward) for more than 1 day
  - OR pericardial effusions
  - OR pericardial rub
  - OR pericarditis by electrocardiography (SLICC criteria)

Pulmonary abnormalities
- Subclinical lung disease (restrictive lung disease)
- Pleuritis - often present with chest pain
- Pulmonary hemorrhage - acute and chronic (rare in children)
- Pulmonary hypertension (due to small multiple pulmonary emboli - dyspnea on exertion, fatigue, lethargy, chest pain and hemoptysis and hoarseness – rare but severe (suspect it if worsening TI on ECHO)
- Acute and chronic pneumonitis – often confused with pneumonia - CT usually helps with diagnosis

Cardiovascular manifestations
- Pericardial disease
  - Common in children esp in 1st 6 months of diagnosis
  - Acute, sharp anterior chest pain with dyspnea
  - Pain is exacerbated by inspiration and alleviated by upright forward leaning position
  - Low grade fever, tachycardial and tachypnea are present.
  - Pericardial rub may be heard
  - ECG and ECHO
  - Severe cases may result in cardiac tamponade and failure
  - Clinically significant myocarditis is rare
  - Valvular heart disease is rare (Libman Sacks Endocarditis)
  - Coronary heart disease
- Increased risk for atherosclerosis

Neurologic
- Seizures
- Psychosis
- Mononeuritis multiplex in the absence of other known causes such as primary vasculitis
- Myelitis
- Peripheral or cranial neuropathy in the absence of other known causes such as primary vasculitis, infection, and diabetes mellitus
- Acute confusional state in the absence of other causes, including toxic/metabolic/uremia/drugs (SLICC )
Neurocognitive functioning in childhood SLE

- *E Muscal et al, Lupus 2010*
- Scores >1.5 SD below age-matched norms in tests of:
  - Executive functioning
  - Visual memory
  - Visual-spatial planning
  - Memory

Prospective (n=24)
- Neurocognitive impairment
  - 47%

Retrospective (n=15)
- Neurocognitive impairment in 71%
- Volume loss in 73% (cerebral) and 68% (cerebellar)
- Depression in 33%
- White matter hyperintensities in 47%
- White matter hyperintensities in 37%

Case: Girl with eye pain

21 year old girl with SLE is complaining of blurry vision and eye pain
- C3 70
- C4 14
- CBC, CMP and ESR nl
- UA – nl

She sees ophthalmology - has loss of vision
She says now that she has severe pain at 6 o'clock position in the L eye.

Posterior scleritis in a patient with systemic lupus erythematosus. Optic disc hyperemia and retinal striae were evident clinically. A, B: Scan ultrasonography showed posterior eye wall thickening with retrobulbar fluid producing the so-called “T-sign” (C).

Causes of red eye in SLE

- **Common**
  - Dry eye (keratoconjunctivitis sicca)
- **Less common**
  - Episcleritis
  - Scleritis
  - Conjunctivitis (non-infective)
- **Rare**
  - Keratitis (other than keratoconjunctivitis sicca)
  - Anterior uveitis

Sivraj et al, 2007

Causes of loss of vision in SLE

- **Anterior segment** – Severe keratoconjunctivitis sicca
- **Lens** – Cataract (secondary to inflammation and/or corticosteroids)
- **Vitreous** – Vitreous haemorrhage (secondary to proliferative retinopathy)
- **Retina**
  - Severe vaso-occlusive retinopathy
  - Central retinal vein occlusion (CRVO)
  - Branch retinal vein occlusion (BRVO)
  - Central retinal arteriole occlusion (CRAO)
  - Branch retinal arteriole occlusion (BRAO)
  - Exudative retinal detachment
  - Toxic maculopathy (secondary to anti-malarial treatment)

Sivraj et al. 2007
Causes of loss of vision in SLE

Choroid
- Lupus choroidopathy
- Choroidal effusion
- Choroidal infarction
- Choroidal neovascular membranes

Neuro-ophthalmic
- Optic neuritis
- Anterior ischaemic optic neuropathy
- Posterior ischaemic optic neuropathy
- Optic chiasmopathy
- Cortical infarcts

Sivraj et al, 2007

The girl with tea colored urine

- 14 yo girl has tea-colored urine, low grade fever and edema over face and feet in the past 2 weeks.
- UA 3+ protein
- CBC and diff – NL
- CMP - low albumin 2.5
- ESR 50mm/hr
- C3 = 50, C4 = 7, ANA 1:1280, DS-DNA 1:160

Renal involvement

- Urine-to-creatinine ratio (or 24-hour urine protein) representing 500 mg protein/24 hours
- OR red blood cell casts
- Clinical nephritis in 75% of children
- Creatinine in <10 year olds is 0.5mg/dl; 1.1 is abnl in that age group!

Focal Proliferative Glomerulonephritis

In one glomerular tuft there is marked hypercellularity and obliteration of capillary lumina. The GBM is thickened and stained a brownish tan in Masson's trichrome stain. The remainder of the glomerulus is normal. (hematoxylin-eosin, high power)

Diffuse Proliferative GN

- "Wire loop" lesions
- Enlarged glomerulus with increased cellularity
- Characteristic GBM thickening and bright red staining of the GBM of peripheral capillary loops ("wire loop" lesion)

Membranous GN

In most areas of the glomerulus, the capillary walls are thickened by pale-staining deposits that stain bright red with periodic acid-Schiff stain. The deposits are most prominent along the outer (epithelial) surface of the GBM, which stain black in the periodic acid-Schiff stain. These deposits are characteristic of lupus nephritis, which is common in patients with SLE. (periodic acid-Schiff, high power)
Leukopenia - nearly 2/3 of the children

- Leukopenia (< 4,000/µL at least once) in the absence of other known causes such as Felty syndrome, drugs, or portal hypertension
- OR lymphopenia (< 1,000/µL at least once) in the absence of other known causes such as corticosteroids, drugs, or infection


Anemia in 50-75% of affected children (≤SD below the mean for age and gender) typically occurs due to

- Anemia of chronic disease - normocytic normochromic typically; may be hypochromic and microcytic
- Autoimmune Hemolytic Anemia - typically mild to moderate
- Iron deficiency - especially in adolescent females with SLE due to:
  - Increase in body mass, but no parallel increase in iron stores
  - Menstruation losses
  - Dietary choices decrease iron intake.

Thrombocytopenia may be the first manifestation of SLE.

Thrombotic thrombocytopenic purpura - rare in children

Thrombocytopenia
**Gastrointestinal manifestations**

- 25–40% of SLE patients
- Abdominal pain
- Pancreatitis
- Hepatitis
- Protein-losing enteropathy
- Mesenteric vasculitis and infarction

**Clinical Characteristics of Patients Who Have SLE**

- Known factors: Autoimmune diseases, age, sex, ethnicity, and others.
- Genetic factors: Association with HLA-B8, DR3, and DR4.
- Environmental factors: UV light, smoking, and pregnancy.

**Mild SLE**

- No renal or life threatening organ involvement
- NSAIDs for musculoskeletal manifestations
- Hydroxychloroquine up to 200mg/day (400mg/day for adults)
- Avoid Sulfa drugs (such as Sulindac)- Sulfa antibiotic allergy more common in SLE (Pope et al, Aceves et al)
- Dapsone in some dermatological manifestations (David et al)
- Low dose glucocorticoids (< 0.35mg/kg/day of prednisone)
- Dose above 0.2mg/kg/dose may impact longitudinal growth (David et al)
- Add 2nd line agent, Mycophenolate mofetil if glucocorticoid dose is >0.35mg/kg/day

**Moderate SLE**

- Clinically significant but not life threatening organ involvement of kidneys or other vital organs/systems
- Daily higher dose glucocorticoids (or alternate day/intermittent IV therapy) (Guiducci et al) with hydroxychloroquine
- Steroid sparing agent:
  - Mycophenolate mofetil
  - Azathioprine
  - Methotrexate (aware of renal toxicity, toxic levels if renal function deteriorates)
  - Cyclophosphamide and Rituximab as steroid sparing agent (Buratti et al, Ravelli et al)

**Severe SLE**

- Substantial Renal (worst DPGN) and CNS involvement
- Glucocorticoids (often high dose IV)
- Cyclophosphamide (IV monthly/ po)
- Rituximab with Cyclophosphamide regimen
- Mycophenolate mofetil
- Azathioprine
- Length may vary with organ involvement (longer for renal vs. 1 year for extra-renal manifestations)

**Neonatal Lupus Erythematosus**

- 1 to 2% percent of babies born to mothers with autoimmune disease, primarily SLE, Sjögren’s syndrome, and antibodies to SSA/Ro and/or SSB/L
- A considerable proportion of mothers of affected infants are asymptomatic (40%).
- If a anti-Ro (SS-A)-positive mother has one child with NLE, risk of recurrence is close to 20%
Skin lesions are transient, lasting weeks to months. Usually resolve without scarring—mild epidermal atrophy. Hypopigmentation. Rarely, remnant telangiectasias can occur at previously affected sites. Cutaneous telangiectasia 6-12 mo (10% of cases)—temples near hairline. To Subacute cutaneous LE (S克莱E)

- Treatment
  - Reassurance
  - Sun avoidance
  - Usually heal w/o scarring
  - Low potency topical mild steroid (increased risk of telangiectasia), Pulse dye laser

Neonatal lupus erythematosus has a very characteristic appearance but the following are in the differential diagnosis:

- Polycyclic lesions: Urticaria, E marginatum, tinea, seborrheic dermatitis
- For Annular erythema: E multiforme, Pityrosporum, Annular erythema of infancy
- A photodistributed drug eruption

### Laboratory exam

**General**

- Hematologic disorder
  - Hemolytic anemia
  - Lymphopenia (< 4,000/µL at least once) in the absence of other known causes such as Felty syndrome, drugs, or portal hypertension
  - OR lymphopenia (< 1,000/µL at least once) in the absence of other known causes such as corticosteroids, drugs, or infection
  - OR thrombocytopenia (< 100,000/µL) at least once in the absence of other known causes such as drugs, portal hypertension, thrombotic thrombocytopenic purpura, or antiphospholipid antibodies
  - Leukopenia—less than 4,000/mm³ total on 2 or more occasions
  - OR lymphopenia—less than 1,500/mm³ on 2 or more occasions
  - OR thrombocytopenia—less than 100,000/mm³ in the absence of offending drugs

- Evidence of immune dysfunction
  - Blistering and blistering abnormalities
  - Liver functions
  - Increased ESR
  - Urine—Blood and protein in urine

### Laboratory abnormalities

- Low complements—C3, C4
- Autoantibodies—ANA, Anti-ds-dna, ENA
- Antiphospholipids

- Immunologic disorder
  - a) Anti-DNA: antibody to native DNA in abnormal titer OR
  - b) Anti-Sm: presence of antibody to Sm nuclear antigen OR
  - c) Positive anti-phospholipid antibody

### ANA

- Antinuclear antibody: An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Disease</th>
<th>Antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rim (peripheral)</td>
<td>SLE</td>
<td>DsDNA</td>
</tr>
<tr>
<td>Homogeneous</td>
<td>Drug induced LE, SLE</td>
<td>Histones, deoxyribonucleoprotein</td>
</tr>
<tr>
<td>Nucleolar</td>
<td>Scleroderma</td>
<td>Nucleolar RNP</td>
</tr>
<tr>
<td>Speckled</td>
<td>Sjogrens, MCTD</td>
<td>Nonhistone proteins, Nuclear RNP</td>
</tr>
</tbody>
</table>

### Sensitivity and specificity of ANA

<table>
<thead>
<tr>
<th>Autoantibodies</th>
<th>Associated CTD</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
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<tbody>
<tr>
<td>ANA</td>
<td>SLE</td>
<td>90</td>
<td>57</td>
</tr>
<tr>
<td>Sjogrens</td>
<td>68</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>MCTD</td>
<td>60</td>
<td>24</td>
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</tr>
<tr>
<td>Anti-ds-dna</td>
<td>40</td>
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<td>20</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>Anti-phospholipid</td>
<td>100</td>
<td>91</td>
<td></td>
</tr>
</tbody>
</table>

Diagnostic Pathology (1996, 1)
**Significance of a +ve ANA test**

<table>
<thead>
<tr>
<th>Table 2: Significance of positive ANA test in CTD and some non-autoimmune conditions [24]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Useful for diagnosis</strong></td>
</tr>
<tr>
<td>1. Lupus erythematosus (LE)</td>
</tr>
<tr>
<td>2. Scleroderma</td>
</tr>
<tr>
<td>3. Polymyositis</td>
</tr>
<tr>
<td>4. Mixed connective tissue disease</td>
</tr>
<tr>
<td>5. Dermatomyositis</td>
</tr>
</tbody>
</table>

**Reproductive Health**

- Protect against STI
- Protect against Pregnancy
- GYN maintenance exam
- Antiphospholipid antibodies, history of thrombosis, BP
- Male and female condoms (use rare in adolescents <40%; failure rate 15-21%)
- IUD
- Nuvaring (ethinyl estradiol)
- Combined estrogen-progesterone (very effective, low cost)
- Progestin only pill
- Depo-provera (decreased BMD)
- Emergency contraception – oral levonorgestrel (decreased thrombosis risk)

**Sexual function and reproductive health in adolescent females with systemic lupus erythematosus**

- Age matched controls for 52 SLE patients
- Mean age of menarche higher in JSLE patients (12.82 ± 1.62 versus 11.55 ± 1.45 years, P = 0.0004).
- Frequency of sexual activity lower in patients with JSLE (23% versus 60%, P = 0.0003).
- Higher percentage of sexual dysfunction, reduced vaginal lubrication, decreased performance, reduced orgasm, and dissatisfaction with one's sex life in JSLE patients (58% versus 23%, P = 0.03; 50% versus 16%, P = 0.046; 58% versus 23%, P = 0.03; 50% versus 26%, P = 0.046, respectively).
- Demographic data, pubertal changes, abnormalities in menstrual cycle, and cervicovaginal cytology were similar in JSLE patients and the control group.

---

### Adverse Pregnancy Outcomes in Adolescents and Young Women with SLE: A National Estimate

- NIS database
- SLE patients: 4442
- Hospitalized women with SLE were:
  - Slightly older (mean age 19.4 vs. 14.19 years, P = 0.0001)
  - More likely to be black (34% vs. 22%)
  - More likely to carry a discharge diagnosis of nephritis (11% vs. 0.02%) or aPL (2.7% vs. 0.2%) and/or to undergo hemodialysis (0.35% vs. 0.0%), all p < 0.0001.

---

### Outcome

<table>
<thead>
<tr>
<th>Maternal Outcomes</th>
<th>SLE N = 4,142</th>
<th>Non-SLE N = 9,121,082</th>
<th>P*</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-eclampsia and Eclampsia</td>
<td>657 (16)</td>
<td>417,676 (4.6)</td>
<td>&lt;0.0001</td>
<td>3.9 (3.3 4.7)</td>
</tr>
<tr>
<td>Death during hospitalization</td>
<td>35 (0.87)</td>
<td>490 (0.005)</td>
<td>&lt;0.0001</td>
<td>69.7 (22.6 214.6)</td>
</tr>
<tr>
<td>Preterm</td>
<td>843 (20)</td>
<td>736,665 (8.1)</td>
<td>&lt;0.0001</td>
<td>2.9 (2.5 3.4)</td>
</tr>
<tr>
<td>Low birth weight or fetal growth retardation</td>
<td>147 (3.9)</td>
<td>34,015 (0.38)</td>
<td>&lt;0.0001</td>
<td>8.1 (5.4 12.5)</td>
</tr>
<tr>
<td>Spontaneous abortion or Intrauterine death</td>
<td>779 (4.3)</td>
<td>99,426 (1.1)</td>
<td>&lt;0.0001</td>
<td>6.9 (5.3 8.8)</td>
</tr>
<tr>
<td>Induced abortion</td>
<td>90 (2.2)</td>
<td>11,749 (0.13)</td>
<td>&lt;0.0001</td>
<td>3.7 (2.4 5.9)</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>643 (15.8)</td>
<td>50,293 (0.63)</td>
<td>&lt;0.0001</td>
<td>9.1 (6.7 12.3)</td>
</tr>
</tbody>
</table>

Allen et al 2014, ACR abstract
### Preeclampsia vs SLE nephritis flare

<table>
<thead>
<tr>
<th>Clinical and laboratory features</th>
<th>Active lupus nephritis</th>
<th>Preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Onset before 20 weeks</td>
<td>Onset after 20 weeks</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>≥300 mg/day</td>
<td>≥300 mg/dl</td>
</tr>
<tr>
<td>Urinary sediment</td>
<td>Active</td>
<td>Inactive</td>
</tr>
<tr>
<td>Uric acid</td>
<td>≤5.5 mg/dl</td>
<td>&gt;5.5 mg/dl</td>
</tr>
<tr>
<td>DNA antibody levels</td>
<td>Rising</td>
<td>Stable or negative</td>
</tr>
<tr>
<td>24 h urine calcium</td>
<td>≥195 mg/day</td>
<td>&lt;195 mg/day</td>
</tr>
<tr>
<td>Complement levels</td>
<td>≥25% drop</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Reproduced with permission from [11].

### Risk assessment

**Previous Obstetric history**
- SGA, preeclampsia, stillbirth, miscarriage, and preterm birth.

**SLE activity**
- APLA(S), Ro, La Ab

Evidence of active SLE, especially lupus nephritis, should be advised to defer pregnancy until the disease is well controlled for at least six months.

### Quotes from my patients with SLE

“I do greatly worry about the future…. passing on this disease to my offspring… Many times I feel I don’t have as much time as everyone else.”

“I can’t do the stuff that kids of my age do... Everything in my life has changed.”

“I wish I never had lupus in my life.”

### Autoimmune Congenital Heart Block Statistics

Friedman and Buyon et al 2003

<table>
<thead>
<tr>
<th>Incidence in +Ro/La pregnancies</th>
<th>3%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrences after first index case</td>
<td>18%</td>
</tr>
<tr>
<td>Mortality</td>
<td>20%</td>
</tr>
<tr>
<td>Need for pacemaker</td>
<td>&gt;60%</td>
</tr>
<tr>
<td>Late onset cardiomyopathy</td>
<td>10%</td>
</tr>
</tbody>
</table>

### Health related quality of life (HRQOL) in pediatric SLE

**Sunflowers**

*With crayons, By Moorby LN*

### SLE (activity and damage) involvement of systems and Health Related Quality of Life (HRQOL)

- **Renal**
  - SLEDAI, SDI

- **Vasculitic**
  - (Raynaud’s phenomenon)

- **MSKS**
  - (arthralgia & arthritis not limiting function)

- **Fatigue**
  - BILAG²

- **Neurologic**
  - (headaches & migraines, ocular)

  BILAG², SLEDAI, SDI

2. Blomkvist, E. et al. Health-Related Quality of Life and its Relationship to Disease Activity and Disability in pediatric and adolescent Juvenile Rheumatoid Arthritis. *Arthritis Care and Research* 2012, 64:445-452
Model of HRQOL for children with SLE