ECHO:
Pediatric Lupus

Pediatric Rheumatology

Pearls for Internist Rheumatologists

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11/2020

Pre-session Questions

Compared to adult onset SLE which of the following systems is most likely to be involved in pediatric or adolescent onset SLE?

a) Musculoskeletal
b) Hematologic
c) Mucocutaneous
d) Renal

Which is the most common manifestation of neuropsychiatric SLE?

a) Psychosis
b) Cognitive disorder
c) Peripheral neuropathy
d) Movement disorder

SLE developing at which age is most associated with long term organ damage?

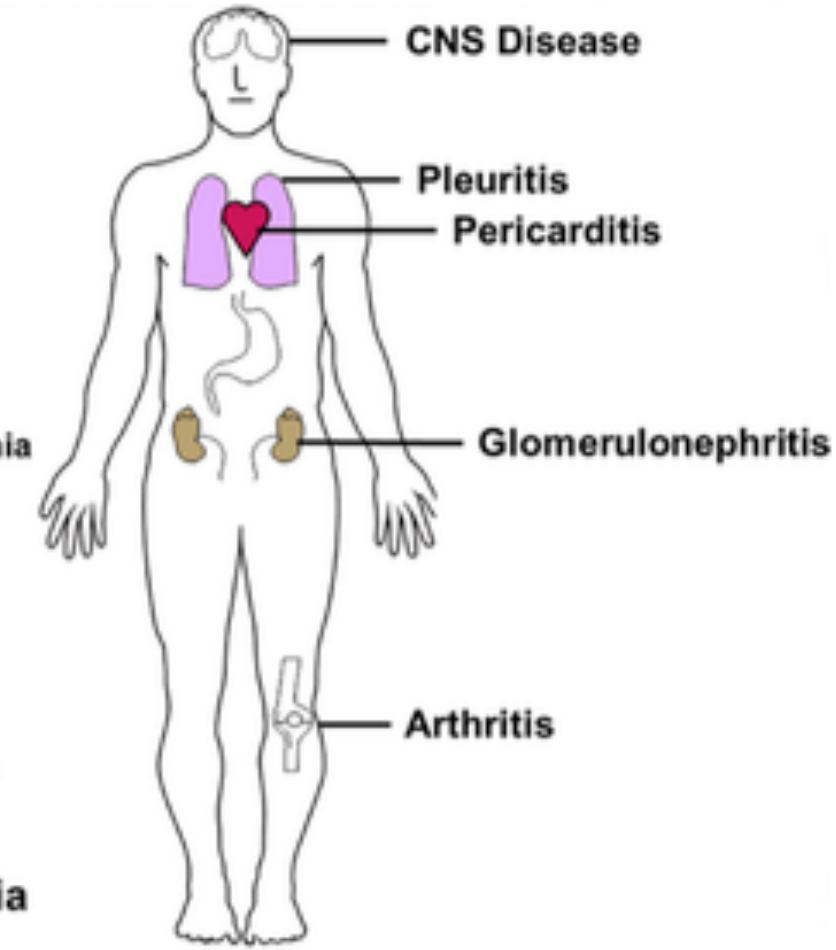
a) Prepubertal
b) Peripubertal
c) Postpubertal adolescent
d) Postpuertal adult

Clinical Criteria

1. Acute Lupus Rash
2. Chronic Lupus Rash
3. Oral Ulcers
4. Alopecia
5. Arthritis
6. Serositis
7. Renal Disorder
8. Neurologic Disorder
9. Hemolytic Anemia
10. Leukopenia/Lymphopenia
11. Thrombocytopenia

Immunologic Criteria

1. Antinuclear antibody
2. Anti-dsDNA
3. Anti-Sm
4. Anticardiolipin
5. Decreased complements
6. Direct Coomb's test



SLICC Revised Criteria

1. Must meet 4 criteria
2. Must have at least 1 clinical and 1 immunologic criteria

OR Biopsy-proven lupus nephritis with anti-dsDNA or ANA

Fig. 1. Systemic Lupus International Collaborating Clinics (SLICC) proposed new SLE classification criteria.

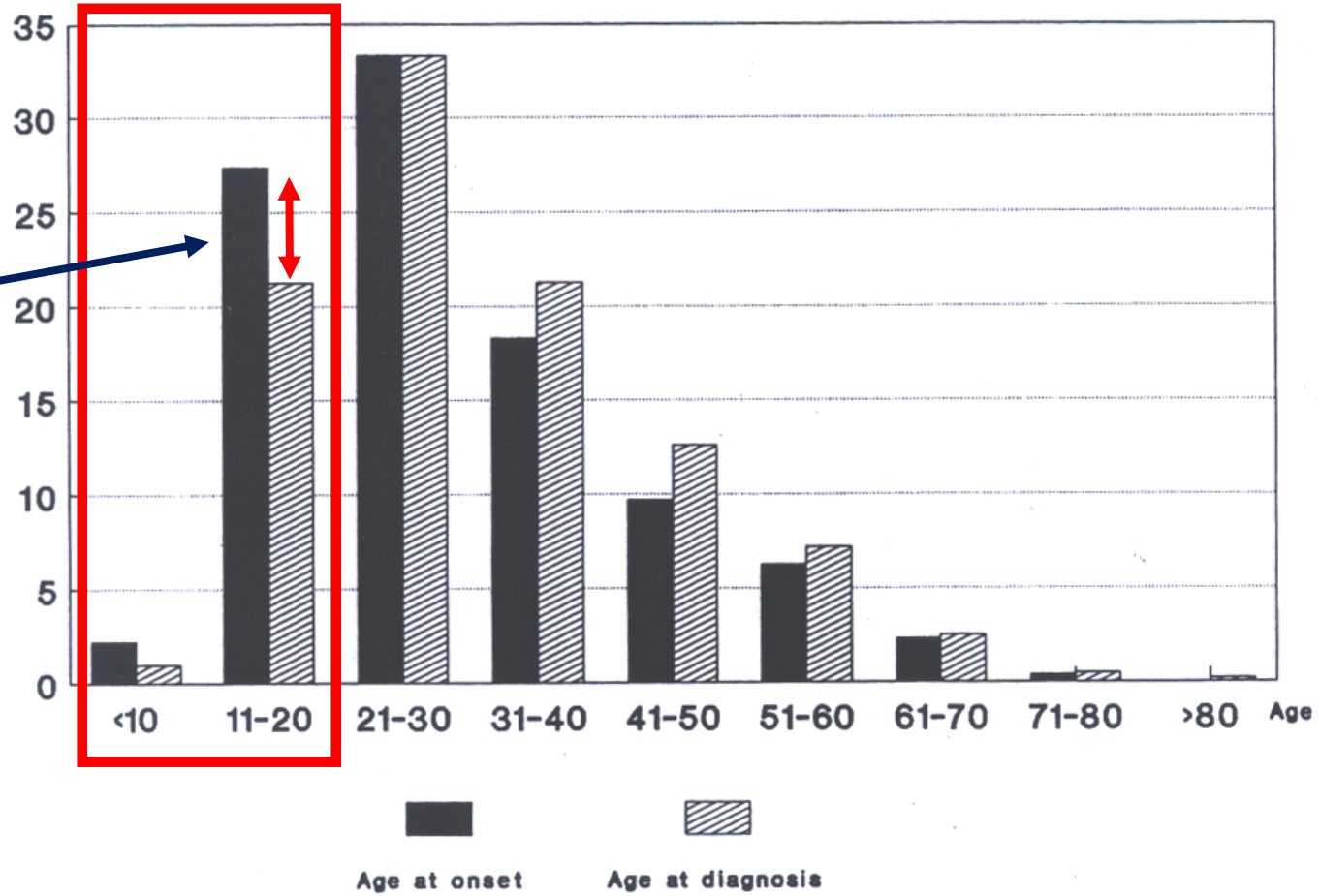
Robertson and James, 2014

Pediatric patients account for ~25% of SLE diagnoses.

Age distribution of SLE development

- 0.36- 0.9 per 100,000 children per year

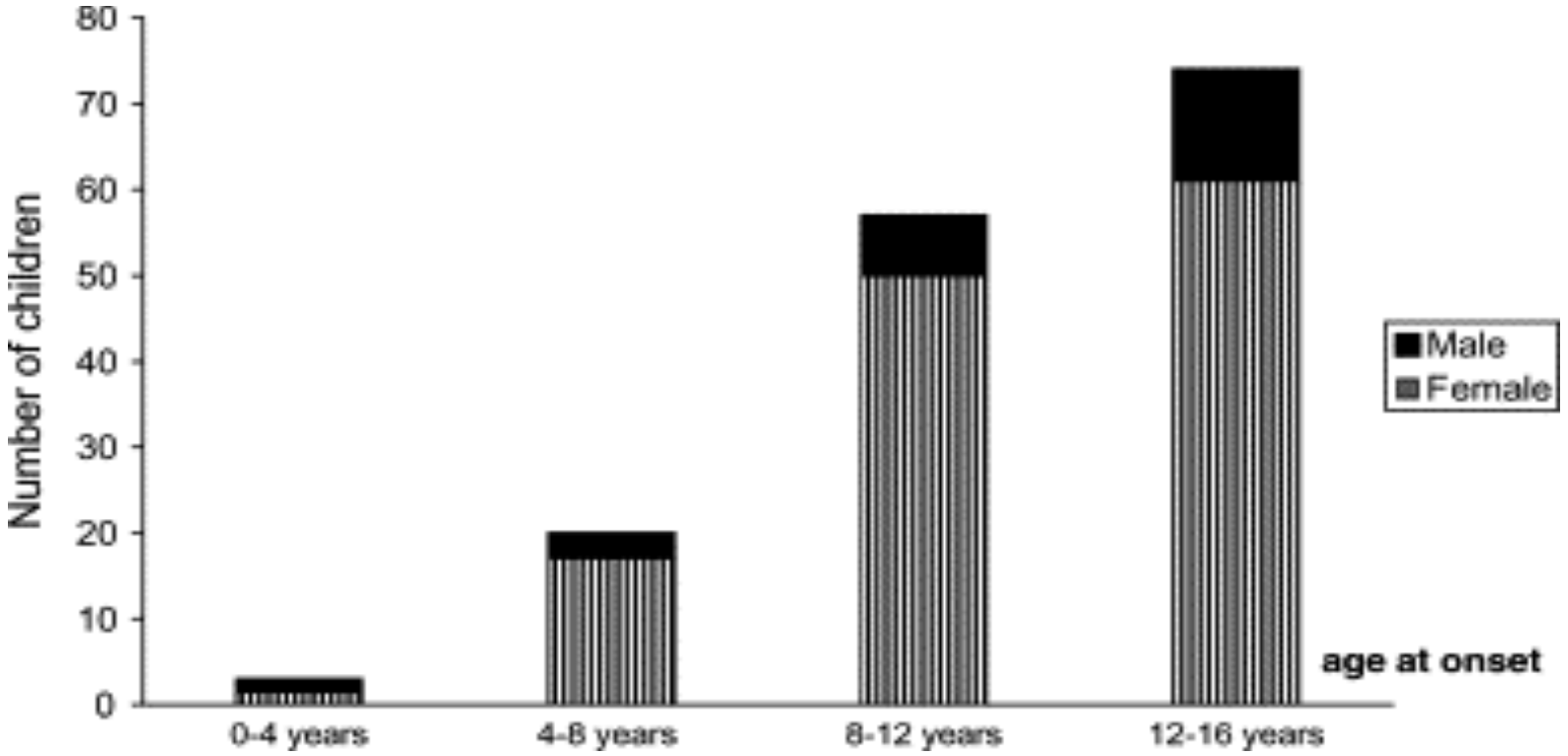
~12%



Percent of SLE patients by decade of age at the onset of symptoms and at diagnosis.

Cervera, 1993

Age distribution of SLE development



Bader-Meunier, 2004

Pediatric SLE (pSLE) is not* subtle.

*It can be subtle, but there are typically significant organ systems involved.

Symptom Development in Pediatrics

Table 1
Clinical features of paediatric-onset and adult-onset SLE.

Clinical features	Paediatric-onset SLE	Adult-onset SLE
Fever	20–67%	43–55%
Lymphadenopathy	6–36%	0–1%
Malar rash	22–79%	35–59%
Discoid lupus	0–19%	3–29%
Oral ulcers	9–49%	13–40%
Photosensitivity	23–53%	20–57%
Arthritis	22–88%	67–94%
Nephropathy	67–82%	33–53%
Pericarditis	16–26%	13–33%
Pleuritis	6–48%	6–33%
Neuropsychiatric disease	15–95%	33–60%
Leucopenia	46–64%	41–57%
Thrombocytopaenia	25–37%	6–25%
Hamolytic anaemia	10–76%	3–13%

Values expressed as percentage.

Adult

Kids

Martini, 2013

Symptom Development in Pediatrics

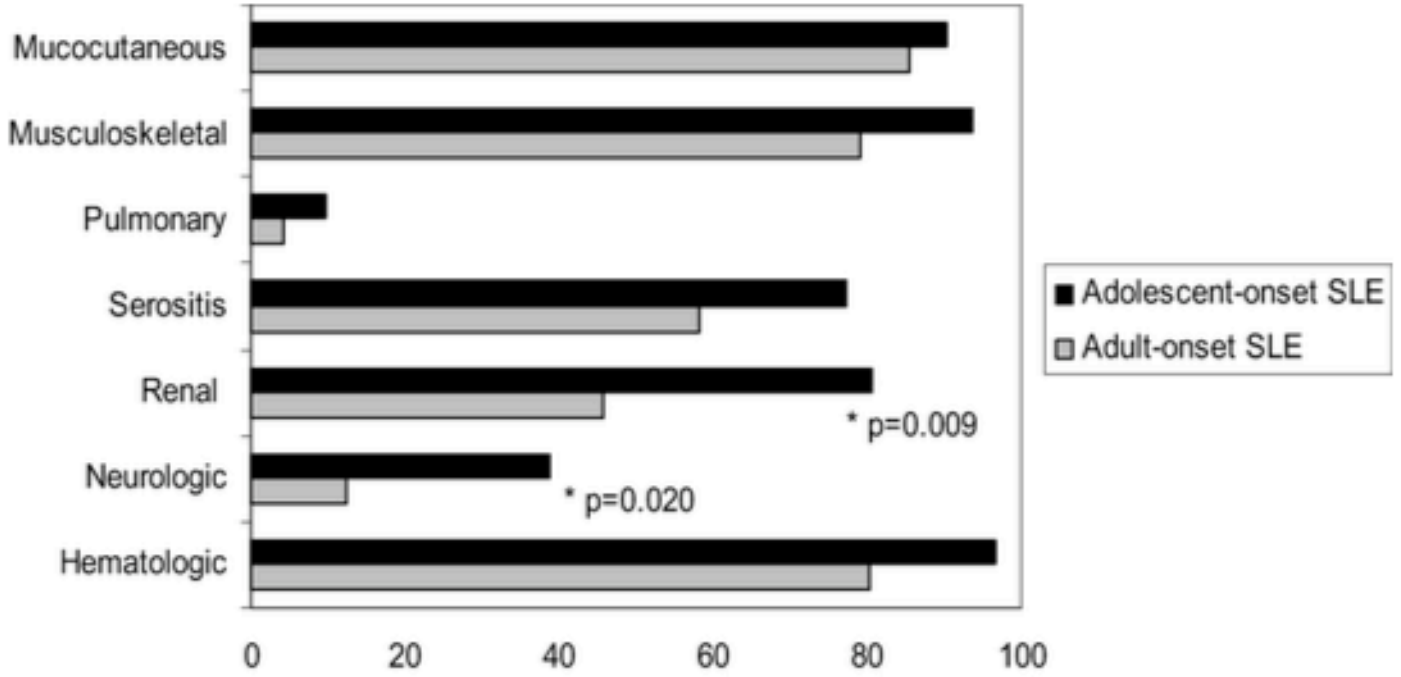


Figure 1 ACR criteria manifestations at baseline in 31 adolescent-onset systemic lupus erythematosus (SLE) and 48 adult-onset SLE patients matched for gender and disease duration. Renal and neurological involvements are significantly increased in adolescent-onset patients. Renal involvement defined as WHO Class II–V and/or proteinuria (>0.5 g/24 h or 3+) attributable to SLE and/or abnormal urinary sediment, proteinuria 2+, elevated serum creatinine/decreased creatinine clearance twice, 6 months apart. Data are presented as percentage of patients.

Tucker, 1998

pSLE is more inflammatory than adult SLE.

Table 3. Differences in disease activity between SLE cohorts, as measured by the SLEDAI*

	Childhood-onset SLE (n = 67)	Adult-onset SLE (n = 131)	*P*
Maximum SLEDAI score in cohort	69	45	
SLEDAI score at diagnosis	16.8 ± 10.1 (0–44)	9.3 ± 7.6 (0–45)	<0.0001
Adjusted mean SLEDAI score	5.70 ± 2.68 (1.3–13.5)	4.59 ± 3.05 (0–18.2)	0.012
Adjusted mean renal SLEDAI score	2.37 ± 2.38 (0–9.7)	0.82 ± 1.59 (0–8.7)	<0.0001

* Except where indicated otherwise, values are the mean ± SD (range) Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score. *P* values were determined by chi-square or Fisher's exact test.

Brunner, 2008

An earlier onset of disease is associated with greater damage accrual.

Damage Accrual

- Higher disease activity
- Longer duration of disease
- Higher side effects and toxicity of therapy

Damage Index

Table 2

Differences in disease damage between pediatric-onset SLE and adult-onset SLE, as measured by the Systemic Lupus International Collaborating Clinics/ ACR (SLICC/ACR) damage index scores (SDI).

SDI domain	LB Tucker et al [9].		Brunner HI et al [10].		Hersh AO et al [11].	
	p-SLE (N=31)	a-SLE (N=48)	p-SLE (N=66)	a-SLE (N=131)	p-SLE(N=90)	a-SLE (N=795)
Mean (SD) total disease duration (years)	6.8 (2.7)	5.6 (3.3)	3.2 (2)	3.5 (2.6)	16.5 (8.5)	13.4 (8.5)
Ocular	9.7%	4.3%	42.4%	13.0% ($p < 0.0001$)		
Neuropsychiatric	29.0%	19.6%	12.1%	9.9%		
Renal	45.2%	17.4% ($p = 0.023$)	9.1%	6.1%	56.2%	37.1% ($p < 0.001$)
Pulmonary	3.2%	6.5%	3.0%	2.3%	23.6%	43.3% ($p < 0.001$)
Cardiovascular	6.5%	4.3%	1.5%	4.6%	7.9%	4.5%
Peripheral vascular	0.0%	8.7%	3.0%	1.5%		
Gastrointestinal	3.2%	10.9%	3.0%	2.3%		
Musculoskeletal	19.4%	15.2%	24.2%	9.9% ($p = 0.007$)		
Skin	9.7%	15.2%	7.6%	6.9%		
Gonadal	12.9%	10.9%	0.0%	1.5%		
Diabetes	3.2%	8.7%	3.0%	4.6%		
Malignancy	3.2%	0.0%	0.0%	3.8%		

Abbreviations: SDI: Systemic Lupus International Collaborating Clinics/ACR (SLICC/ACR) damage index scores, pSLE: paediatric-onset systemic lupus erythematosus, aSLE: adult-onset systemic lupus erythematosus, Only p-values <0.05 are shown.

Martini, 2013

Damage Index

Table 2. Differences in medication requirements between the SLE cohorts*

	Childhood-onset SLE (n = 67)	Adult-onset SLE (n = 131)	*P*
Oral corticosteroids	65 (97)	92 (70)	<0.0001
Pulse methylprednisolone	20 (30)	15 (11)	0.001
Antimalarial agents	54 (81)	95 (73)	0.21
Immunosuppressive medications	44 (66)	48 (37)	0.0001
Azathioprine	28 (64)	36 (75)	0.24
Cyclophosphamide	11 (25)	10 (21)	0.63
Methotrexate	4 (9)	15 (31)	0.009
Cyclosporine	1 (2)	0	0.48
Mycophenolate mofetil	0	1 (2)	1.00

* Values are the number (%) of patients. *P* values were determined by chi-square or Fisher's exact test. SLE = systemic lupus erythematosus.

Brunner, 2008

How early is too early (for long term damage)?

Damage Studies

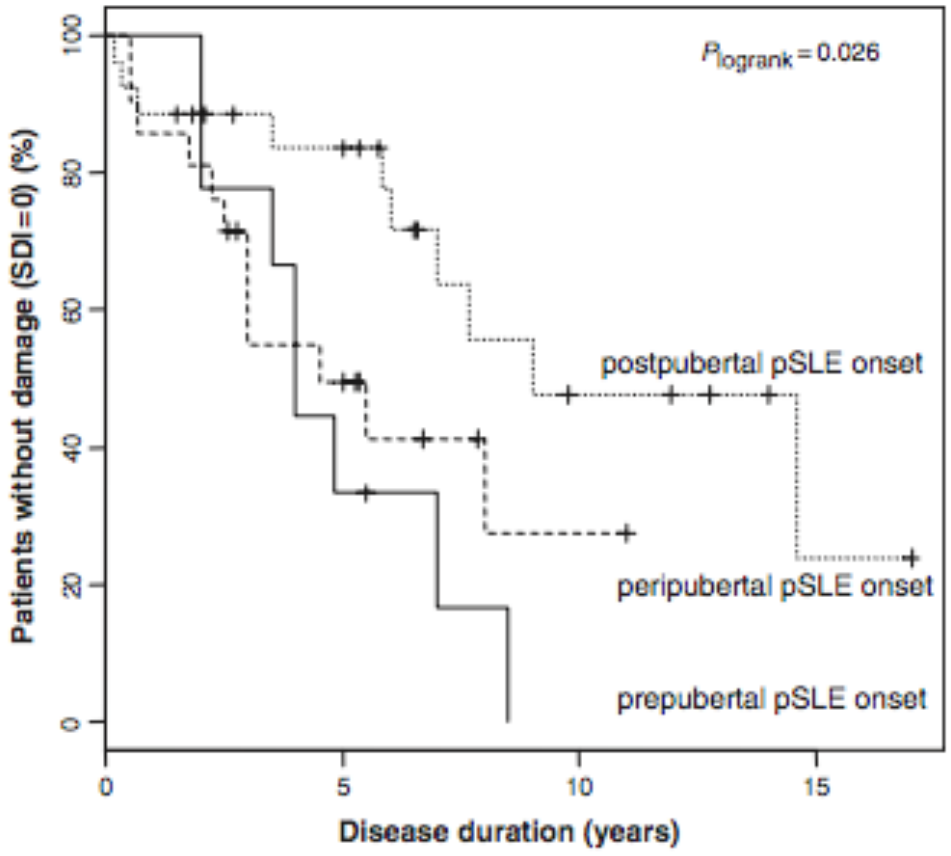


FIG. 2. Kaplan–Meier type plot of time to damage occurrence in pSLE according to age at disease onset.

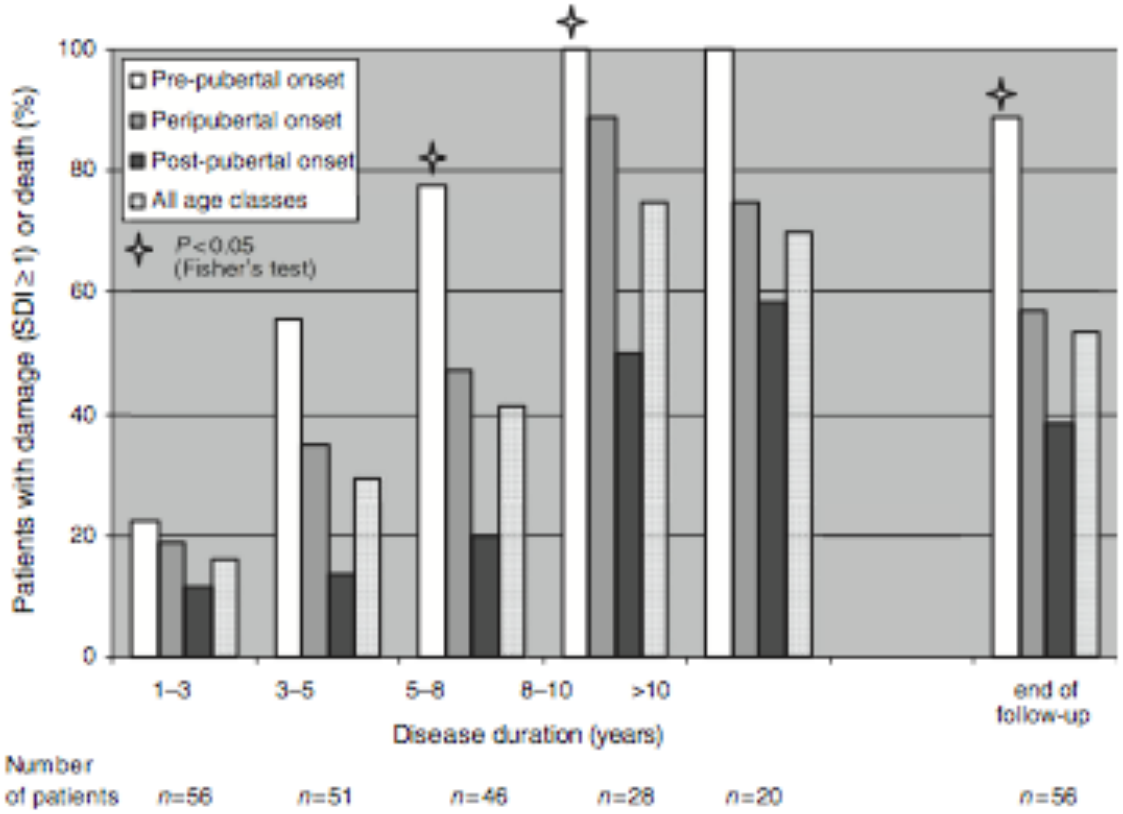


FIG. 3. Risk of damage (SDI ⩾1) or death in 56 patients with pSLE according to age at disease onset.

Descloux, 2009

Subclinical damage…

- Caused by disease (uncontrolled inflammation) and treatment (steroids):
  - Pubertal development is delayed (on average by 12-18 months) in 15.3% of children
  - Growth failure is prevalent

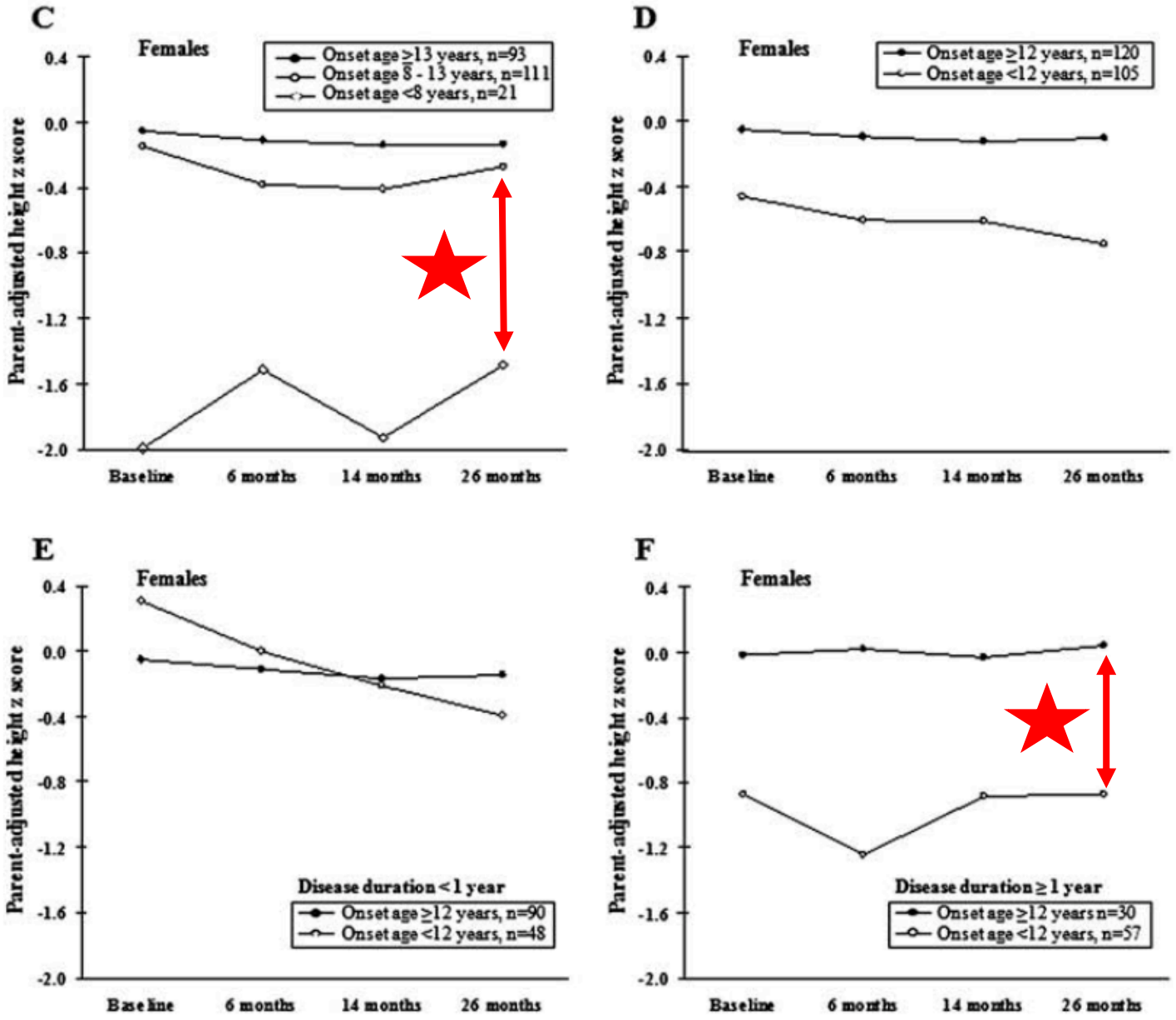
Table 3 Pubertal characteristics of the 147/276 (53.3%) evaluable females with juvenile SLE

	Patients included for pubertal evaluation* (N=147)
Patients who had menarche registered, n	104/147 (70.7%)
Age at menarche, median (1st, 3rd quartile)	13.6 (12.6, 14.5)
Tanner ≥B2 at last visit	141/147 (95.9%)
Age at B2, median (1st, 3rd quartile)	11.9 (11.1, 12.7)
Delayed pubertal onset†	11/72 (15.3%)
Delayed pubertal tempo‡	37/96 (38.5%)
Delayed or absent menarche	25/114 (21.9%)
Delayed menarche§	15/114 (13.1%)
Absent menarche¶	10/114 (8.8%)
Normal menarche	89/114 (78.1%)
Delayed puberty**	53/147 (36.1%)
Irregular menses or postmenarche amenorrhoea	48/104 (46.2%)

Numbers are medians (1st, 3rd quartiles) or frequencies (%).
*A total of 147 female patients were included in pubertal evaluation, and 129 were excluded as 114 patients had already completed puberty before disease onset and 15 patients had no menarche but were <13 years of age at last follow-up (too young to be informative).
†Age at B2 ≥13 years.
‡Delayed pubertal tempo (stable Tanner stage for ≥1 year in late-maturing girl or ≥2 years in normal-maturing girl).
§Age at menarche ≥15 years.
¶No menarche and age at last follow-up ≥15 years.
**Delayed puberty was defined as either delayed pubertal onset, delayed pubertal tempo (stable Tanner stage for ≥1 year in late-maturing girl or ≥2 years in normal-maturing girl), or delayed or absent menarche.

Rygg, 2011

Subclinical damage…



Rygg, 2011

Autoantibodies are a defining feature of SLE.

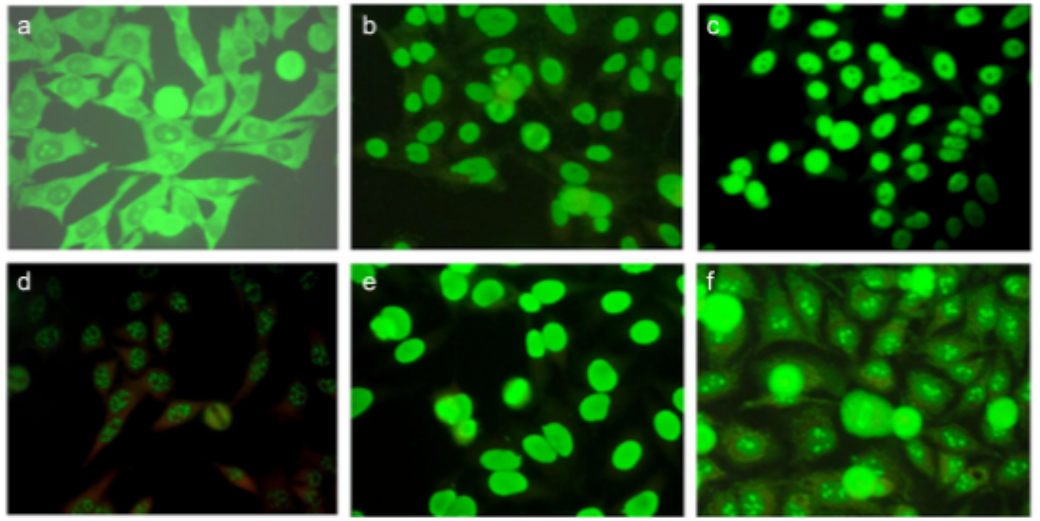
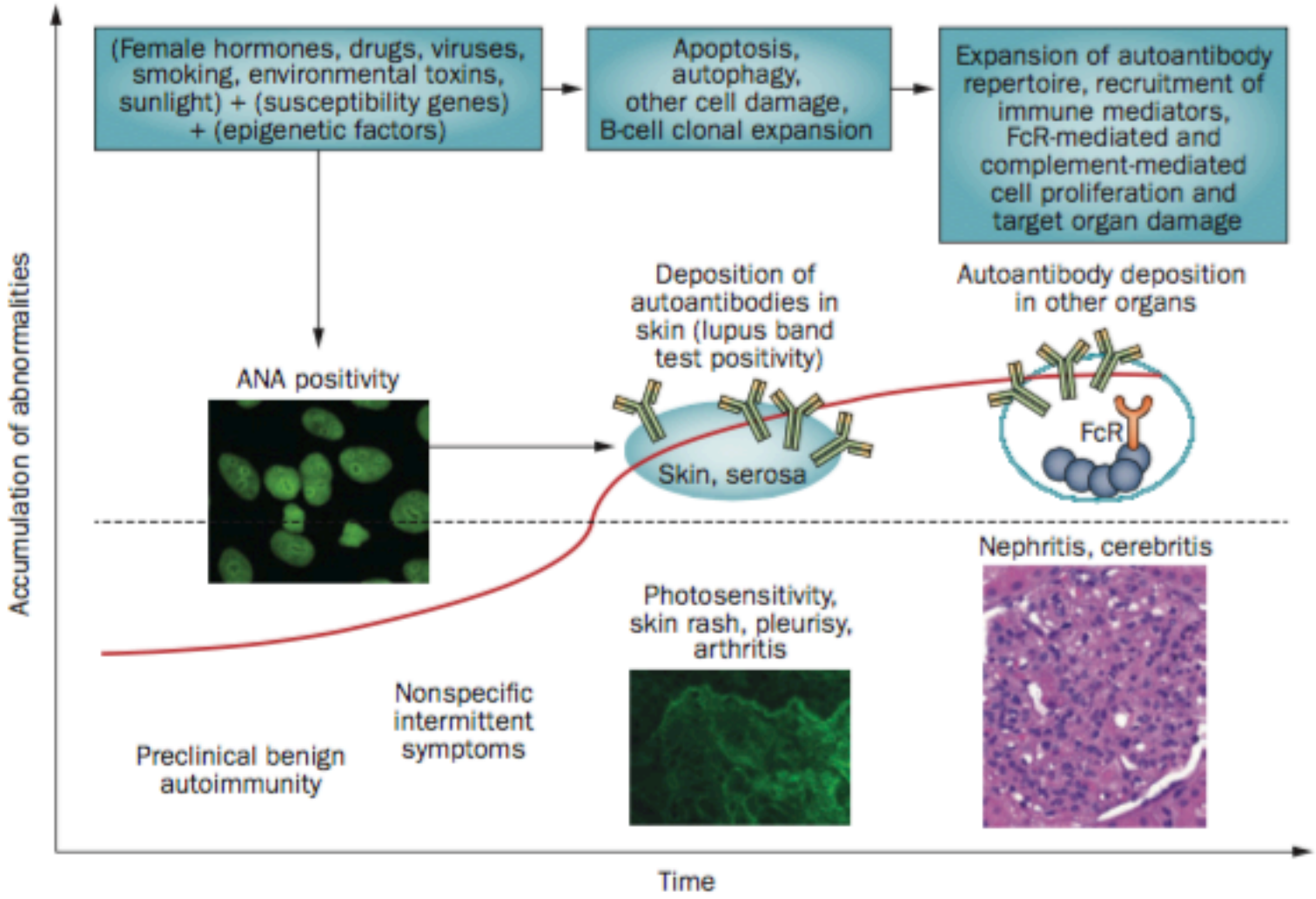


Fig. 1. Microphotographs of indirect immunofluorescence of specific antibodies in Hep2 cells. (a) Cytoplasmic P-ribosomal pattern. (b) NuMA-1 pattern. (c) Centromeric or discrete speckled pattern. (d) SSA discrete speckled pattern. (e) Homogeneous pattern. (f) Nucleolar with mitochondrial pattern.

Autoantibodies progress into disease



Olsen and Karp, 2014

Autoantibodies progress into disease

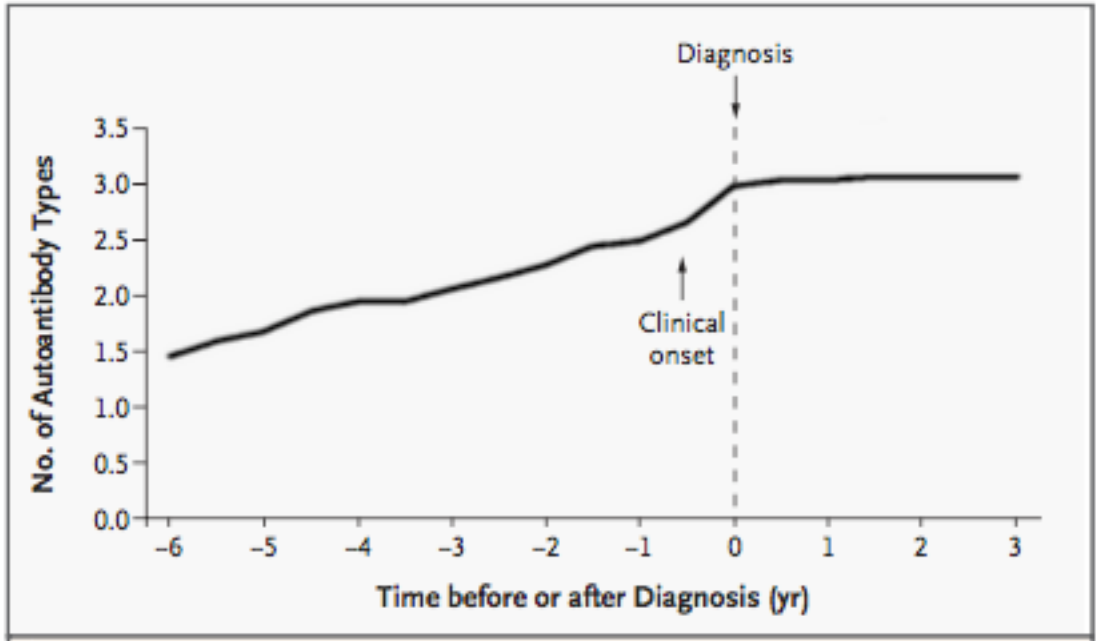
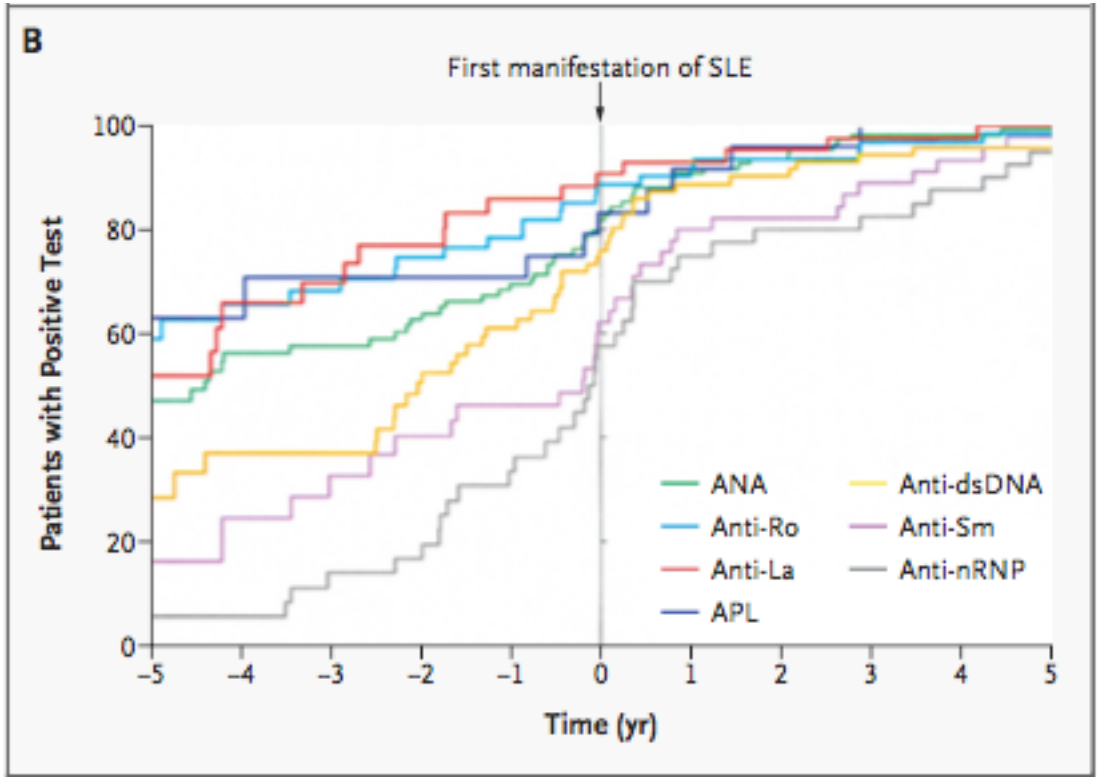


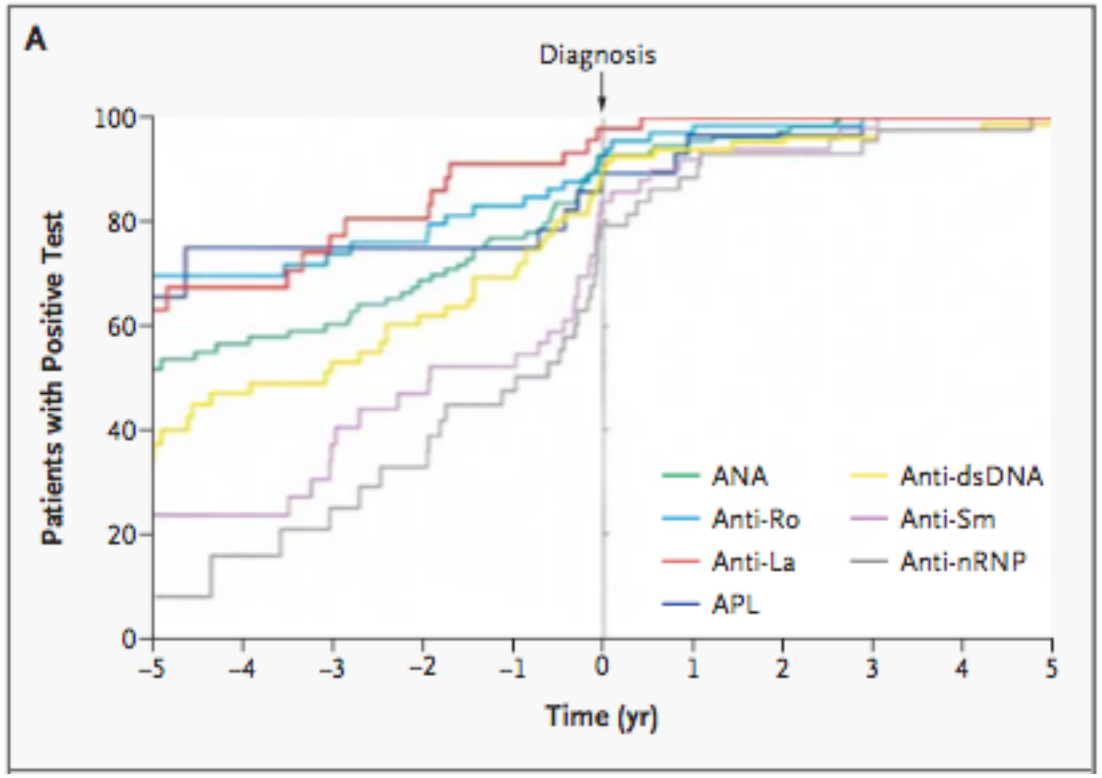
Figure 2. Accumulation of Systemic Lupus Erythematosus Autoantibodies.

The curve shows the average number of types of autoantibody in relation to the time of diagnosis of systemic lupus erythematosus. Seven autoantibodies were evaluated, which bind cellular constituents (antinuclear antibodies), Ro, La, double-stranded DNA, Sm, phospholipid, and nuclear ribonucleoprotein. The time of diagnosis and the median time of the first appearance of any clinical criterion useful for the classification of systemic lupus erythematosus (clinical onset) are indicated by arrows.

Arbuckle, et. al., 2003

Autoantibodies progress into disease





Arbuckle, et. al., 2003

Can we treat to delay the escalation of immunosuppression?

Lupus (2007) 16, 401–409
http://lup.sagepub.com

PAPER

Hydroxychloroquine sulfate treatment is associated with later onset of systemic lupus erythematosus

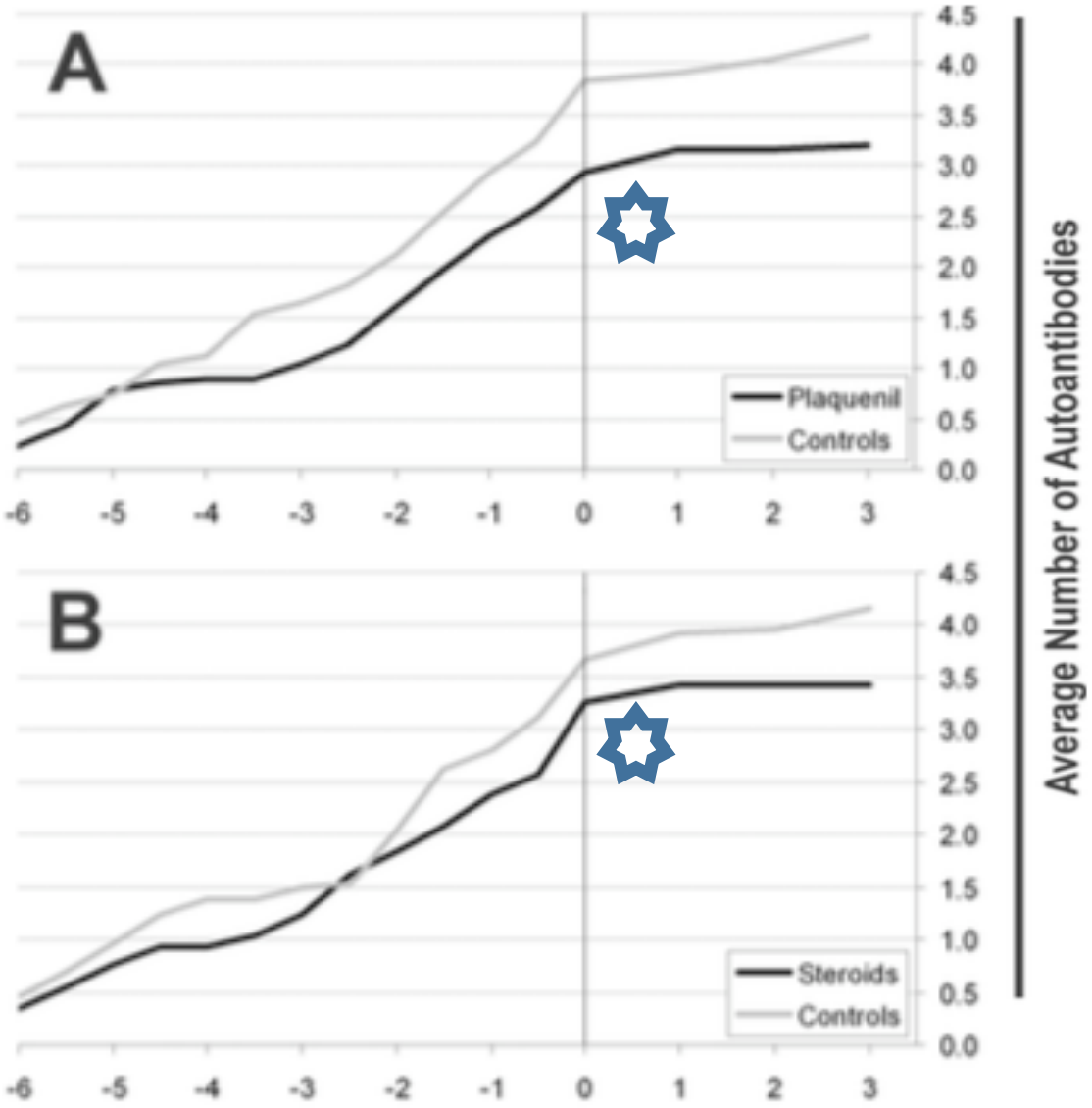
JA James[1,2]*, XR Kim-Howard[1,3], BF Bruner[1,2], MK Jonsson[4], MT McClain[1], MR Arbuckle[1], C Walker[5], GJ Dennis[5,6], JT Merrill[7] and JB Harley[1,2,8]

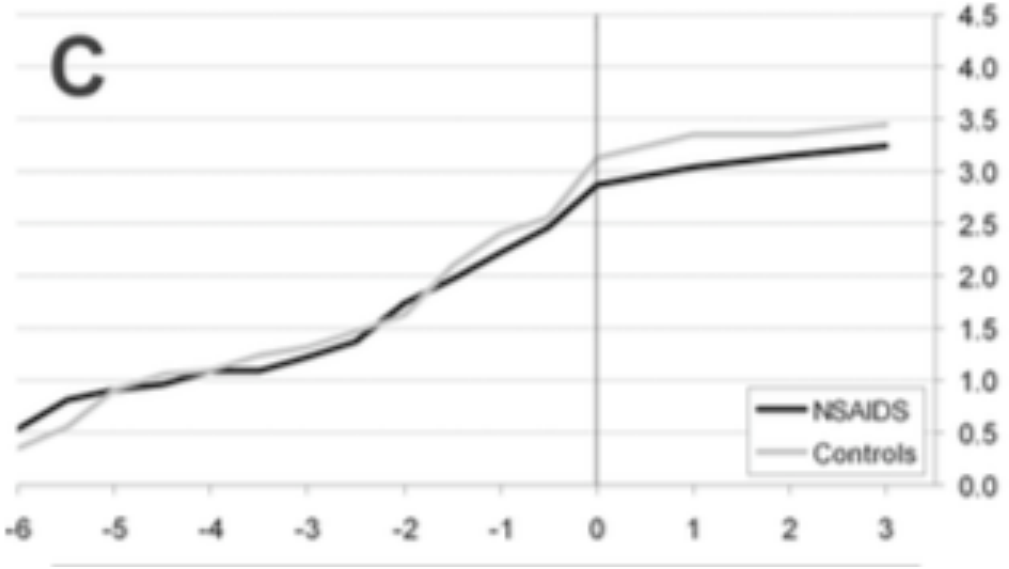
- Chart review
  - 130 individuals with incomplete SLE inclusion criteria followed over time for development of additional criteria
  - 26 were treated with HCQ prior to full criteria/ these were matched to no-HCQ controls

Table 2 Cumulative autoantibody information for SLE patients treated with HCQ before diagnosis and matched SLE controls

	SLE HCQ preDX n = 26	*SLE No HCQ preDx n = 26*
ANA	22 (85%)	24 (92%)
Ro	9 (35%)	15 (58%)
La	7 (27%)	10 (38%)
aPL	7 (27%)	7 (27%)
dsDNA	14 (54%)	18 (69%)
Sm	7 (27%)	10 (38%)
nRNP	7 (27%)	10 (38%)
Ribosomal P	2 (8%)	8 (31%)
C1q	9 (35%)	9 (35%)
Avg. # of autoantibodies	3.23	4.27

HCQ seems to delay the onset of serologic disease.





James, 2007

HCQ seems to delay the onset of clinical disease.

Table 1 Length of SLE disease onset from the first criterion to classification in SLE patients treated with hydroxychloroquine (HCQ) ($n = 26$), corticosteroids (Steroid) ($n = 27$), or non-steroidal anti-inflammatory drugs (NSAID) ($n = 32$) before diagnosis compared to matched SLE patients without pre-diagnosis medication use

	Time (years) from first recorded criterion			
	Median	*Mean*	*Std. dev*	*Range*
HCQ Status				
Pre-Dx HCQ	1.08	2.69	3.51	0.08–13.58
No Pre-Dx HCQ	0.29	1.07	1.87	0–7.72
Steroid Status				
Pre-Dx Steroid	0.92	2.76	4.29	0.08–14.75
No Pre-Dx Steroid	0.42	1.32	2.22	0.02–14.83
NSAID Status				
Pre-Dx NSAID	0.88	2.15	3.27	0.02–13.58
No Pre-Dx NSAID	0.42	1.45	2.66	0–14.83
HCQ + Sterioids				
Pre-Dx both ($n = 13$)	1.43	3.49	4.5	0.17–13.58
Neither HCQ/Steriods ($n = 93$)	0.33	1.23	2.22	0.02–14.83

There was significant overlap in the HCQ/ steroids groups.

They felt that the HCQ was more representative of the effect.

James, 2007

Clinical Criteria

1. Acute Lupus Rash
2. Chronic Lupus Rash
3. Oral Ulcers
4. Alopecia
5. Arthritis
6. Serositis
7. Renal Disorder
8. Neurologic Disorder
9. Hemolytic Anemia
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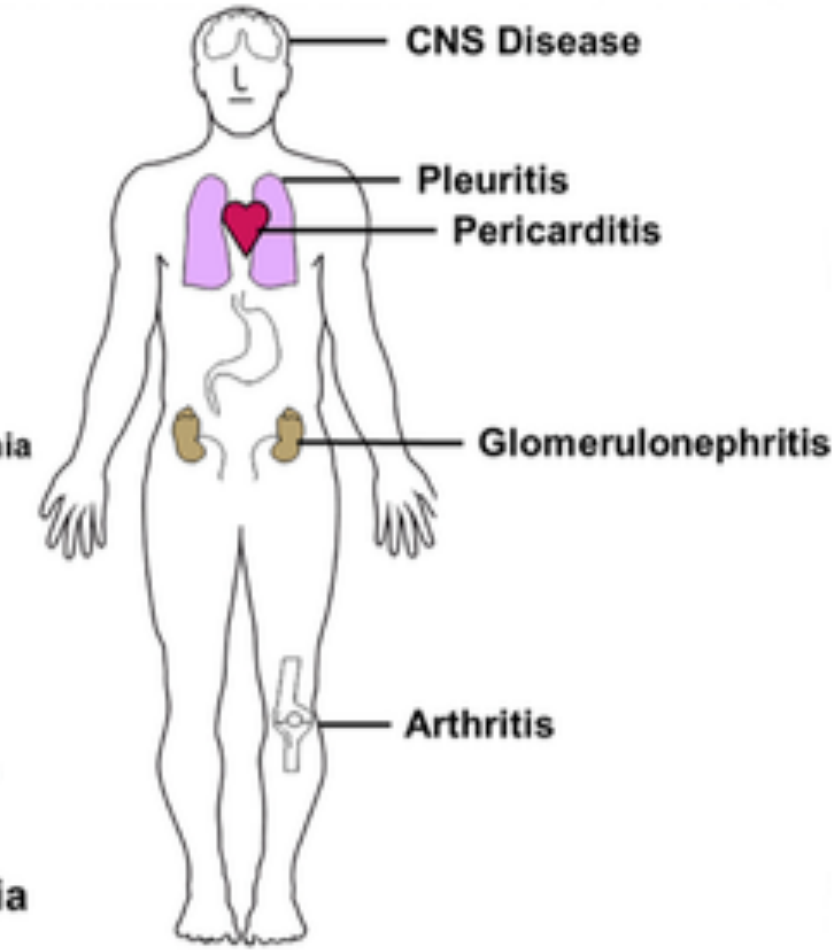

SLICC Revised Criteria

1. Must meet 4 criteria
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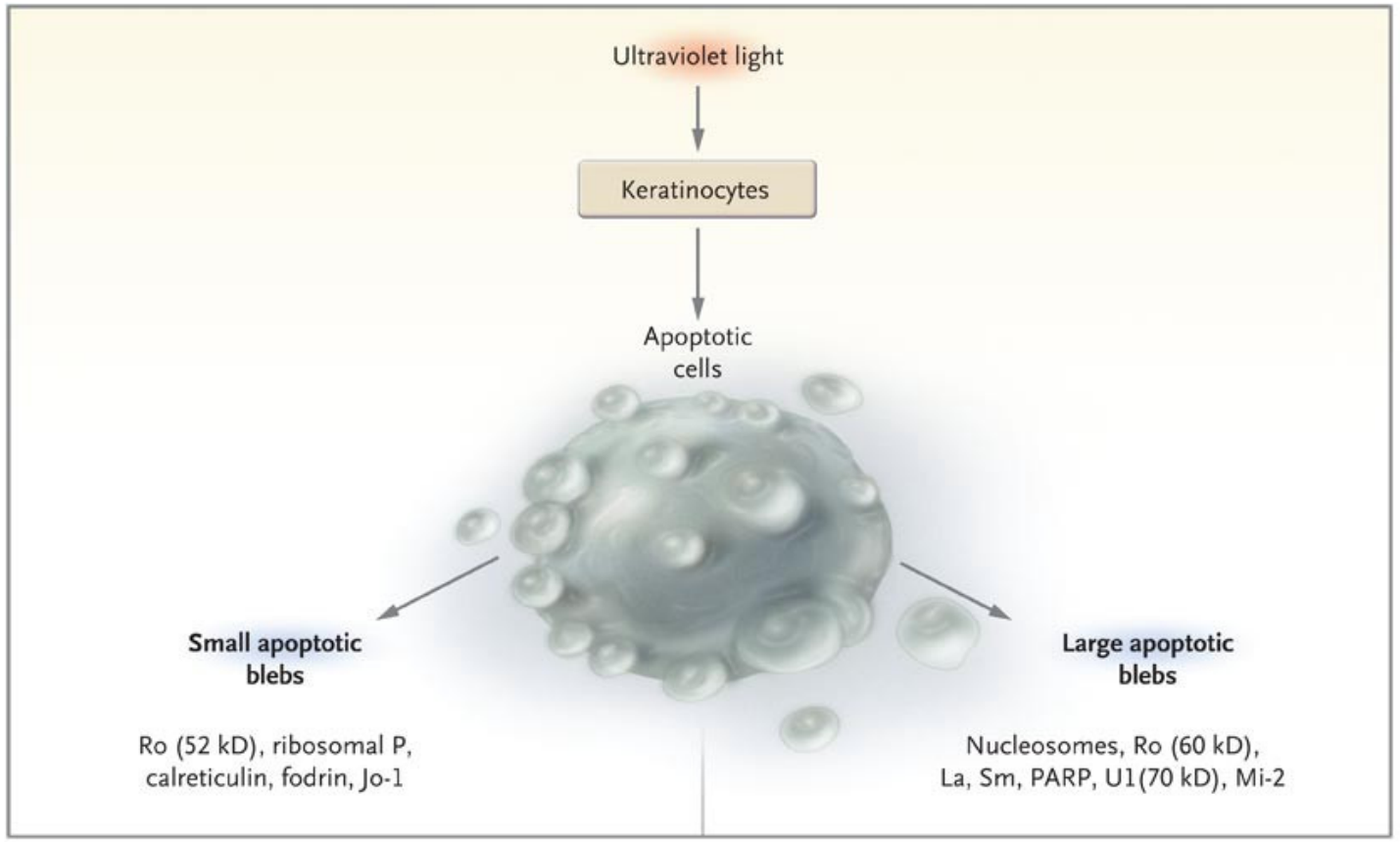
OR Biopsy-proven lupus nephritis with anti-dsDNA or ANA

Fig. 1. Systemic Lupus International Collaborating Clinics (SLICC) proposed new SLE classification criteria.

Robertson and James, 2014

Cutaneous Lupus

- Acute cutaneous lupus (Malar rash)
- Chronic cutaneous lupus (Discoid rash)
- Subacute cutaneous lupus
- Non- scarring Alopecia



Rahman, 2008

Malar Rash

- Erythematous
- Raised
- Non- pruritic
- Non- scarring
- Extends over the nasal bridge
  - Spares the nasolabial folds
  - May effect the chin and ears
- Photosensitive

Discoid Rash

- Rare in children
  - < 10%
- Scarring rash
- Heaped up borders, atrophy and ulceration in the center

Subacute Cutaneous Lupus

Musculoskeletal Manifestations

- Arthralgias → about 90%
- Arthritis → about 75%
- Bone abnormalities:
  - Avascular necrosis (<5%)
  - Bone fragility fractures
  - Osteoporosis
- Secondary pain amplification

R
63

R
TA

Cardiac Manifestations of SLE

- Pericarditis
  - Most common cardiac manifestation (~25% incidence)
  - If longstanding and untreated, can result in fibrous connections in the pericardium
- Myocarditis
  - Inflammatory infiltrate
  - Ischemia (small vessel inflammation, clotting predilection, atherosclerosis)
  - Adult studies → Uncommon (~6%); although 80% have evidence on autopsy
- Endocarditis (valve)
  - Libman-Sacks → Valve fibrosis, most common of the mitral valve, that results from new vessel formation and active inflammation
  - Associated with active SLE disease and APLs.

Hematologic Manifestations

- Hematological → Up to 80%
  - Thrombocytopenia 8-74%
  - Leukopenia 27-52%
    - Lymphopenia 30-59%
  - Anemia 72-84%

Leucopenia

- **Immune – mediated**
- Bone marrow suppression
- Peripheral antibody formation

- **Non-immune mediated**
- Drug induced
  - Azathioprine
  - MMF
  - Cyclophosphamide
  - MTX
  - HCQ
  - NSAIDS
- Sepsis
- Viral
  - parvovirus

Anemia

- **Immune mediated**
- Autoimmune hemolytic anemia
- Pure red cell aplasia
- Hemophagocytic syndrome
- Aplastic anemia
- TTP/microangiopathic

- **Non-immune mediated**
- Chronic disease
- Chronic renal insufficiency
- Iron deficiency
- Drug-induced
- Infection
- Myelofibrosis
- Myelodysplasia

Thrombocytopenia

- **Non- immune**
- Drug induced BM suppression
- DIC
- Myelodysplasia
- Myelofibrosis

- **Immune – mediated**
- Anti-platelet Ab
- Anti-thromboetin Ab
- TTP/microangiopathy
- APLa
- Evans sydnrome

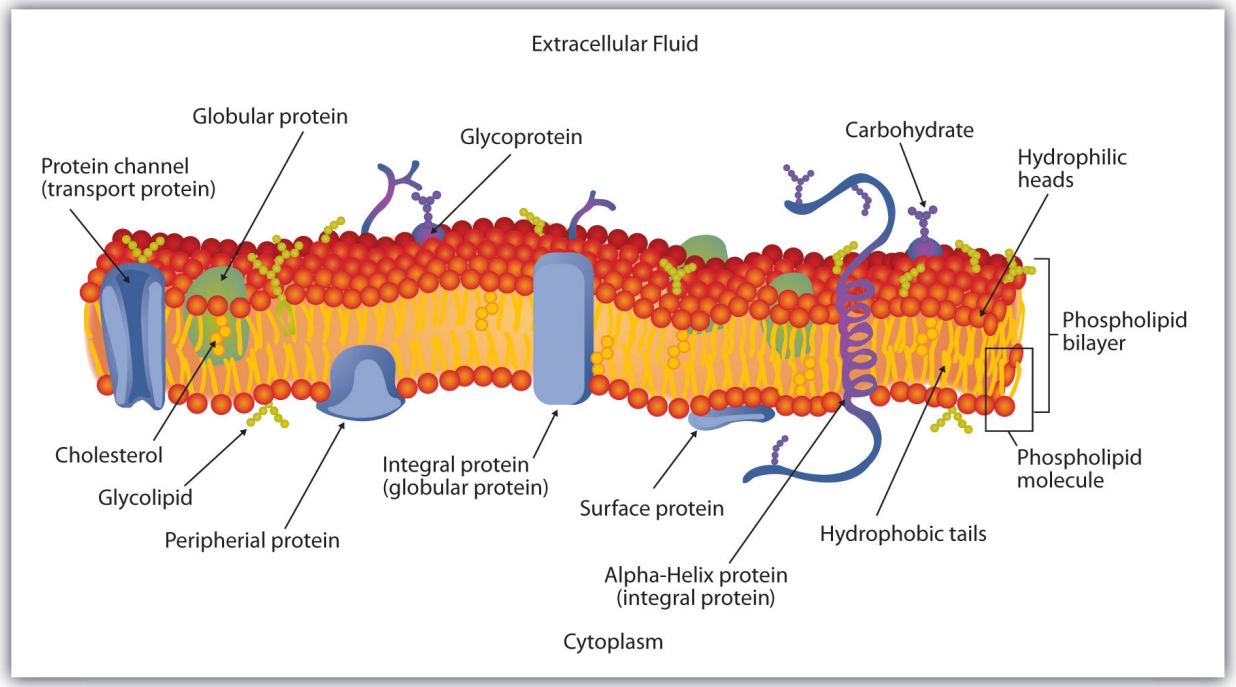
Anti-phospholipid antibody syndrome

Phospholipids are components of all cell membranes

There are (+) or (-) charged

The balance and location is critical to function

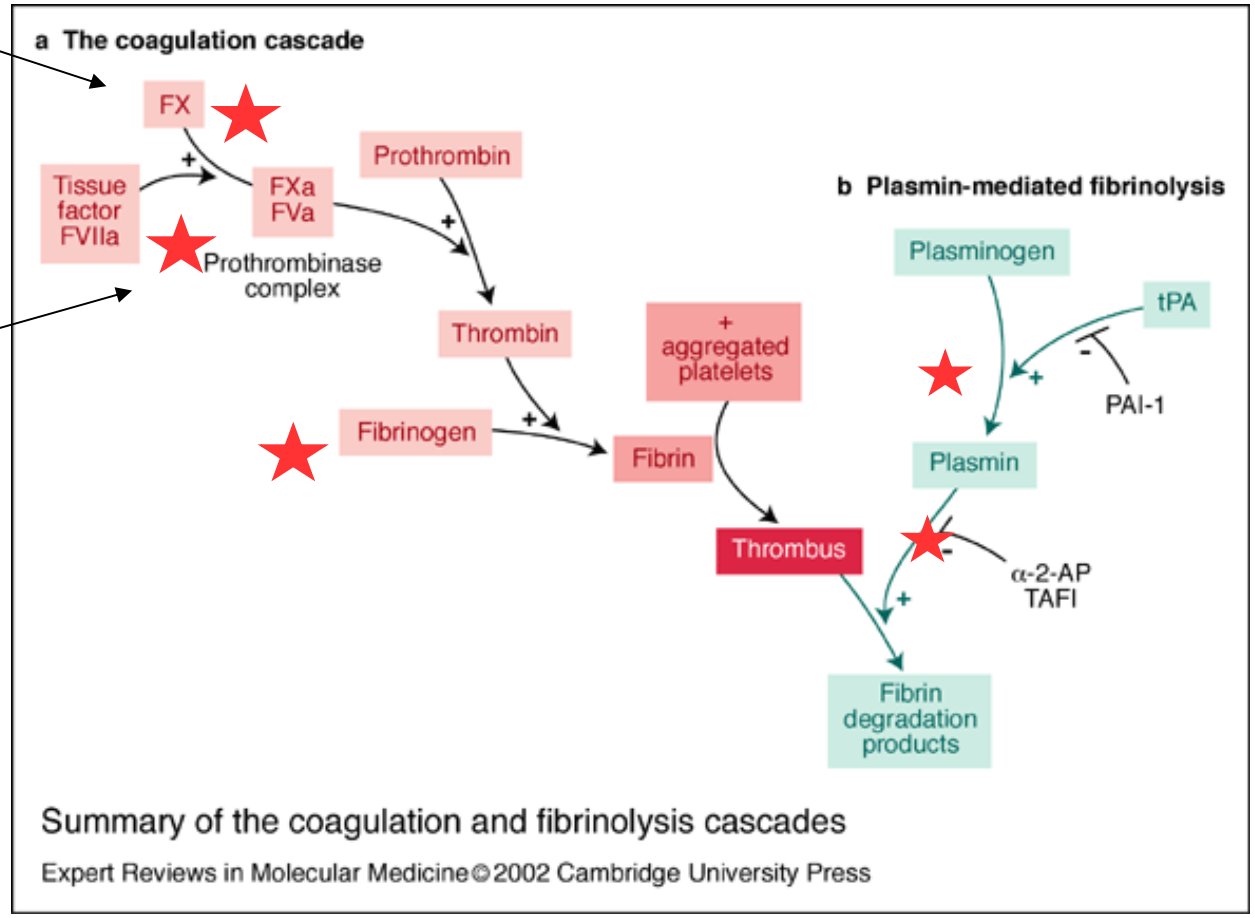
aPLs will disrupt the normal interactions between cells and alter the membranes biological function.



Procoagulant Effect

Protein C

Protein S



aPLs have been shown to inhibit the actions of many inhibitors of thrombus formation.

Platelet Effect

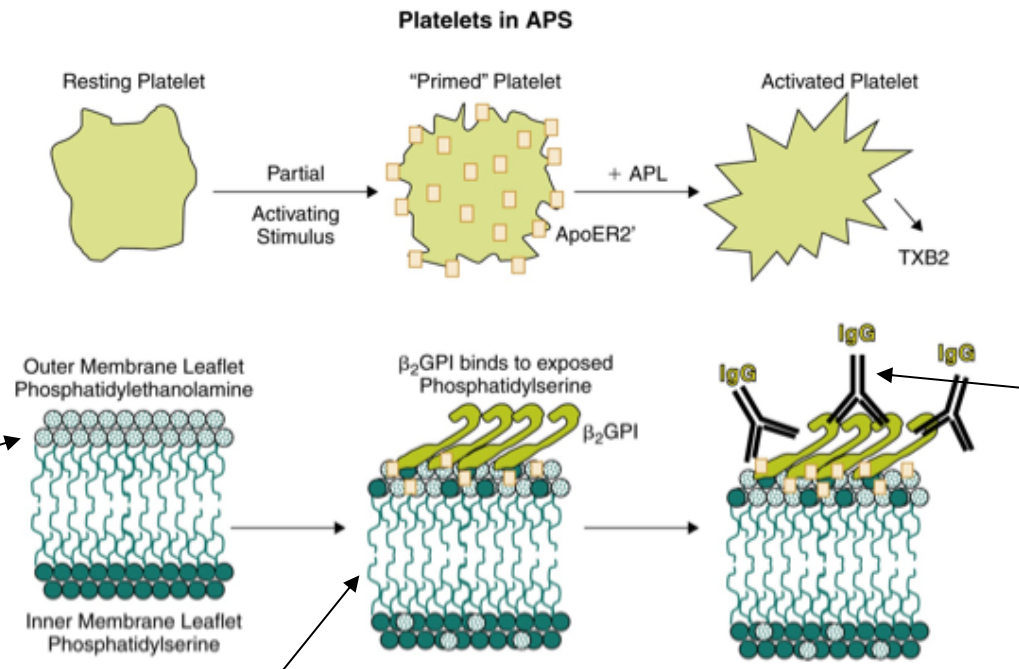


FIGURE 22–1 Effects of antiphospholipid antibodies on ...

Platelet stress causes the negatively charged PTS to move to the outer membrane

This allows the antibodies to bind the platelet. And the platelets to aggregate.

β2 glycoprotein will bind the negative PL. Typical function of β2 glycoprotein is to inhibit platelet aggregation in excess.

Cassidy et. al. 2010.

Endothelial Effect

Critical for platelet and leukocyte adhesion to endothelium.

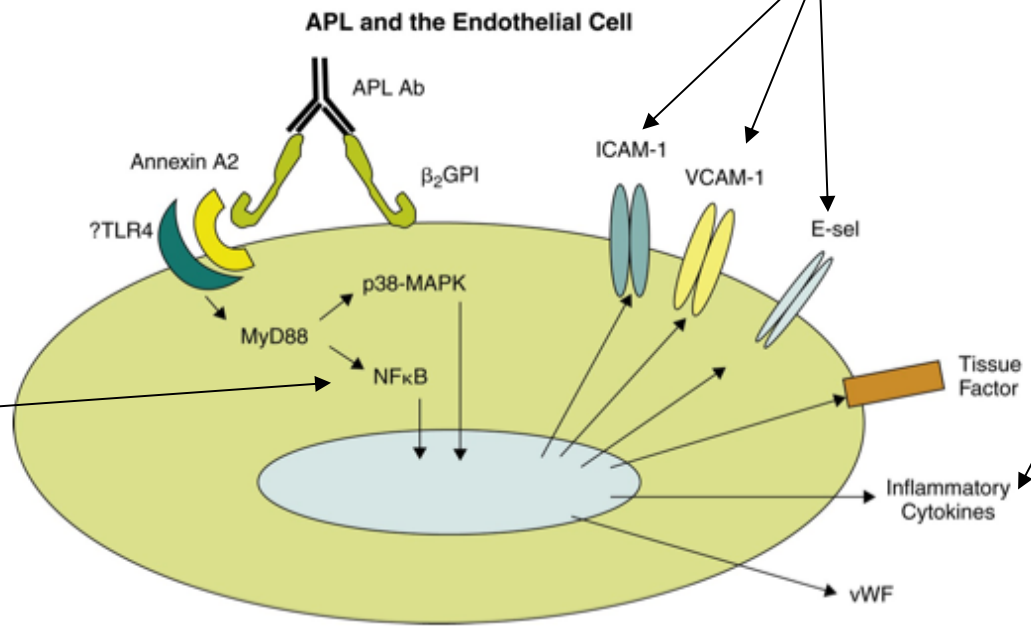


FIGURE 22–2 Effects of antiphospholipid antibodies on ...

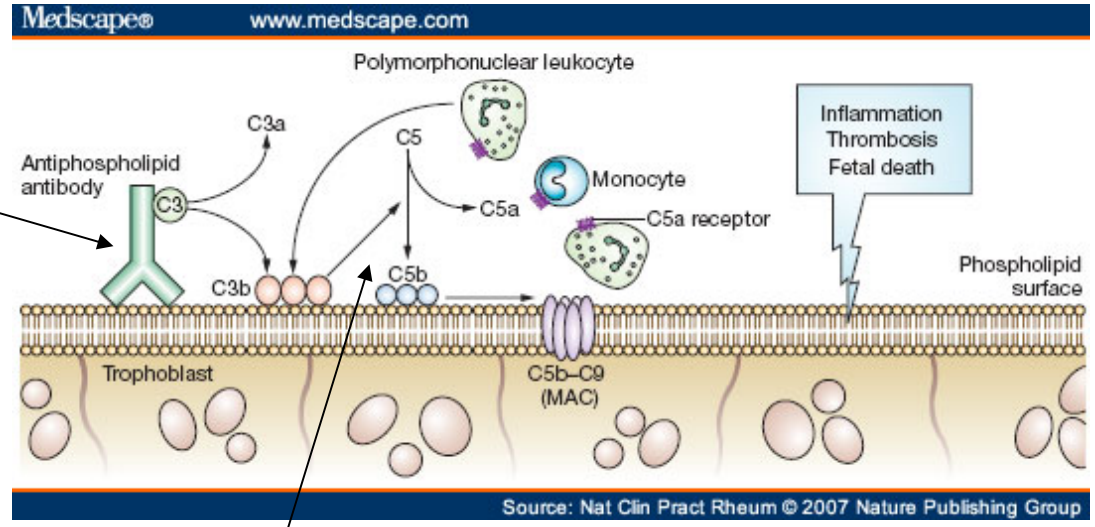
Direct upregulation of inflammation in cells.

Increases inflammation in vessel wall and platelet adhesion.

Cassidy et. al. 2010.

Organ Effect

Bound aPLs will activate the classical complement pathway.



This results in the production of serine proteases which activate cell death and begin the process of thrombus formation. Also recruits more inflammatory cells to the area.

Manifestations

TABLE 3 Associated Nonthrombotic Clinical Manifestations at the Time of the Initial Thrombotic Event

Clinical Manifestation	No. (%) of Patients
Hematologic disorders	46 (38)
Evans syndrome	15 (12)
Thrombocytopenia	10 (8)
Leucopenia/lymphopenia	10 (8)
Autoimmune hemolytic anemia	9 (7)
Bleeding disorder	2 (2)
Skin disorders	22 (18)
Livedo reticularis	7 (6)
Raynaud phenomenon	7 (6)
Skin ulcers	4 (3)
Pseudovasculitic lesions	3 (2)
Chronic urticaria	1 (1)
Nonthrombotic neurologic disorders	19 (16)
Migraine headache	8 (7)
Chorea/athetosis	5 (4)
Epilepsy	4 (3)
Pseudotumor cerebri	1 (1)
Mood disorder	1 (1)

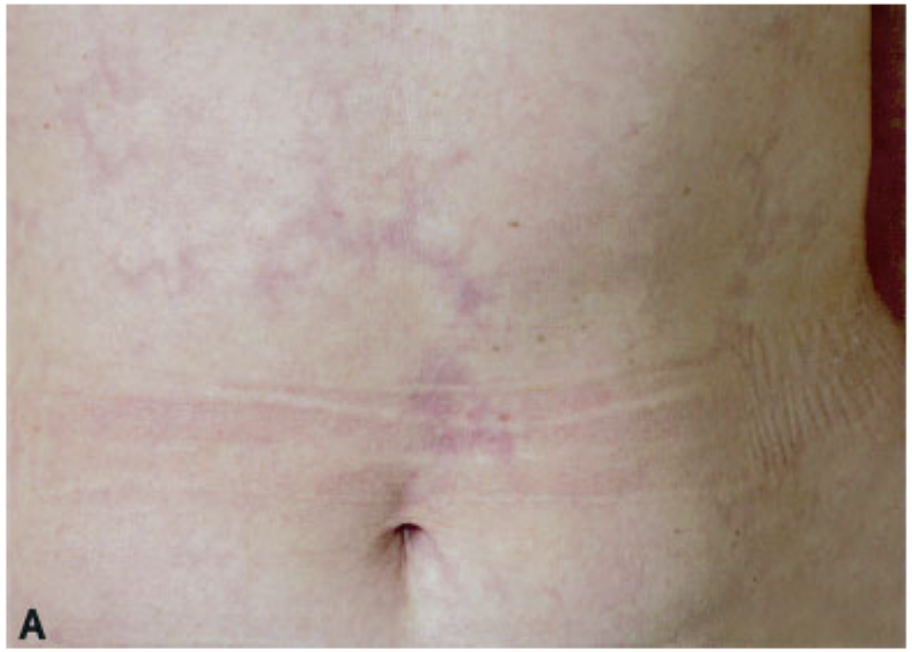
Prospective studies in adult patients with SLE show an association of persistent aPL and decreased cognitive function

- Attention
- Concentration
- Executive functioning

Check aPL in children with unexplained neurologic disorders

Avcin, 2012

Livedo reticularis

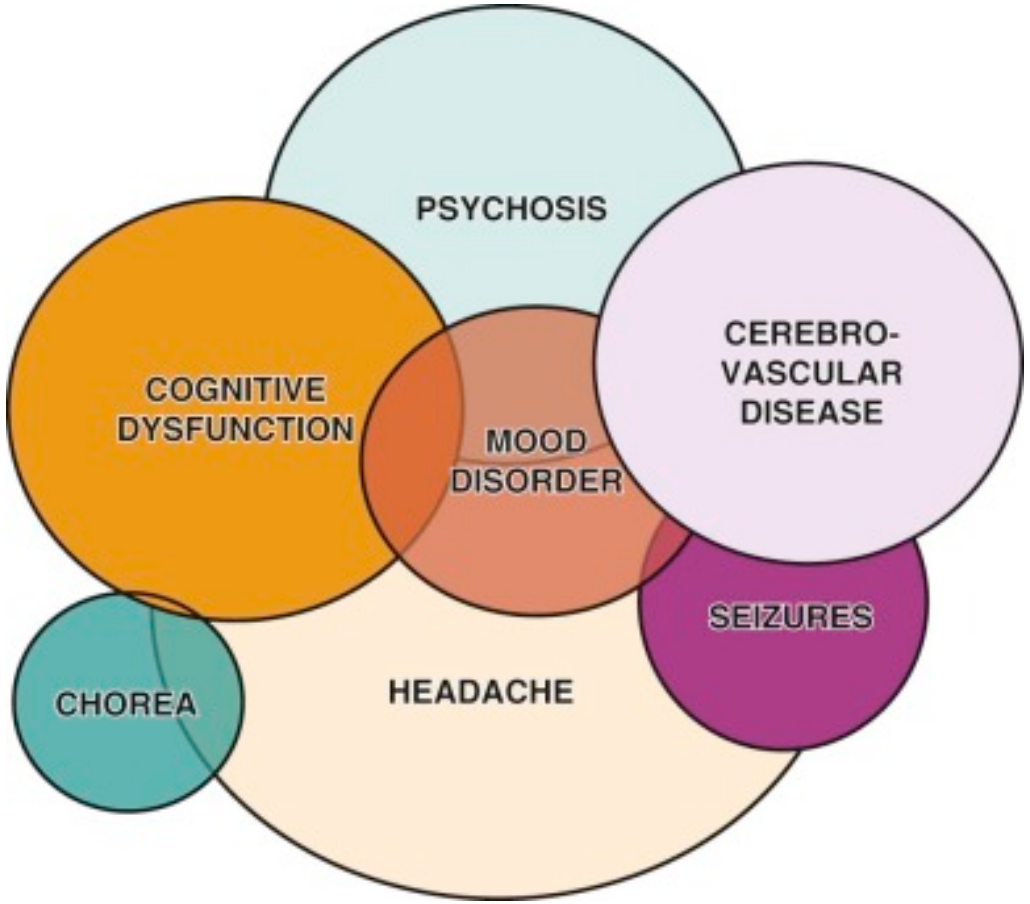


Livedo racemosa

**Presence is associated with arterial thrombotic events

ACR Image Bank

Neuropsychiatric Lupus



Robbins and Cotran, 2016

Neurologic Manifestations

- Central nervous system 20-95%
  - Headaches 43-72%
  - Seizures 26-51%
  - Psychosis 10-12%
  - Myelopathy 1%
  - Cerebral vascular disease 12%
  - Cognitive disorder 55%
  - Mood disorder 57%
  - Movement disorder 7-9%

- New onset or change of headaches may be red flag for serious process!
  - Increased intracranial pressure
  - Posterior reversible encephalopathy syndrome
  - Cerebral vein thrombosis
  - Cerebritis
  - Infection

Neurologic Manifestations

- Peripheral nervous system
  - Acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barre syndrome)
  - Autonomic disorder
  - Mononeuropathy, single/multiplex
  - Myasthenia gravis
  - Neuropathy, cranial
  - plexopathy
  - polyneuropathy

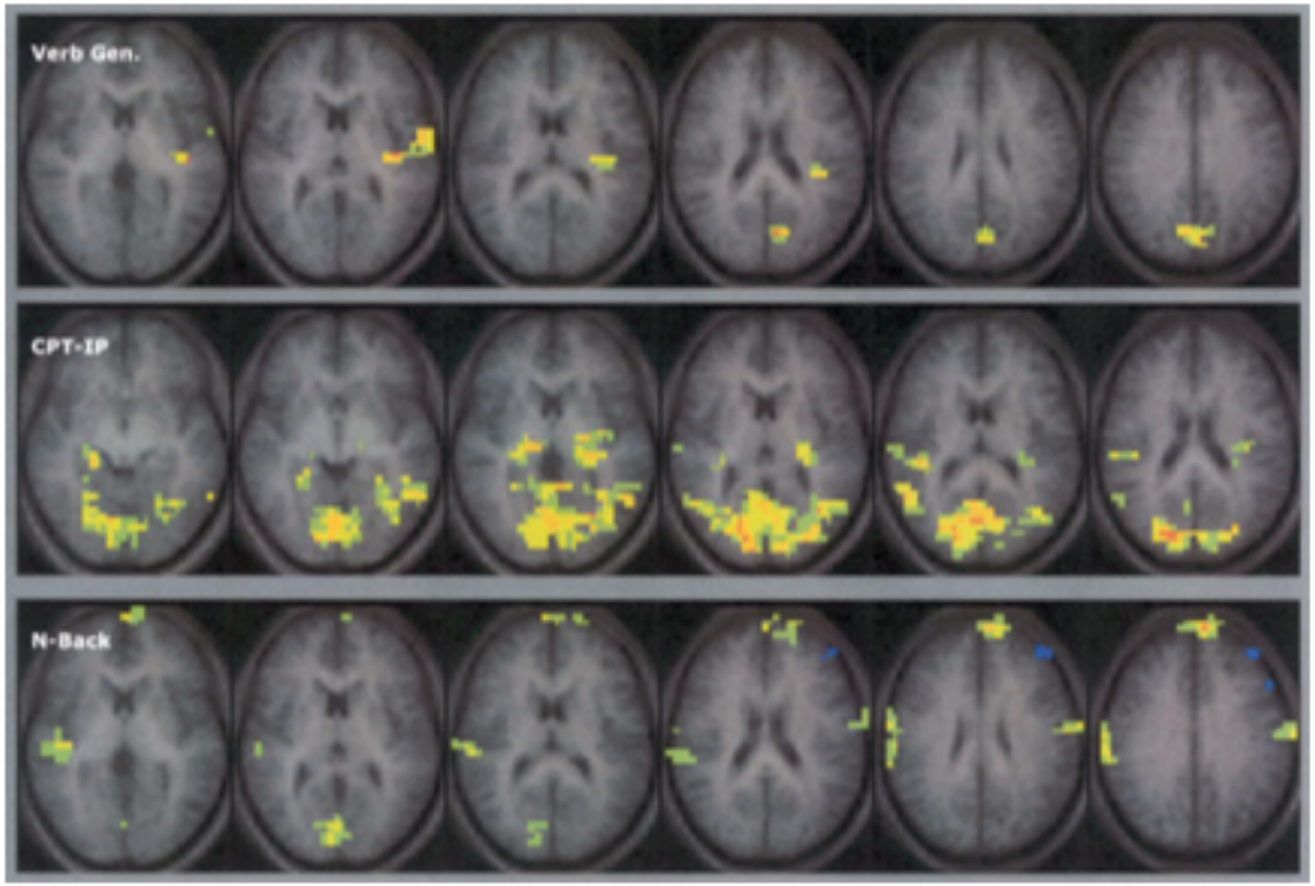
Neuropsychiatric testing (and persistent treatment) is one of the most effective ways to reduce morbidity from npSLE

FMRI Studies

Verb generation

Attention

Memory



Activation in pSLE
Activation in control

Imbalance in the activation in the Broca area. (Wernicke suppression.)

Imbalance in the activation suggests abnormal attention ability.

Imbalance in the activation suggests that pSLE patients have to work much harder for a given task

DiFrancesco, 2007

Lupus Nephritis

Table 2
Clinical features in pediatric and adult systemic lupus erythematosus over time[a]

Study	Hoffman 2009[b]			Ramirez-Gomez 2008[c]			Rood 1999[d]			Carreno 1999[e]			Font 1998[f]		
Organ Systems	pedSLE (n = 56)	aSLE (n = 194)	*P* Value	pedSLE (n = 230)	aSLE (n = 984)	*P* Value	pedSLE (n = 31)	aSLE (n = 135)	*P* Value	pedSLE (n = 49)	aSLE (n = 130)	*P* Value	pedSLE (n = 34)	aSLE (n = 396)	*P* Value
Renal															
Proteinuria	63.6	4.2	<0.01	49.1	45.3	NS	61	43	NS	—	—	—	—	—	—
Urinary cell casts	57.1	32	<0.001	—	—	—	65	53	NS	—	—	—	—	—	—
Nephropathy	62.5	36	<0.001	—	—	—	—	—	—	67.3	48.4	<0.05	50	34	NS

Although similar frequency, renal disease is often the presenting symptom and occurs within 2 years of diagnosis (90%).

Table 1. Comparison of renal involvement between the SLE cohorts*

	Childhood-onset SLE (n = 67)	Adult-onset SLE (n = 131)
Patients with *any* renal involvement†	52/67 (78)	68/131 (52)‡
Patients with at least 1 renal biopsy	43/67 (64)	24/131 (18)
WHO classification of the first renal biopsy		
Class I	0	0
Class II	10/43 (23)	5/22 (23)
Class III	11/43 (26)	4/22 (18)
Class IV	17/43 (40)	7/22 (32)
Class V	5/43 (11)	6/22 (27)

* Values are the number of patients/number evaluated (%). SLE = systemic lupus erythematosus; WHO = World Health Organization.
† Defined as a score of >0 in the renal domain of the SLE Disease Activity Index during the followup period.
‡ $P = 0.0005$.

Mina and Brunner, 2010

Classification of lupus nephritis

- Class I - minimal mesangial lupus nephritis
  - Normal glomeruli by light microscopy, but mesangial immune deposits by immunofluorescence
- Class II - mesangial proliferative lupus nephritis
  - Mesangial hypercellularity or mesangial matrix expansion bilaterally across the, with mesangial immune deposits by immunofluorescence

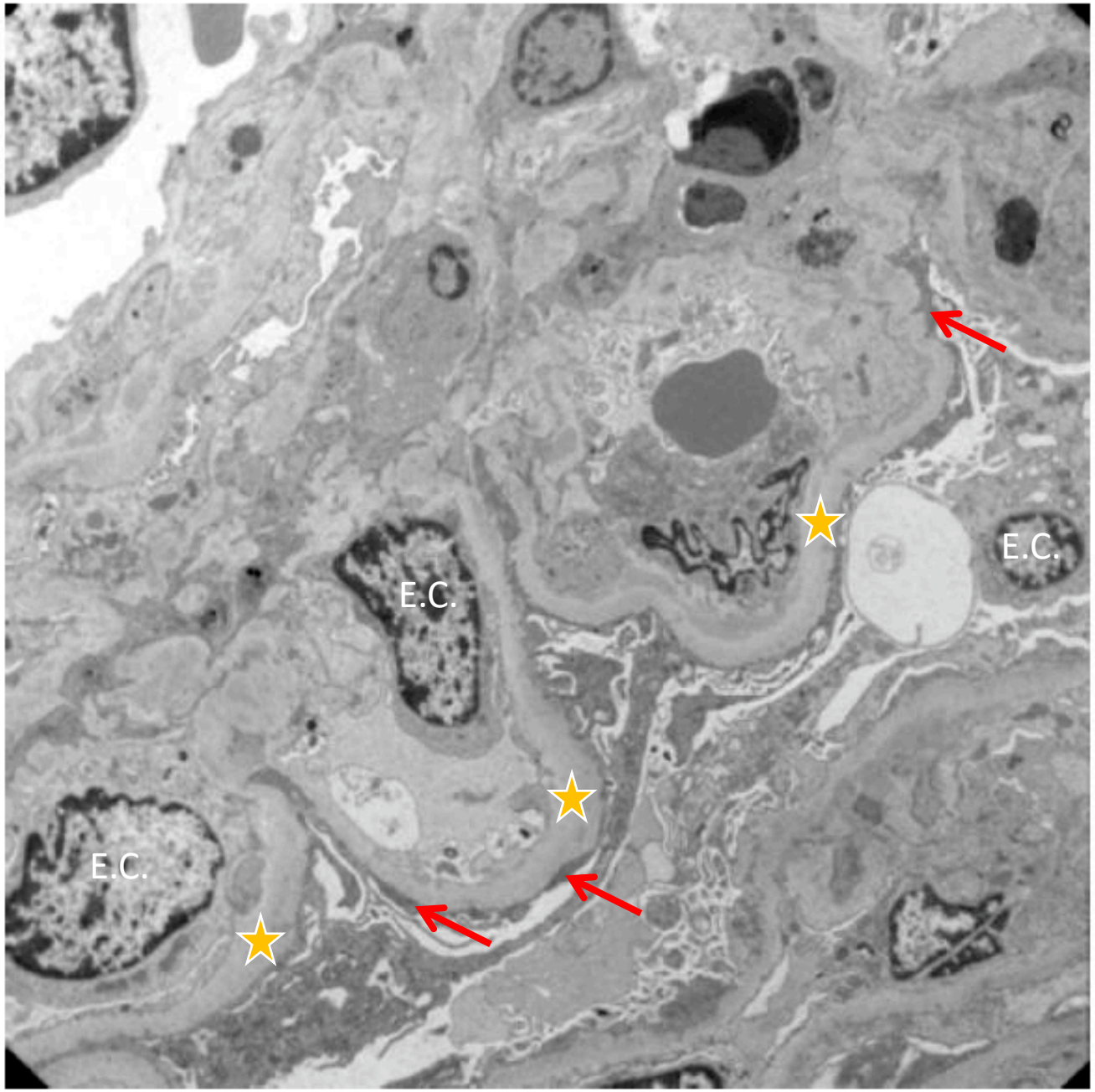
Treat the lupus.

- Class III - Focal lupus nephritis
  - active or chronic focal, segmental or global glomerular involving **less than 50% of all glomeruli** with diffuse subendothelial immune deposits
- Class IV - diffuse lupus nephritis
  - active or chronic diffuse, segmental or global glomerulonephritis involving **more than 50% of all glomeruli** with diffuse subendothelial immune deposits

Treat the lupus, aggressively.

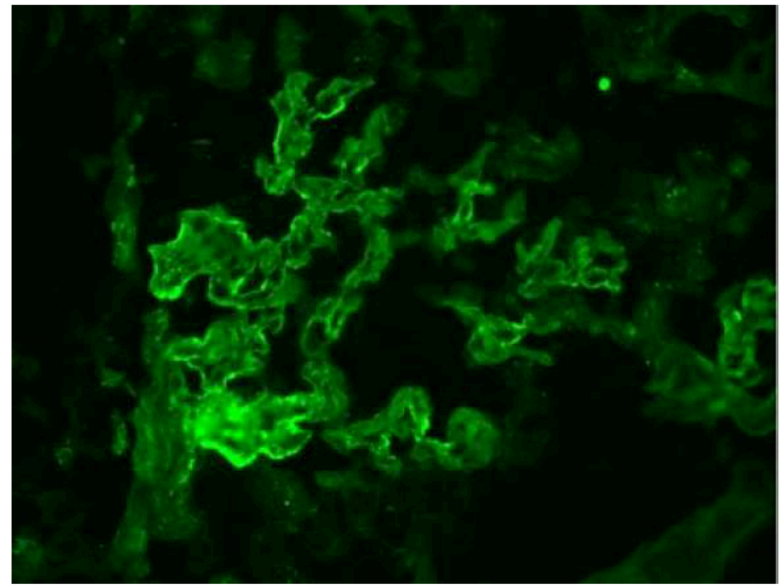
- Class V membranous lupus nephritis
  - global or segmental sub-epithelial immune deposits by immunofluorescence or electron microscopy
- Class VI advanced sclerosing lupus nephritis
  - > 90% glomeruli globally sclerosed without residual activity

Call the transplant team.

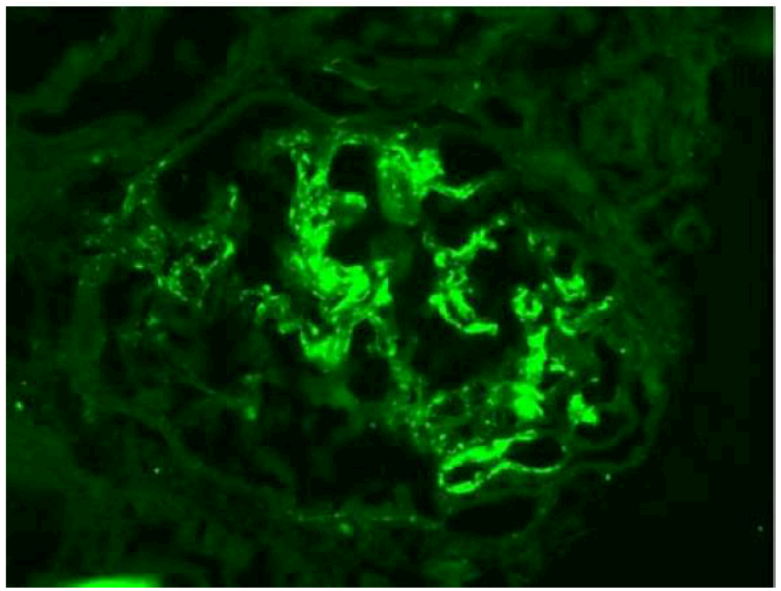


Electron Micrograph

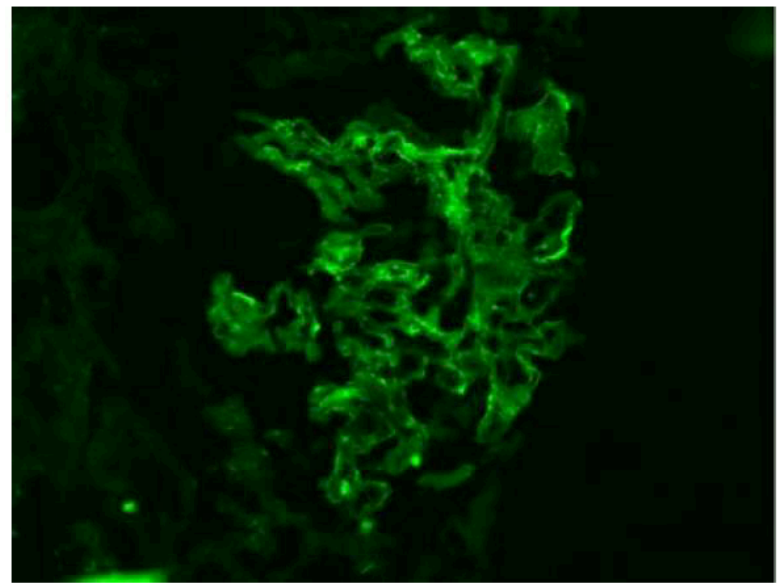
Immune complexes are highly anionic and cannot cross the GBM; this results in subendothelial deposits.



Igg

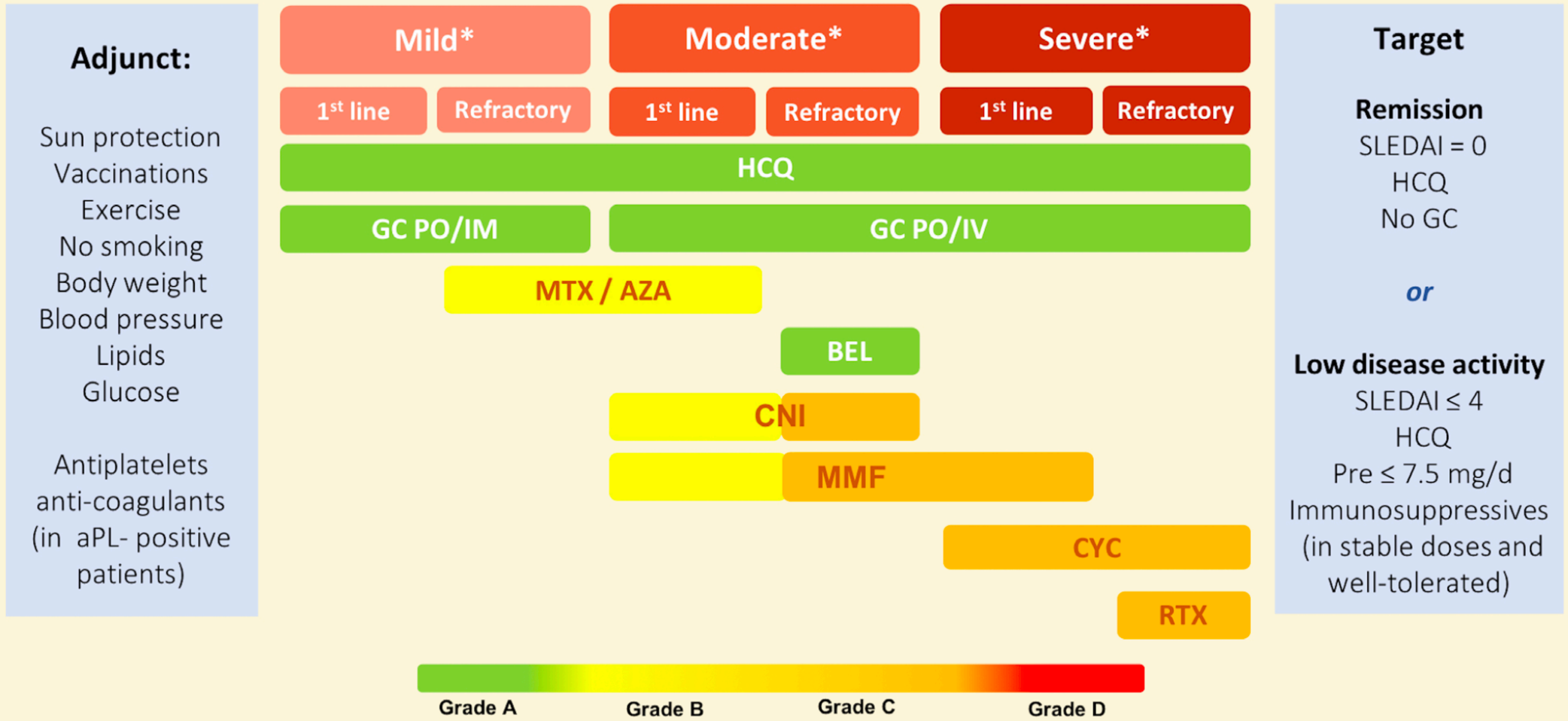


C3



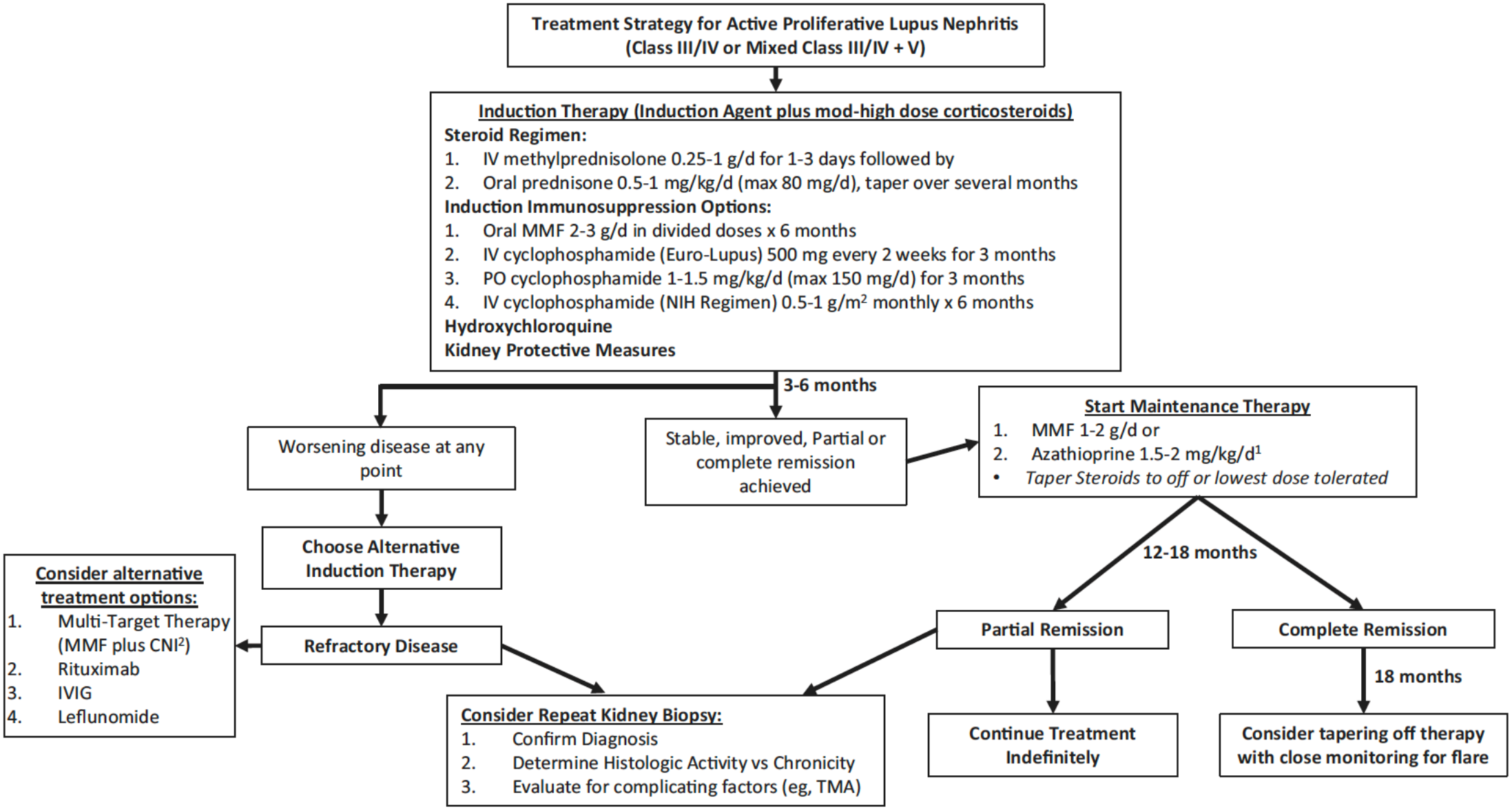
Iga

Treatment of non-renal Systemic Lupus Erythematosus

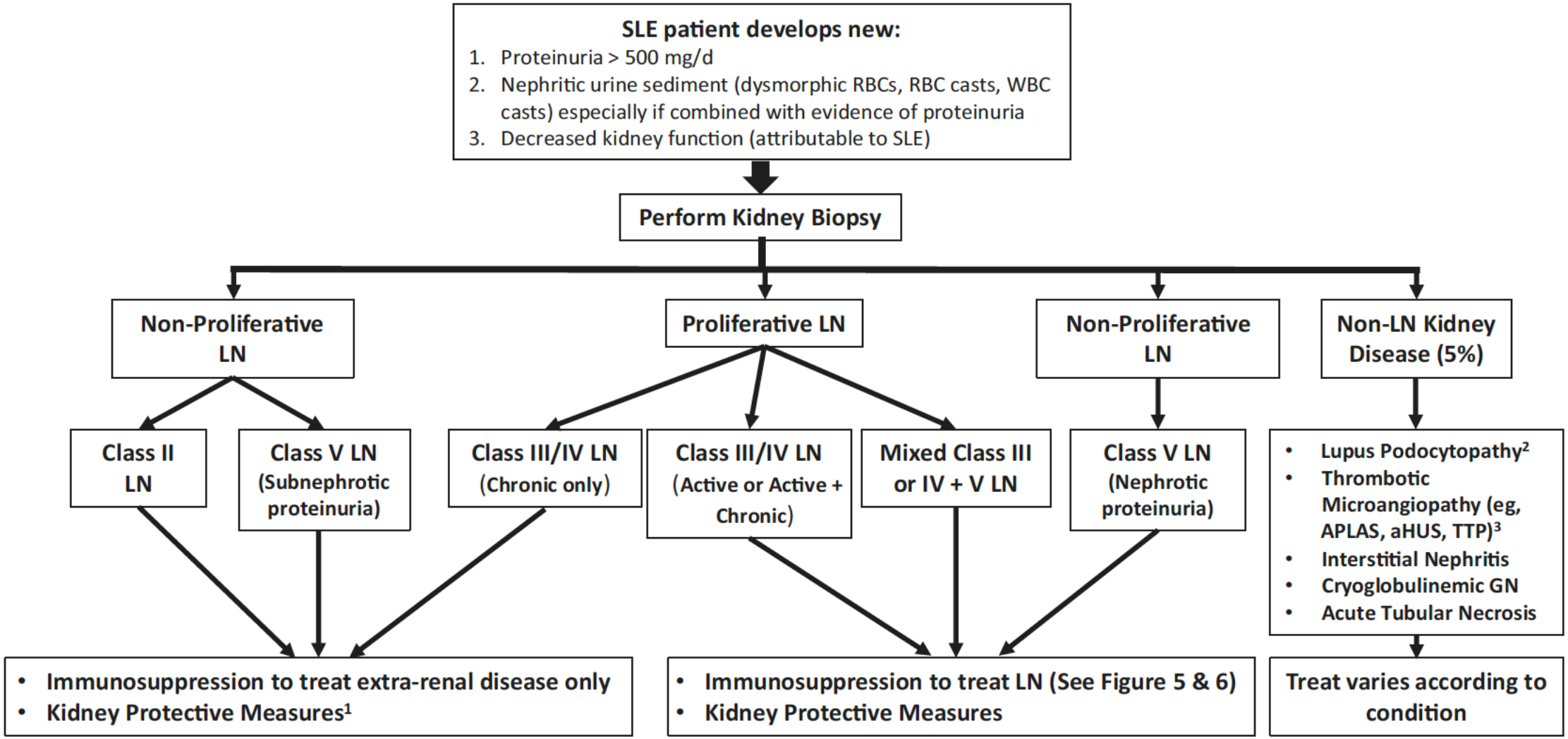


Mild: constitutional symptoms/ mild arthritis/ rash ≤9% BSA/PLTs 50-100 x 10^3/mm^3; SLEDAI≤6; BILAG C or ≤1 BILAG B manifestation
Moderate: RA-like arthritis/ rash 9-18% BSA/cutaneous vasculitis ≤18% BSA; PLTs 20-50x103/mm3/serositis; SLEDAI 7-12; ≥2 BILAG B manifestations
Severe: major organ threatening disease (nephritis, cerebritis, myelitis, pneumonitis, mesenteric vasculitis; thrombocytopenia with platelets <20x103/mm3; TTP-like disease or acute hemophagocytic syndrome; SLEDAI>12; ≥1 BILAG A manifestations

Fanouriakis, 2019


Treatment Strategy for Active Proliferative Lupus Nephritis (Class III/IV or Mixed Class III/IV + V)
Induction Therapy (Induction Agent plus mod-high dose corticosteroids)
Steroid Regimen:
1. IV methylprednisolone 0.25-1 g/d for 1-3 days followed by
2. Oral prednisone 0.5-1 mg/kg/d (max 80 mg/d), taper over several months
Induction Immunosuppression Options:
1. Oral MMF 2-3 g/d in divided doses x 6 months
2. IV cyclophosphamide (Euro-Lupus) 500 mg every 2 weeks for 3 months
3. PO cyclophosphamide 1-1.5 mg/kg/d (max 150 mg/d) for 3 months
4. IV cyclophosphamide (NIH Regimen) 0.5-1 g/m2 monthly x 6 months
Hydroxychloroquine
Kidney Protective Measures
3-6 months
Worsening disease at any point
Stable, improved, Partial or complete remission achieved
Start Maintenance Therapy
1. MMF 1-2 g/d or
2. Azathioprine 1.5-2 mg/kg/d1
• Taper Steroids to off or lowest dose tolerated
12-18 months
Choose Alternative Induction Therapy
Consider alternative treatment options:
1. Multi-Target Therapy (MMF plus CNI2)
2. Rituximab
3. IVIG
4. Leflunomide
Refractory Disease
Partial Remission
Complete Remission
18 months
Consider Repeat Kidney Biopsy:
1. Confirm Diagnosis
2. Determine Histologic Activity vs Chronicity
3. Evaluate for complicating factors (eg, TMA)
Continue Treatment Indefinitely
Consider tapering off therapy with close monitoring for flare

Parikh, 2020.


SLE patient develops new:
1. Proteinuria > 500 mg/d
2. Nephritic urine sediment (dysmorphic RBCs, RBC casts, WBC casts) especially if combined with evidence of proteinuria
3. Decreased kidney function (attributable to SLE)
Perform Kidney Biopsy
Non-Proliferative LN
Proliferative LN
Non-Proliferative LN
Non-LN Kidney Disease (5%)
Class II LN
Class V LN (Subnephrotic proteinuria)
Class III/IV LN (Chronic only)
Class III/IV LN (Active or Active + Chronic)
Mixed Class III or IV + V LN
Class V LN (Nephrotic proteinuria)
• Lupus Podocytopathy[2]
• Thrombotic Microangiopathy (eg, APLAS, aHUS, TTP)[3]
• Interstitial Nephritis
• Cryoglobulinemic GN
• Acute Tubular Necrosis
• Immunosuppression to treat extra-renal disease only
• Kidney Protective Measures[1]
• Immunosuppression to treat LN (See Figure 5 & 6)
• Kidney Protective Measures
Treat varies according to condition

Parikh, 2020.

Case Presentation

- Why did I pick this case?
  - Adolescent lupus from peri-to-post puberty
  - Multiple organ system involvement
  - Subjective versus objective disease activity

Rheumatology Care History

As a brief synopsis of her care; her initial HPI was:

The patient is a 13-year-old female who was referred from Pediatric Hematology Oncology here at Yale after being discharged from the hospital, where she is evaluated for pancytopenia. Her mother reports that her complaints started approximately 3 months ago with an insidious onset of fever and pallor. This continued for several weeks until eventually the fatigue had been too significant and was impacting her life, so she was brought to the Emergency Department. At that time, they recall that she had been febrile more days than not, approximately 5 days a week, to 100.1 occasionally. She had been treated with Tylenol with some effect, but fever seemed to be persistent. In the Emergency Department she was noted to have an anemia, thrombocytopenia, and leukopenia. She was admitted to the Hematology Oncology service for neutropenia and fever, and was started on broad-spectrum antibiotics. During her fairly short stay here received serial CBCs with no other intervention. She was discharged to follow up in Hematology Oncology Clinic, and she has regularly, with CBCs that show continued leukopenia with ANCs around 1000, but never so significant as to require repeat hospitalization. Her anemia has fluctuated between 6 and approximately 8 g/dL of hemoglobin. The other pertinent lab was an ANA, which was listed as 1-640. She had a lactate dehydrogenase of 436. She had mild elevations of her liver enzymes on admission, but after hydration those seemed to normalize, and she had a normal electrolyte panel. Her mother reports that the most concerning complaint is the fatigue and her ill appearance. Her general review of systems is pertinent for occasional headaches, although nothing with any neurological issues. She does not complain of any eye redness or pain. She does not describe any oral or nasal ulcerations. She says that she is very fatigued and she has lost about 15 pounds in the past 3 months, and her mother said she is looking significantly ill. She has no difficulty swallowing food or water. She has no difficulty with daily ambulation; however, when she walks up a flight of stairs, she notes that she is more short of breath than previous. She does not appreciate any palpitations when this happens. She has no nausea, vomiting, diarrhea. She does not describe any particular skin rash. **ANA1:640;dsDNA --> 700;C3/C4 --> C4- undetectable; C3-41; Pancytopenia; G6PD levels --> normal**

Past Medical History
Past diagnoses: Sickle cell trait (Recent hospitalization was her first.)
Medications: None
Surgeries: None.
Allergies: NKDA
Immunizations: Up to date.

Family history
She has 2 older siblings (one brother and one sister)
There is no significant illnesses throughout the family; maternal grandmother with elevated thyroid growth.
Diabetes in mulitple people
Maternal side with "blood issues" and difficulty maintaining pregnancy (no specific members)

Social History
School information: Aurelia is going into the 8th grade.
Social Activity: She used to do cheerleading, has not been able to do anything in the summer due to illness
Physical activity: Limited since the onset of the summer.

8/2015 --> Diagnosed with SLE; admitted for steroid pulse and starting medications
9/2015 --> No complaints, continued all medications.
12/2015 --> Continued steroid wean, tolerating medications well
3/2016 --> Off steroids, doing well
5/2016 --> Doing well.
8/2016 --> Doing well; question of full medication adherence. (low complement, high dsDNA, normal inflammatory markers)
1/2017 --> Doing well.
5/2017 --> Sporadic dosing of medication, admitted to hospital for fatigue (abnormal labs)
6/2017 --> Feeling well; restarted all medication
12/2017 --> Feeling well; reasonable adherence to medication regimen (rising dsDNA titer, normal inflammatory markers, mild low complement)
3/2018 --> Feeling well; reasonable adherence to medication regimen
9/2018 --> Poor adherence to med regimen (C3- 51/ C4- 8; ESR 10)
11/2018 --> Poor adherence to med regimen (C3- 54/ C4- <10; ESR 15; dsDNA 177)
2/2019 --> Poor adherence to med regimen (C3- 61/ C4- <10; ESR 18; dsDNA 147)
6/2019 --> Poor adherence to med regimen (C3- 30/ C4- 5; ESR 41; dsDNA >379); Added steroids
9/2019 --> hospitalization with gram-negative rod sepsis (diagnosed as pasteurella canis, completed course of intravenous antibiotics); C3- 22/ C4 <2; ESR 30; dsDNA >1000).
11/2019 --> persistent cytopenia
1/2020 --> Received 1st course rituximab
3/2020 --> Doing well.
6/2020 --> initially reported doing well, lab shows significant anemia. (C3- 34/ C4- 8; ESR 85; IgG 1995; dsDNA >379)
7/2020 --> anaphylaxis with rituximab administration; subsequent hospitalization for renal biopsy showed significant small-vessel vasculitis in the glomeruli, no chronicity or significant scarring in the kidney, difficulty controlling hypertension; admitted again for enteritis which was seemingly associated with a poor absorption of medications
8/2020 --> Starting cytoxan; large volume of hypertension
9/2020--> C3- 75/ C4- 14; ESR 17; dsDNA 36
10/1/2020 --> 4th dose of cyclophosphamide
10/15/2020 --> 5th dose of cyclophosphamide; C3- 89/ C4- 15; ESR 17; dsDNA 44

Initial Admission

- Admitted to hematology for pancytopenia → transfused and discharged, follow-up in heme clinic and rheumatology

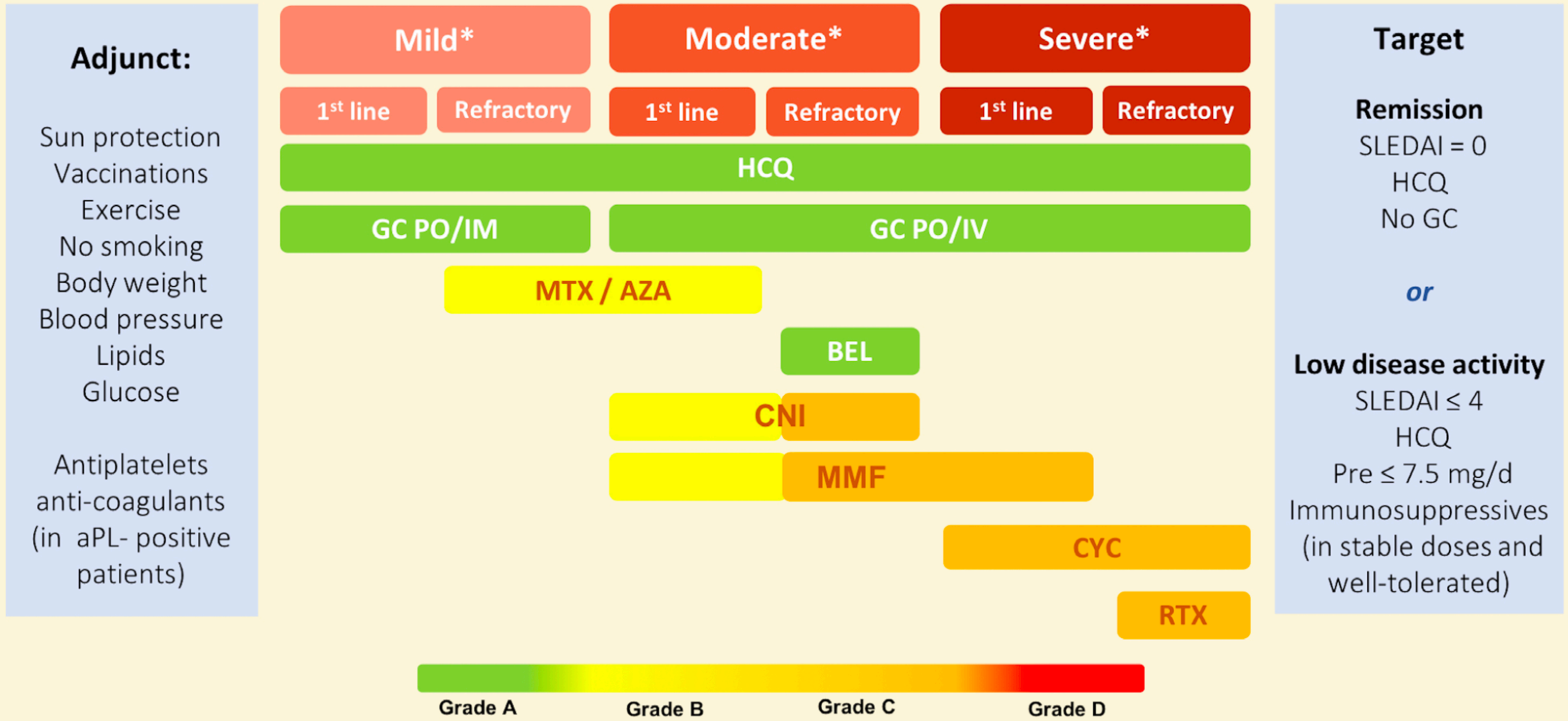
CBC	
CBC with Differential	See Below
WBC	1.4 * c
RBC	3.6
Hemoglobin	8.0
Hematocrit	25.8
MCV	72
MCH	22.5
MCHC	31.1
RDW-CV	13.9
Reticulocyte Count	1.0
Absolute Reticuloc...	37.6
Retic Ct Pct	
Absolute Reticuloc...	
Immature Retic Fract	
Reticulocyte Hgb E...	
nRBC	
Platelets	104 *
MPV	9.9
Neutrophils	51
Lymphocytes	17
Monocytes	8
Eosinophils	1
Basophils	1
Atypical Lymphocytes	3
Metamyelocytes	
ANC (Abs Neutrophi...	1.0
Lymphocyte Absolute	
Absolute Lymphocyt...	0.2
Monocytes (Absolute)	

CHEMISTRY GENERAL	
Sodium	135
Potassium	3.8
Chloride	98
CO2	21.0
Anion Gap	16
BUN	10
Creatinine	0.5
BUN/Creatinine Ratio	20.0
eGFR (NON African-...	
eGFR (Afr Amer)	
Glucose	109
Calcium	8.1
Calcium, Ionized, ...	
Magnesium	2.1 *
Phosphorus	4.1 *
Uric Acid	3.3
Total Bilirubin	0.27
Bilirubin, Direct	
Alkaline Phosphatase	40
Alanine Aminotrans...	23
Aspartate Aminotra...	47
AST/ALT Ratio	
LD	500
Haptoglobin	
Total Protein	6.4
Albumin	2.8
Globulin	3.6
A/G Ratio	0.8

Physical Examination
BP 96/47 mmHg | Pulse 57 | Temp(Src) 99.7 °F (37.6 °C) (Temporal) | Ht 5' 4.13" (1.629 m) | Wt 40.4 kg | BMI 15.22 kg/m2
General appearance: NAD, conversant, ill appearing cachexic
Eyes: PERRL, EOMI, no injection or erythema of the sclera, no abnormalities noted in the iris.
HEENT: Oropharynx clear with moist mucous membranes and no mucosal ulcerations; normal hard and soft palate. Normal aperture of the mouth.
Neck: Full range of cervical spine motion, no thyromegaly or lymphadenopathy
Lungs: CTA, with normal respiratory effort
CV: RRR, no murmurs appreciated
Abdomen: Soft, non-tender; no masses or HSM; difficult to palpate as the patient reports that she is very ticklish
Skin: No malar rash but a lacy appearance with sandpaper feel to the extremities.
Musculoskeletal examination:
Joint space: No synovitis, no limitations in the range of motion, no tenderness.
Muscle: Normal strength, no tenderness, no allodynia.
Psych: Appropriate affect, alert and oriented to person, place and time

IgA		304 *
IgM		354 *
Immunoglobulin G		2,110 *
Creatinine, Urine,...		
Beta-2 Microglobulin		
C3 Complement		41 *
C4 Complement		<10 *
Total Complement, ...		
ANA	Positive *	
ANA Titer	1:640	
ANA Pattern	Homogeneous	
ANA Titer 1		
ANA Pattern 1		
ANA Titer 2		
ANA Pattern 2		
ANA Titer 3		
ANA Pattern 3		
dsDNA Ab (Crithidia)		
Sm Antibody		
Sm/RNP Antibody		
SS-A Sjogrens Ab		
dsDNA Ab		607.2 *
dsDNA Ab Titer		
ENA Smith (SM) Ab		*Negative* *
Smith and RNP (ENA...		*Negative* *
ENA SSA (RO) Ab		*Negative* *
ENA SSB (LA) Ab		*Negative* *
SS-B Sjogrens Ab		
Scleroderma (Scl-7...		*Negative* *
Jo-1 IgG Antibody		*Negative* *
ANCA Screen		*Negative* *
Anticardiolipin IgG		4.1 *
Anticardiolipin IgA		<1.4 *
Anticardiolipin IgM		3.8 *
Beta-2 Glycoprotei...		<6.4 *
Beta-2 Glycoprotei...		2.3 *

Treatment of non-renal Systemic Lupus Erythematosus



Mild: constitutional symptoms/ mild arthritis/ rash ≤9% BSA/PLTs 50-100 x 10^3/mm^3; SLEDAI≤6; BILAG C or ≤1 BILAG B manifestation
Moderate: RA-like arthritis/ rash 9-18% BSA/cutaneous vasculitis ≤18% BSA; PLTs 20-50x103/mm3/serositis; SLEDAI 7-12; ≥2 BILAG B manifestations
Severe: major organ threatening disease (nephritis, cerebritis, myelitis, pneumonitis, mesenteric vasculitis; thrombocytopenia with platelets <20x103/mm3; TTP-like disease or acute hemophagocytic syndrome; SLEDAI>12; ≥1 BILAG A manifestations

Fanouriakis, 2019

8/27/2015

- Evaluated in outpatient clinic → admitted for continued evaluation
  - Pulse dose solumedrol (30mg/kg/day or 1g)
  - PPI
  - Start HCQ and MMF
  - [IVIg if no improvement in the platelets: did not need]
- Tentative Dx: pSLE with concern for additional MAS
  - DDx: ANCA associated vasculitis; APS; JDMS

	WBC	Hemoglobin	Platelets	C3 Complement	C4 Complement	dsDNA Ab	BUN	Creatinine
Ref. Range	Latest Ref Rai	Latest Ref Ran	Latest Ref F	Latest Ref Range: !	Latest Ref Range: '	Latest Ref Ra	Latest Re	Latest Ref Ra
8/27/2015 1510				41 *	<10 *	607.2 * !	11 *	0.7 *
8/27/2015 2040	1.7	7.6	146					
8/28/2015 1419						555.8 * !		
8/28/2015 1853	1.6 *	7.2 *	163 *					
8/29/2015 0712			163 *					
8/30/2015 0908	3.1	7.5	170 *					
8/31/2015 0630	4.3 *	7.4 *	175 *				13 *	0.4 *
9/1/2015 0641	6.0	7.6	207					
9/4/2015 1600	11.4	8.2	190	50 *	<10 *	789.9 * !	26	0.5
10/14/2015 1355	10.9	12.8	221			87.2 * !		
12/10/2015 1417	11.6	14.8	190	104 *	<10 *	48.2 * !	11	0.6

10/9/2015

6. Prednisone to taper:

30 mg in am, 20 mg in pm x 3 weeks,
20 mg in am, 20 mg in pm x 3 weeks,
20 mg in am, 10 mg in pm x 3 weeks,
Follow-up visit to determine the continued taper from there.

12/10/2015

1. Steroid wean:

This Saturday to 10mg with breakfast and dinner. Keep for 2 weeks...
Then 10mg in the morning, 5mg in the evening. Keep for 2 weeks
Then 5mg in the morning, 5mg in the evening. Keep for 2 weeks.
Then 5mg in the morning only. Keep for 2 weeks.
Then off

	Sedimentation Rate (ESR)
Ref. Range	Latest Ref Range: 0 - 20 mm/hr
8/27/2015 1510	58 *
8/31/2015 0630	60 *
9/4/2015 1600	31
12/10/2015 1417	8
3/21/2016 1516	6

	Sedimentation Rate (ESR)
Ref. Range	Latest Ref Range: 0 - 20 mm/hr
3/21/2016 1516	6
5/16/2016 1554	5
8/22/2016 1449	11
1/30/2017 1134	24 ▲
5/28/2017 1901	20
5/29/2017 1244	16
6/23/2017 1142	21 ▲
12/19/2017 1618	15
3/20/2018 1446	12
9/21/2018 1118	10
9/25/2018 1502	14
11/27/2018 1433	15
2/5/2019 1558	18
6/11/2019 1550	41 ▲
9/3/2019 1610	47 ▲

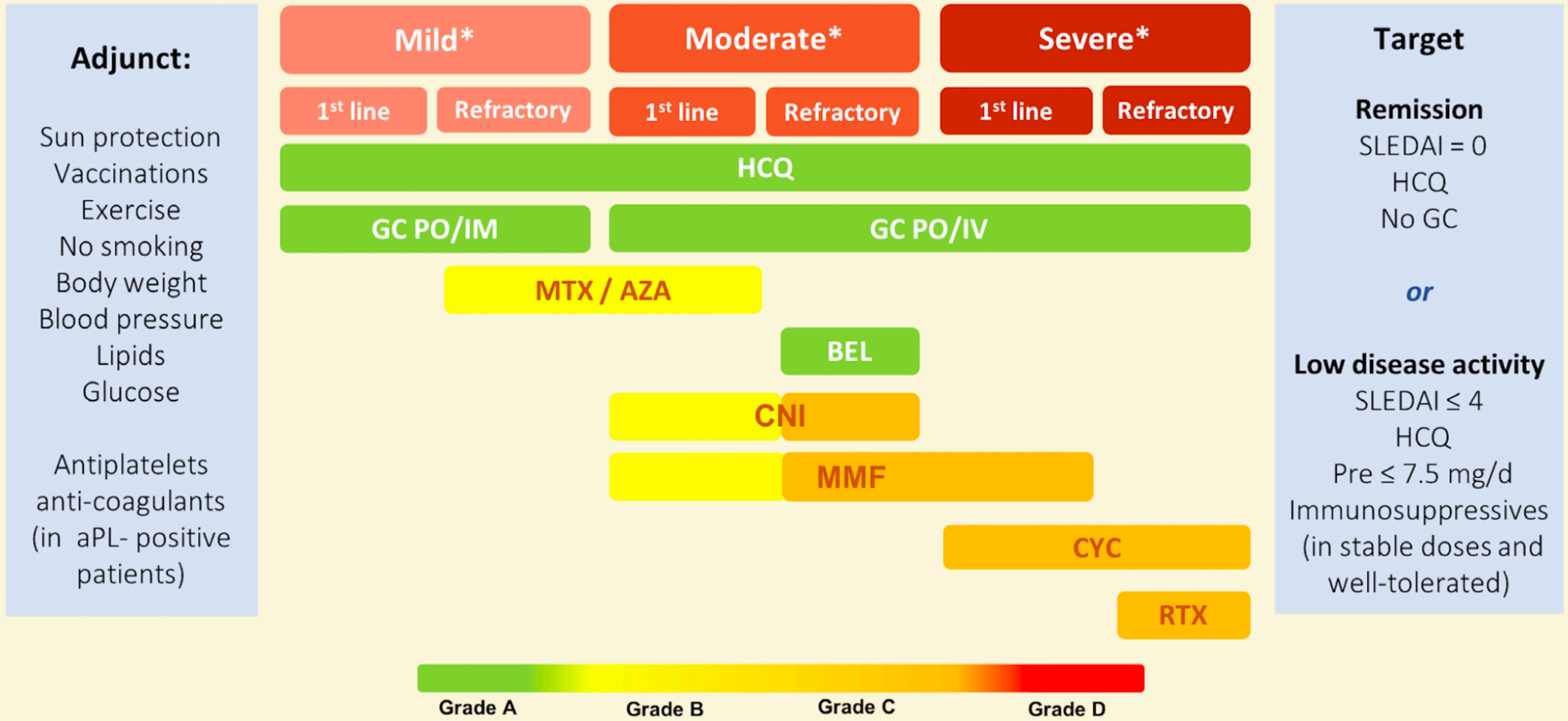
5/2017- Admission

General appearance: NAD, conversant.
Eyes: PERRL, EOMI, no injection or erythema of the sclera, no abnormalities noted in the iris.
HEENT: Oropharynx clear with moist mucous membranes and no mucosal ulcerations; large multidirectional palatal ulceration. Normal aperture of the mouth.
Neck: Full range of cervical spine motion, no thyromegaly or lymphadenopathy
Lungs: CTA, with normal respiratory effort
CV: RRR, no murmurs appreciated
Abdomen: Soft, non-tender; no masses or HSM.
Skin: Mild erythematous macules/plaques over the cheeks and bridge of the nose (classic malar rash); no hair loss.
Musculoskeletal examination:
Joint space: No synovitis, no limitations in the range of motion, no tenderness.
Muscle: Normal strength, no tenderness, no allodynia.
Psych: Appropriate affect, alert and oriented to person, place and time

Assessment:
Aurelia is a 15 year old female with a history of SLE who is admitted for pancytopenia and skin rash, likely associated with SLE flare. She has been poorly compliant with medications in the past several weeks and has also described sun exposure without sunscreen use; these are all likely contributors to SLE flare. (likely not MAS with normal ferritin; normal ESR and pancytopenia are likely a combination of smoldering SLE activity and moderate medication usage.)

Component	Latest Ref Rng & Units	5/30/2017	5/29/2017
WBC	4.0 - 13.0 x1000/uL	**2.6 (L)**	
RBC	3.6 - 5.8 M/uL	4.8	
Hemoglobin	12.0 - 15.0 g/dL	**10.5 (L)**	
Hematocrit	37.0 - 48.0 %	**34.0 (L)**	
MCV	78.0 - 98.0 fL	**71.1 (L)**	
MCHC	31.0 - 36.0 g/dL	**30.9 (L)**	
RDW-CV	11.0 - 18.0 %	14.8	
Platelets	140 - 465 x1000/uL	215	
MPV	6.0 - 11.0 fL		
ANC (Abs Neutrophil Count)	1.0 - 10.0 x 1000/uL	1.6	
Neutrophils	32.0 - 79.0 %	61.8	
Lymphocytes	13.0 - 52.0 %	30.9	
Absolute Lymphocyte Count	1.0 - 4.0 x 1000/uL	**0.8 (L)**	
dsDNA Ab	<30.0 IU/mL		**>1,000.0 (H)**
C3 Complement	81 - 145 mg/dL		**37 (L)**
C4 Complement	16 - 39 mg/dL		**<10 (L)**
Sedimentation Rate (ESR)	0 - 20 mm/hr		16
CRP, High Sensitivity	0.1 - 3 mg/L	2.7	

Treatment of non-renal Systemic Lupus Erythematosus



Mild: constitutional symptoms/ mild arthritis/ rash ≤9% BSA/PLTs 50-100 x 10^3/mm^3; SLEDAI≤6; BILAG C or ≤1 BILAG B manifestation
Moderate: RA-like arthritis/ rash 9-18% BSA/cutaneous vasculitis ≤18% BSA; PLTs 20-50x103/mm3/serositis; SLEDAI 7-12; ≥2 BILAG B manifestations
Severe: major organ threatening disease (nephritis, cerebritis, myelitis, pneumonitis, mesenteric vasculitis; thrombocytopenia with platelets <20x103/mm3; TTP-like disease or acute hemophagocytic syndrome; SLEDAI>12; ≥1 BILAG A manifestations

Fanouriakis, 2019

5/2017

- Treatment:
  - Solumedrol 1g for 3 days → Prednisone 60mg BID
  - MMF 1500mg PO BID
  - HCQ 300mg PO qday
  - Discussion of additional DMARD, rituximab, family was against additional medication because adherence to MMF and HCQ was very poor and she felt these were otherwise working well

9/2019

- Fever and syncope while at home
- Admitted to BH in shock
  - Epinephrine and dopamine drips
  - Acute renal failure
  - ICU, Rheumatology, and Nephrology consults
    - stress dose steroid

9/2019

Mr. Whiskers (representation)

Blood Culture	Abnormal Stain !! Pasteurella canis !
Blood Culture Gram Stain	!! Aerobic and Anaerobic Bottle Gram negative rods

Resulting Agency: BH LAB

Susceptibility

	Pasteurella canis Not Specified	
Cefazolin	<=4 ug/mL	**Susceptible**
Meropenem	0.5 ug/mL	**Susceptible**
Piperacillin + Tazobactam		**Susceptible**
Tigecycline	<=0.5 ug/mL	**Susceptible**

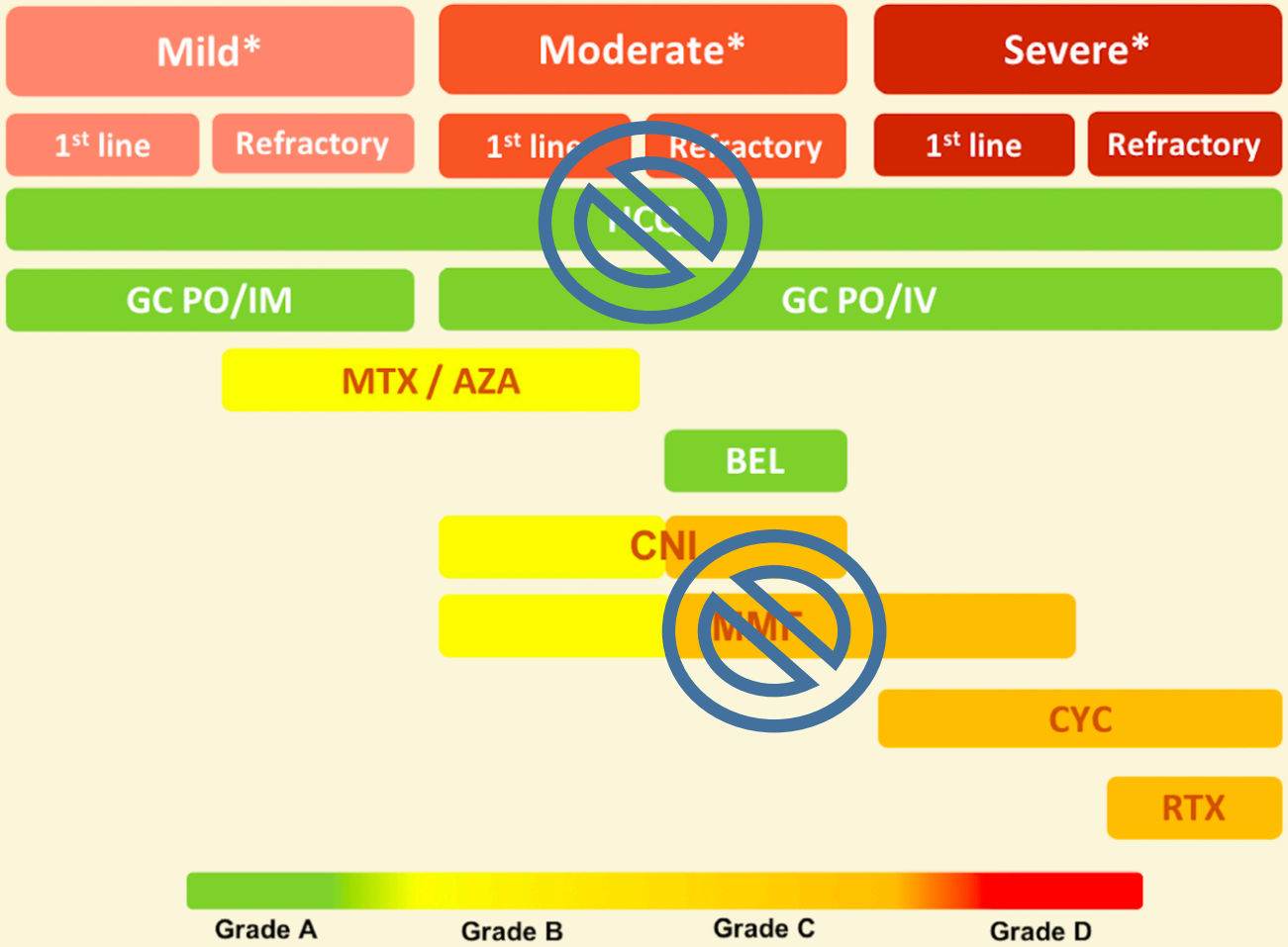
	WBC	Hemoglobin	Platelets	C3 Complement	C4 Complement	dsDNA Ab	BUN	Creatinine
Ref. Range	Latest Ref Rai	Latest Ref Ran	Latest Ref F	Latest Ref Range: !	Latest Ref Range: '	Latest Ref Ra	Latest Re	Latest Ref Ra
9/3/2019 1610	2.9 *	6.9 *	77 *	28 *	5 *		9	0.54
9/18/2019 0917	10.1 *	6.7 *	63 *				32	2.53
9/18/2019 1840							31	2.15
9/18/2019 2310		9.6						
9/19/2019 0411	5.9 *	9.9 *	37 *				34	2.03
9/19/2019 0809							33	1.79
9/19/2019 1514				22	<2	>1,000.0 *		
9/19/2019 2119	7.4 *	9.5 *	28 *				34	1.41
9/20/2019 0650	7.1 *	8.8 *	24 *				34	1.27
9/20/2019 2107	5.8 *	8.0 *	17 *				39	1.28
9/21/2019 0438	5.5 *	7.9 *	15 *				42	1.20
9/22/2019 1044	7.4 *	8.3 *	14 *				45	0.86
9/23/2019 0552	6.3 *	8.4 *	17 *				41	0.73
9/24/2019 0935	6.4 *	8.0 *	33 *				27	0.60
9/25/2019 0613	6.6 *	8.1 *	49 *				19	0.51
9/26/2019 0519	5.0 *	7.2 *	71 *				14	0.47
9/26/2019 1009	7.8 *	7.0 *	78 *					

Treatment of non-renal Systemic Lupus Erythematosus

Adjunct:

Sun protection
Vaccinations
Exercise
No smoking
Body weight
Blood pressure
Lipids
Glucose

Antiplatelets
anti-coagulants
(in aPL- positive patients)



Target

Remission
SLEDAI = 0
HCQ
No GC

or

Low disease activity
SLEDAI ≤ 4
HCQ
Pre ≤ 7.5 mg/d
Immunosuppressives
(in stable doses and well-tolerated)

Mild: constitutional symptoms/ mild arthritis/ rash ≤9% BSA/PLTs 50-100 x 10^3/mm^3; SLEDAI≤6; BILAG C or ≤1 BILAG B manifestation
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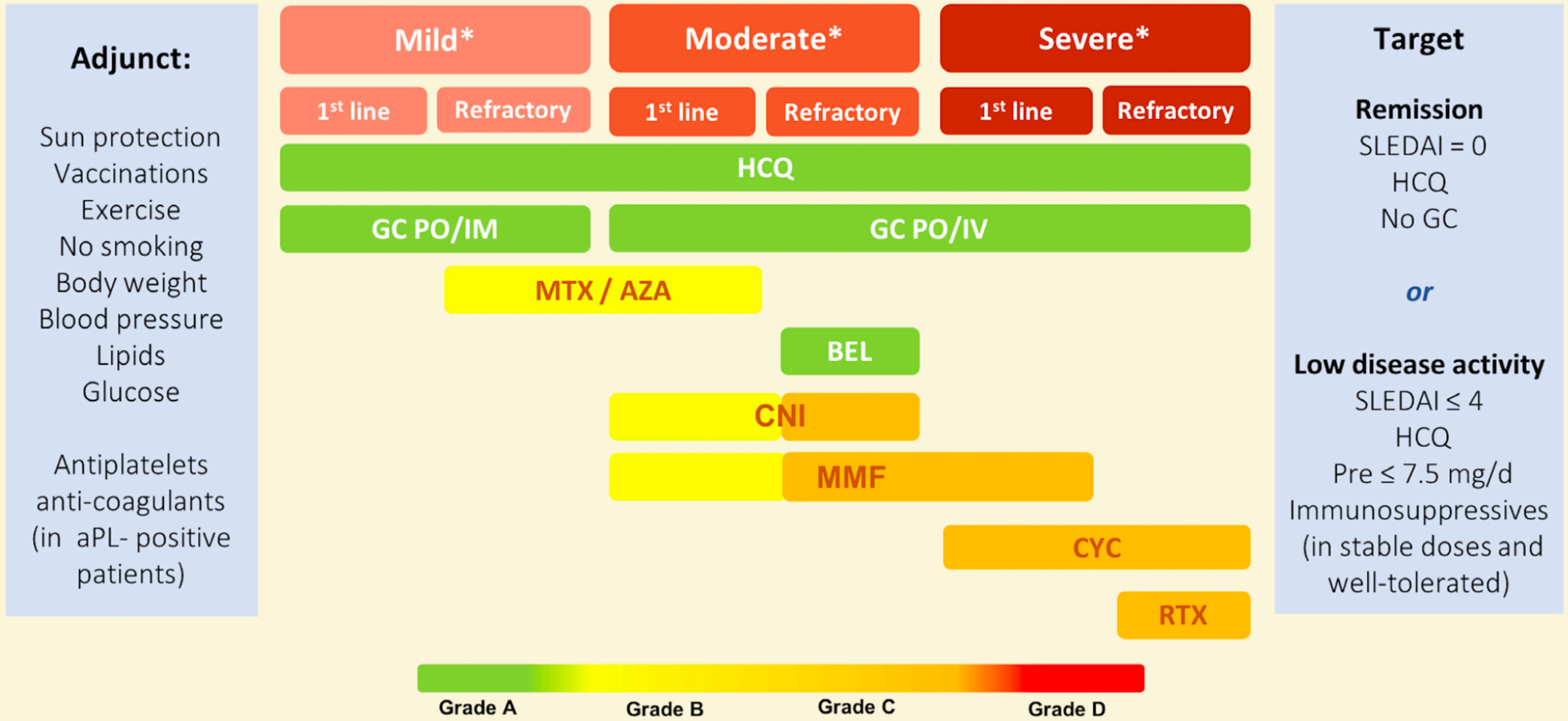
Fanouriakis, 2019

11/2019-1/2020

- 11/2019 → First follow-up after hospitalization, MMF never restarted, HCQ is taken daily. Bilateral knee arthritis. Labs show persistent cytopenia
- 1/2020 → Feels well; interval evaluation with hematology shows persistent cytopenia. Gave 1st course of rituximab, restarted MMF.

Component	Latest Ref Rng & Units	1/21/2020	1/17/2020	1/3/2020
WBC	4.0 - 10.0 x1000/µL	**2.1 (L)**	**2.3 (L)**	**2.5 (L)**
RBC	3.8 - 5.9 M/µL	**3.4 (L)**	3.8	**3.5 (L)**
Hemoglobin	12.0 - 18.0 g/dL	**8.6 (L)**	**9.7 (L)**	**8.8 (L)**
Hematocrit	37.0 - 52.0 %	**28.1 (L)**	**31.9 (L)**	**28.4 (L)**
MCV	78.0 - 94.0 fL	82.4	84.2	81.4
MCHC	31.0 - 36.0 g/dL	**30.6 (L)**	**30.4 (L)**	31.0
RDW-CV	11.5 - 14.5 %	**16.8 (H)**	**16.6 (H)**	**15.2 (H)**
Platelets	140 - 440 x1000/µL	**51 (L)**	**44 (LL)**	**45 (LL)**
MPV				
ANC (Abs Neutrophil Count)	1.0 - 11.0 x 1000/µL	1.5	1.5	1.6
Neutrophils	37.0 - 84.0 %	72.2	66.7	66.2
Lymphocytes	8.0 - 49.0 %	15.1	20.9	23.6
Absolute Lymphocyte Count	1.0 - 4.0 x 1000/µL	**0.3 (L)**	**0.5 (L)**	**0.6 (L)**
Monocytes	4.0 - 15.0 %	8.5	10.2	6.1
Monocytes (Absolute)	0.0 - 2.0 x 1000/µL	0.2	0.2	0.2
Eosinophils	0.0 - 7.0 %	0.0	0.0	0.0
Eosinophil Absolute Count	0.0 - 1.0 x 1000/µL	0.0	0.0	0.0
Basophils	0.0 - 4.0 %	0.0	0.4	0.4
Basophils Absolute	0.0 - 0.0 x 1000/µL	0.0	0.0	0.0
Immature Granulocytes	0.0 - 3.0 %	**4.2 (H)**	1.8	**3.7 (H)**
Immature Granulocytes (Abs)	0.0 - 0.3 x 1000/µL	0.1	0.0	0.1
C4 Complement	10 - 40 mg/dL		**7 (L)**	**5 (L)**
C3 Complement	90 - 180 mg/dL		**34 (L)**	**21 (L)**
CRP, High Sensitivity	See comment mg/L			**6.2 (H)**
Sedimentation Rate (ESR)	0 - 20 mm/hr		**42 (H)**	**42 (H)**
Immunoglobulin G	768-1,632 mg/dL		**1,930 (H)**	
dsDNA Ab, IgG	<10.0 IU/mL		**160.0 (H)**	

Treatment of non-renal Systemic Lupus Erythematosus



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Fanouriakis, 2019

6/2020-8/2020

- 6/2020 → Worsening fatigue and musculoskeletal pain
- 7/2020 → B-cells have returned; decided to re-dose rituximab
  - First dose- uneventful
  - Second dose- anaphylaxis → during hospitalization developed HTN and worsening elevation in the creatinine

8/2020- Present

- Biopsy: Class IV lupus nephritis with multiple glomerular thrombi
- Hold MMF and start Cytoxan (Eurolupus protocol)

LIGHT MICROSCOPY:

The biopsy consists of four fragments which are stained with H&E, PAS, Trichrome, Jones Silver, and HPS stains. Review of all stains reveals at least glomeruli, none of which are sclerotic. The architecture of the kidney is mildly distorted. There is interstitial scarring involving 5-10% of the biopsy tissue. There is a patchy interstitial infiltrate consisting of lymphocytes and plasma cells involving 10-20% of the interstitium. The tubules show tubular injury. The glomeruli show endocapillary proliferation in six glomeruli and necrosis in at least two glomeruli. Glomerular capillary thrombi are noted in some glomeruli. The mesangium shows increased cellularity. The vessels show severe vasculitis with transmural mononuclear cell infiltration along with fibrinoid necrosis.

IMMUNOFLUORESCENCE MICROSCOPY:

Frozen sections are stained for IgA, IgG, IgM, C3, C1q, and fibrinogen. There is a full-house staining pattern with capillary loop and mesangial staining for IgG(1-2+), IgA(2+), IgM(1+), C3(1+), and C1q(1+). There is also trace staining for fibrinogen.

	WBC	Hemoglobin	Platelets	C3 Complement	C4 Complement	dsDNA Ab	BUN	Creatinine
Ref. Range	Latest Ref Rai	Latest Ref Ran	Latest Ref F	Latest Ref Range:	Latest Ref Range:	Latest Ref Ra	Latest Re	Latest Ref Ra
11/19/2019 1424	3.1 *	8.9 *	145 *				20	0.65
12/18/2019 1249	1.7 *	8.6 *	47 *				14	0.73
1/3/2020 0842	2.5 *	8.8 *	45 *	21 *	5 *		14	0.73
1/17/2020 0958				34 *	7 *		19	0.69
1/17/2020 0959	2.3 *	9.7 *	44 *					
1/21/2020 1021	2.1 *	8.6 *	51 *					
3/2/2020 1126	5.1 *	7.8 *	85 *	37 *	7 *		15	1.00
6/1/2020 1537	4.4	6.2	85 *	34 *	8 *		25	1.30
8/6/2020 0821	3.4	8.2	62	34 *	6 *		19	1.52
8/13/2020 1050	4.6	6.2	72					
8/13/2020 2053							19	2.08
8/13/2020 2054	30.8	4.2 *	123					
8/13/2020 2242	23.5	3.9 *	116					
8/14/2020 0553	8.5	5.2 *	67	32 *	5 *		23	2.62
8/14/2020 1319							23	2.65
8/14/2020 1320	10.1	7.2	64					
8/14/2020 1958	9.2	6.9	62					
8/15/2020 0530	5.2	5.9 *	54				23	2.24
8/15/2020 1759	5.9	8.2	59					
8/16/2020 0627	6.2	7.6	58				31	1.97
8/17/2020 0607	5.9	7.4	58				38	1.82
8/18/2020 1408	19.7	7.7	96				46	1.73
8/19/2020 1005	26.0	9.8	105				47	1.97
8/20/2020 1512	20.5	10.2	49	55 *	10 *		43	2.02
8/20/2020 1650	22.2	9.4	49 *					
8/21/2020 0448	14.6	8.0	40 *				37	1.70
8/22/2020 1208	20.6	7.6	59				25	1.76
8/23/2020 0555	13.9	6.6	78				24	1.83
8/23/2020 1606	17.9	7.4	118					
8/24/2020 0559	12.6	8.4	112				29	1.96
8/25/2020 0556	10.2	7.8	116				29	1.75
8/26/2020 0641	10.4	8.7	112	57 *	9 *		28	1.61
8/27/2020 0559	9.9	9.4	112				30	1.50
8/28/2020 0535	12.5	9.6	119				32	1.49
8/29/2020 0613	11.5	9.5	110	58 *	9 *		34	1.45
8/29/2020 1548	13.7	10.4	115				37	1.46
9/3/2020 0937	12.7	9.9	80	59 *	10 *		36	1.59
9/17/2020 0902	7.0	9.8	102	75 *	14 *		19	1.22
10/1/2020 0907	9.5	10.9	96				17	1.30
10/15/2020 0928	10.8	10.9	105	89	15		24	1.49
10/29/2020 0859	10.1	11.2	126	101	18		27	1.32

	Protein/Creatinine Ratio, Urine, Random
Ref. Range	Latest Ref Range: <0.10 mg/mg Cr
8/31/2015 1442	0.7
9/4/2015 1600	0.3
12/10/2015 1417	0.1
3/21/2016 1516	0.1
5/16/2016 1554	0.1
8/22/2016 1449	0.12 *
1/30/2017 1134	0.14 *
6/23/2017 1142	0.08
3/20/2018 1448	0.10
9/21/2018 1220	0.04
9/25/2018 1458	0.13
9/3/2019 1610	0.35
9/19/2019 2119	1.98
3/2/2020 1126	0.47
8/6/2020 0821	1.95
8/18/2020 1409	2.95
8/30/2020 1003	2.00
9/15/2020 1358	2.88
10/15/2020 1341	1.03

9/3/2019 1610	>379.0 *
1/17/2020 0959	160.0 *
3/2/2020 1126	>379.0 *
6/1/2020 1537	>379.0 *
8/6/2020 0821	>379.0 *
8/21/2020 0448	30.0 *
8/26/2020 0641	17.0 *
8/29/2020 1548	10.0 *
9/3/2020 0937	19.0 *
9/17/2020 0902	36.0 *
10/15/2020 0928	44.0 *
10/29/2020 0859	48.0 *

Post-session Questions

Compared to adult onset SLE which of the following systems is most likely to be involved in pediatric or adolescent onset SLE?

a) Musculoskeletal
b) Hematologic
c) Mucocutaneous
d) Renal

Which is the most common manifestation of neuropsychiatric SLE?

a) Psychosis
b) Cognitive disorder
c) Peripheral neuropathy
d) Movement disorder

SLE developing at which age is most associated with long term organ damage?

a) Prepubertal
b) Peripubertal
c) Postpubertal adolescent
d) Postpuertal adult

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d) Postpuertal adult

Final thoughts on caring for these patients…

- Establishment of good therapeutic relationship
  - Partnership versus caretaker
- Multidisciplinary approach
- Education of affected child, parents, siblings and school and peer environment
- Anticipatory guidance
- Vigilance in close monitoring
- Limiting disease intrusiveness

Final thoughts on caring for these patients…

- Take into consideration
  - developmental phase and associated challenges
    - Discuss “life goals” in the setting of chronic disease
  - Adolescents:
    - striving for independence and autonomy vs. regressive dependent needs
    - Dramatic change through growth of body and mind vs. holding on to status quo

Additional resources

- ACR website www.rheumatology.org
  - Lots of free stuff for residents
- ACR slide collection
- ACR session select
  - Issues in SLE
  - APLS
  - SLE new treatments
  - Genetics, genomics, proteomics: SLE
- CARRA