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Systemic Lupus Erythematosus and the Arthralgias

HPI of ARTHRITIS

Articular symptoms:

- **Morning stiffness**
- **Loss of function**
- **Deformity**
- **Swelling**
- **Pain**
- **Symptoms AGGRAVATED BY REST**
  (OA aggravated by movement and relieved by rest)

Morning stiffness happens with every variety of inflammatory arthritis- BUT ONLY WITH RHEUMATOID is it going to last for longer than an hour!
Stiffness is a rough measure of the degree of inflammation

Could it be
TRAUMA?
WAS THERE AN
INJURY?
What was its mechanism?

bugs, blood, and crystals (BBC) cause the **most intense joint pain.**
Degeneration pain is dull and irritating.

High fever, big swelling, mono or pauciarthritis, extremely painful joint; Inflammation extending past the joint and up and down the limb – plus a systemically ill patient- → **IMMEDIATE ARTHROCENTESIS! Start antibiotics without waiting for cultures**

Extra-articular symptoms:

- **Raynaud's phenomenon** RA or SLE
- **Rash (malar?…)** SLE
- **Fever** any non-degenerative arthropathy eg. gout, RA, SLE, infectious arthritis
  → **WHAT KIND OF FEVER?? High grade = infectious cause!!**
- **Fatigue** renal involvement, sleep loss or anaemia of chronic disease?
- **Anorexia** renal involvement, and/or chronic inflammation
- **Weight loss** renal involvement, and/or chronic inflammation
- **Malaise** chronic inflammation
- **Diarrhoea** irritable bowel syndrome or Crohns disease (associated with arthritis)
- **Mucosal ulcers** non-specific sign of autoimmune disease
- **Red, dry, gritty eyes** active inflammatory process
- **Urethritis +/- Balanitis** reactive arthritis (Reiter's syndrome)

Diagnostic Questions: which arthritis is this?

ACUTE or CHRONIC?
- If its been going on for months, its probably not infective.
- If the joint gets red, hot and swollen within 1 hour, it's haemarthrosis
- If it within days and in the big toe, ankle or knee its probably gout

LARGE or SMALL joints involved?
- LARGE usually crystalline or infective arthritis
- SMALL usually autoimmune arthritis

ITS NOT Rheumatoid if it's a monoarthritis OR the hands are not involved

HOW MANY JOINTS??
- MONOARTICULAR (1 joint) if ACUTE = infective until proven otherwise !
  → Usually *Staph A.*
  Must beware of non-gonococcal monoarthritis- very serious complications
- PAUCIARTICULAR (2-5 joints)
- POLYARTICULAR (>6 joints)

MIGRATING, with FEVER, and TENOSYNOVITIS and DERMATITIS its likely gonococcal arthritis

RELAPSING / REMITTING COURSE?
…is characteristic of autoimmune disease.

DEFORMITY IS TAKING PLACE?
Only Rheumatoid Arthritis regularly deforms; not much else.

DEMOGRAPHICS: Young thin pre-menopausal women DO NOT GET GOUT

PATTERN OF INVOLVEMENT: which was the first joint, next joint etc…

Symmetrical polyarticular MCP, PIP& MTP joints	RA, SLE & Psoriatic arthritis
DIP joint(s), Bony swelling of DIP or PIPs or 1st CMC joint (base of thumb)	Psoriasis, OA
Proximal girdle joints	Polymyalgia Rheumatica & RA
Asymmetrical large joint, oligoarticular disease	Reactive arthritis, Psoriasis, AS
Acute monoarticular disease	Infection, psoriasis, gout, pseudogout
Chronic monoarticular	Psoriasis, RA, AS, OA & chronic infection (e.g. tuberculosis)
Axial, sacroiliac & girdle joint	Ankylosing spondylitis.
Axial joints	Lumbar & cervical spondylosis/OA

BOTTOM LINE: IT'S the CHITS

Crystals **H**aemarthrosis **I**nfectious **T**raumatic **S**ynovial or bone tumour

PAST HISTORY

- Obesity
- Alcoholism
- Renal impairment
- Diuretic use

} GOUT

SEXUAL HISTORY

- Sexually active
- IV drug user

} Gonococcal or reactive arthritis

MEDICATIONS

- Hydrallazine
- Procainamide
- Antibiotics

} Drug SLE

FAMILY HISTORY

- Psoriasis in the family?
- RA in the family?

You must exclude fracture.

IS THE LUMBAR SPINE INVOLVED?
!! PROBABLY A SERONEGATIVE ARTHROPATHY !!

PHYSICAL EXAMINATION

General observation

- **Sick pale and weak- could be SEPSIS!!**

Joint observation

- **Compare right and left**
- **Erythema?** Underlying arthritis or infection
- **Scars?** Previous joint operations or trauma
- **Rash** psoriasis or vasculitis
- **Swelling-** effusion, osteophyte or hypertrophy?
- **Deformity-** chronic destructive, usually RA
- **Muyscle wasting and atrophy** = chronic disease

Palpation

- **Warmth** means active inflammation
- **Tenderness** grades 1 to 4 (4= pt wont let you do it)
- **Spongy boggyness** synovitis or effusion

Active + Passive Movement

Look for

- **Stability**
- **Joint crepitus**
- **Fixed flexion/extension deformity**

Specifically for SLE:
OBSERVE the cushingoid appearance due to corticosteroid treatment (and the stigma thereof)
Palpate PIP and MCP for arthritis;
look for Raynauds (cold intolerance)
look for Sjogren's (dry eyes and mouth)
Auscultate for pericarditis, pleuritis, pulmonary fibrosis
Feel for hepatosplenomegaly
Do urinalysis and measure blood pressure

So, its INFECTIOUS ARTHRITIS…

WHATS THAT BUG, THEN?

Skin breakdown, previously healthy, joint replacement or concommitant RA
→ **STAPHYLOCOCCUS AUREUS**

Ask about RECENT MUMPS or PARVOVIRUS

Splenic dysfunction, otherwise well
→ **STREPTOCOCCUS Sp.**
Pustules, tenosynovitis, fever, migrating, young sexually active drug-user
→ **NEISSERIA GONORHHOEA**
Immune suppressed host, and/or gastrointestinal infection
→ **AEROBIC or ANAEROBIC Gram-Neg**
Recent travel history, immune compromise
→ **MYCOBACTERIUM Sp.**
Immune compromise
→**FUNGUS**
Exposure to ticks, antecedent rash, knee joints
→ **SPIROCHETE: BORELLIA BURGDORFERI**

So, its CRYSTALLINE SEDIMENTATION…

WHAT IS GROWING IN THOSE JOINTS?

Clue: its either **GOUT** or **PSEUDOGOUT**.

Monosodium Urate crystals	Calcium Pyrophosphate
Needle-shaped	Rod or log crystals
Usually monoarticular	Usually monoarticular
Big toe, ankles, knees	Knee, wrist
Not in young women	Old people
DUE TO: Hyperuricaemia, obesity, alcoholism, lead poisoning, hyperlipidaemia, diuretics, Cyclosporine	DUE TO: Hypothyroidism, hemochromatoisis, chronic renal failure, diabetes, hyperPTH, hypercalcaemia
ACUTE management: NSAIDs and steroids Chronic management Allopurinol Colchicine Dietary restrictions	ACUTE management: steroids, NSAIDS Chronic management NSAIDS colchicine

IF YOU CAN PASSIVELY MOVE THE LIMB WITHOU PAIN, ITS NOT A JOINT PROBLEM
and if active movement causes pain in just one plane its probably a tendon or bursa problem

IF YOU FIND SYNOVITIS, IT MUST BE INFLAMMATORY OR SYSTEMIC RHEUMATIC.

Looking for

- Joint effusion with fluid
- Warmth over a joint
- Boggy swelling
- Soft tissue swelling

(eg. the sausage fingers of psoriatic tenosynovitis)

INVESTIGATIONS:

ESR non-specific marker of inflammation

CRP non-specific marker of inflammation (NORMAL IN RHEUMATOID)

FBC looking for

- Anaemia of chronic disease
- Thrombocytopenia of lupus
-

Coagulation studies

coagulopathy of lupus + Antiphospholipid syndrome

Urine microscopy + biochemistry

Looking for protein and cast characteristic of lupus nephritis

X-ray Looking for characteristic degenerative changes to support clinical diagnosis

Arthrocentesis If unsure which infective agent is responsible , or which crystals are being deposited

Electrolytes, urea, creatinine

Not terribly useful, as kidney function must drop by 75% before differences in creatinine clearance become measurable

Serology:

RHEUMATOID FACTOR: 80% of RA patients have a positive RF

ANTINUCLEAR ANTIBODY: 95% of SLE patients have a positive ANA expecting homogenous pattern

ANTI-2-STRANDED DNA: 65% to 80% of SLE patients have a normal AdsNA

!! VALUABLE: AdsNA decreases with successful therapy and increases with disease activity

DIAGNOSTIC CRITERIA: 4 or more of the following = LUPUS

- **Malar cheek rash**
- **Discoid lupus rash**
- **Photosensitivity**
- **Mouth or nasal ulcers**
- **Joint swelling + stiffness**
- **Pleuritis**
- **Pericarditis**
- **Urine sediment with protein and red cell casts**
- **Sizures and psychosis (or merely an intractable headache)**
- **Anaemia**
- **Thrombocytopenia**
- **Previous miscarriage of unknown cause (or due to recognised placental thrombosis)**
- **Positive ANA or other autoimmune serology characteristic of systemic lupus**

Seronegative Spondyloarthropathies

DIAGNOSE THE PRESENCE NOT THE SUBTYPE

CHARACTERISTICS:

- **No Rheumatoid factor** (hence **seronegative**)
- **Involvement of spinal and sacroiliac joints** (hence spondyloarthropathy)
- **Peripheral arthritis** (predominantly lower limb)
- **ENTHESOPATHY:** inflammation of the attachment of tendon to bone
- **Familial clustering**
- **HLA-B27** (immune phenotype which accounts for racial differences)
  i.e aboriginals have 0% incidence, Haida indians have 50%
- **Spectrum of extra-articular features (common to all)**

	Male	Both	Female
Young	Reactive Ank. Spond.	Post viral Psoriatic Enteropathic	RA SLE
Middle aged	Gout		RA PGOA
Elderly		PMR Pseudogout Malignancy	

DIAGNOSTIC CRITERIA:

PRIMARY:
- Inflammatory spinal pain
- Or
- Asymmetric lower limb Synovitis

SECONDARY:
- Positive family history
- Psoriasis
- Inflammatory bowel disease
- Preceding urinary or GI infection
- Buttock pain
- Enthesopathy in the Heel
- Sacroiliitis (X-ray diagnosis)

MUST SATISFY ONE OR BOTH PRIMARY CRITERIA plus one secondary

So how do you know if its inflammatory back pain? = 4 of 5 criteria:

- onset before age 40
- insidious onset
- present for over 3 months
- morning stiffness of over 30min
- improves with exercise

REITERS SYNDROME
A TRIAD: Uveitis, Urethritis and Arthritis

Reiters is the same thing as reactive arth.

CARDIOVASCULAR INVOLVEMENT:
long standing and severe disease causes INVOLVEMENT OF AORTIC ROOT (and thus, aortic regurg)

PERIPHERAL EXTRA-ARTICULAR SIGNS:

- enthesopathy
- skin lesions, mucosal lesions;
- inflammatory eye disease (! Iritis! Difficult t
- inflammatory bowel disease
- cardiovascular lesions
- AIDS (associated with Reiters syndrome)

ONYCHOLYSIS
Is PSORIATIC Arthritis
Otherwise hard to tell apart from RA, but nail changes are in 90%
= PITTING + BREAKDOWN

SYNDESMOPHYTES of the SPINE:
the anlylosing spondylitis lesion
order of progression:
1. The vertebral body become squared
2. A degenerative Romanus lesion eats away at a corner of the vertebral body
3. Bony destruiction of the romanus lesion is followed by bony overproduction, causing a spike of bone to descend from the lip of one vertebral body down towards the next body (= that's a syndesmophyte)
4. **The syndesmophytes fuse ("bridge") the vertebral bodies together.**

Peripheral arthritis:

In **psoriatic arthritis mutilans**, the bones literally dissolve, leaving behind floppy deformed fingers and wrists

- Acute onset
- Lower limbs
- Assymmetric
- Large effusions
- Usually pauciarthritis

DACTYLITIS = an enthesopathy!
Ask the patient about "SAUSAGE FINGERS"

Enthesopathy- Specific for seronegative arthropathy!

- Associated with HLA-B27
- Enthesis is highy vascular and thus susceptible to antigen/antibody deposition and bacterial invasion
- BONE EROSION and new bone formation results
- Achilles + plantar fascia enthesitis = painful walking
- Chest wall enthesitis= pleuritic pain

Sclerosis on ONE SIDE
= normal adaptation to childbirth

SACROILIITIS: → bottom of the SIJ is synovial← so look there first

EARLY CHANGES: blurring of joint lines, widening of joint, sclerosis (opacity) on **both sides** of joint
- **IN SACRO-ILIITIS PROPER, the JOINT LINE IS FUSED AND INVISIBLE**

WHATS IMPORTANT FOR ANKYLOSING SPONDYLITIS: males much more common
Peripheral arthritis is common, 50% of cases; EXTRA-SPINAL FEATURES = iritis, aortitis, SC compression, amyloidosis
!!! APICAL FIBROSIS IS PATHOGNOMIC! Nothing else fibroses the apex of lung except ank spond. !!!

MUST MAKE SURE THE PATIENTS SPINE IS NOT FIXED IN FOETAL CURL! Make them sleep prone!!

SYSTEMIC LUPUS ERYTHEMATOSUS

An AUTOIMMUNE CT disease with auto-abs, circulating immune complexes and widespread tissue damage.

EPIDEMIOLOGY:

female:male 9:1
1/1000 whites
1/250 black women
onset 20s & 30s

PROGNOSIS
Course: chronic relapse & (long) remission, flares rare post-menopause
Complications from therapy: Infections – immunosuppression
Coronary artery disease – chronic steroid use
Must control initial acute phase well ? early diagnosis is key
Range of disease severity but 10yr survival in western world >95%

PATHOGENESIS:

disturbance of immune regulation. Defective suppressor T cells cause polyclonal B cell activation ? uncontrolled auto-ab production against nucleic acids, RBCs, coagulation proteins, phospholipids, lymphocytes, platelets et al. *Typically the abs target nucleic material.*
Circulating immune complexes are deposited in the kidney, brain (choroid plexus), heart, spleen, lung, GIT, skin & peritoneum causing inflammation & tissue damage.
Exacerbations happen when there is more circulating DNA as a result of infection, trauma, drugs.

MULTIFACTORIAL CAUSE:

genetic: families display SLE, CT disease, antinuclear ab's, immune complexes
assoc with histocompatibility Ags: HLA-B8 and DR3

environmental: worsened by sunlight & oestrogen, triggered by drugs (HYDRALAZINE – antiHT, PROCAINAMIDE – antiarrhythmic)

HISTORY:

CLINICAL FEATURES

1. **Malar rash**
2. **Discoid lupus**
3. **Photosensitivity**
4. **Oral ulcers**
5. **Arthritis** (non erosive)
6. **Pericarditis / pleuritis**
7. **CNS**
   -seizures -npathy
   -psychosis -aphasia
   -mental ? -mvt ?
   -visual field dfx

LABS

8. **proteinuria / casts**
9. **anemia / leucopenia / lymphopenia / thr-penia**
10. **+ANA**
11. **anti-dsDNA or –Sm**

4 out of the 11 makes SLE a possibility

PRESENTATION

General: malaise (100%), weight loss (60%), nausea & vomiting (50%), thrombosis (15%)
Musculoskeletal: (95%) arthralgia, arthritis, myositis
Skin: (85%) skin rash (BUTTERFLY, DISCOID, VASCULITIC), alopecia
Fever: (77%)
Neuro: (60%) delirium, dementia, convulsions, chorea, neuropathy, MS symptoms
Renal: (50%) haematuria, oedema, renal failure
Respiratory: (45%) pleurisy
Cardio: (40%) pericarditis
Haematogical: (50%) lymphadenopathy, anaemia
Thrombophlebitis, recurrent Miscarriage *lupus anticoagulant*
Sjogren's ?

PMH **Meds:** procainide, hydralazine (cessation of drug?)
Treatment given & complications of treatment

FHX

SHX

EXAMINATION:

CORONARY ARTERY DISEASE AND STROKE ARE THE BIGGEST KILLERS in SLE

GENERAL INSPECTION
Cushingoid
Weight
Mental state

HANDS
Vasculitis
Rash – photosensitivity, mac-pap
Raynaud's
Arthropathy

ARMS
Livedo reticularis (vasculitis)
Purpura (thrombocytopenia)
Prox myopathy (SLE, steroids)

HEAD
Alopecia, lupus hairs
Eyes – scleritis, keratoconj. sicca, anemia, **fundi** (hard exud)
Mouth – ulcers, infection
Nose – nasoseptal perforation
Rash – butterfly, discoid, diffuse mac-pap
CN lesions
Lymphadenopathy

CHEST
Cardiovasc system – pericarditis, murmurs
Respiratory – pleural effusion, pleurisy, pulm fibrosis, atelectasis

ABDOMEN
big Spleen
big Liver

HIPS
Aseptic necrosis

LEGS
Feet – red soles, sml joint synovitis
Rash
Prox myopathy
Cerebellar ataxia
neuro exam – npathy, hemiplegia, mononeuritis multiplex
ulceration

OTHER
urine analysis - proteinuria
blood pressure - HT
Temp chart

PROXIMAL MYOPATHY

SJOGREN'S ? of SLE
1. **keratoconj. sicca**
2. **dry mouth**

PERICARDITIS (chronic constrictive)
1. **low BP**
2. **pulsus paradoxis** (??BP on inspiration)
3. **? JVP**
4. **apex beat impalpable**
5. **heart sounds** – distant, early 3rd heart sound & early pericardial knock
6. **big Liver, ascites, oedema**

LIVEDO RETICULARIS (capillaries dilate and blood stagnates within these vessels)
1. **mottled cyanotic skin discolouration surrounding pale central areas**
2. **legs, arms and trunk** (worse in cold weather)

PULM FIBROSIS
1. **clubbing**
2. **cyanosis**
3. **crackles** (fine, late, inspirat)

PLEURISY – describes disease process affxng pleura
1. **pleuritic pain**
2. **? chest movt**
3. **pleural rub**

PLEURAL EFFUSION
1. **dysnnoea**
2. **? breath sounds**
3. **? chest mvt**
4. **dull percussion**
5. **? vocal resonance**
6. **± pleural rub**

INVESTIGATIONS:

HAEMATOLOGICAL TESTS:
- **Anaemia** (normochromic normocytic)
- **Leucopenia**
- **Clotting defics** – abs to VII, IX, X
- **Lupus anticoagulant** – (10% cases)
- **Thrombocytopenia** – (15%)

SEROLOGICAL TESTS
- *SPECIFIC* for SLE (even when quiescent)
- **Antinuclear Ab** (99%)
- **Anti-double stranded DNA**
- **Anti-Sm**
- *EXACERBATIONS:* complement weirdness
- **? Total haemolytic complement CH50**
- **? C3, C4**

SKIN BIOPSY
- **+ immunofluorescence of BM**
  - -affected skin (95% cases)
  - -non-affxd skin (50%)

+ RHEUMATOID FACTOR (10%)

if patient doesn't match criteria exactly, may have other CT disease or **Mixed CT disease (MCTD). Profile of auto-abs determine specific disease.

TREATMENT

MUSCULOSKELETAL

NSAIDS avoid gastrotoxic NSAIDS, counter with cytoprotective Rx

Antimalarials Hydroxychloroquine is the antimalarial drug used most often in the United States; ophthalmologic monitoring is recommended every six to 12 months

Glucocorticoids Individual joints may benefit from intra-articular injection of triamcinolone; severe polyarthritis flare-ups may be treated with intravenous "pulse therapy" consisting of 1,000 mg of methylprednisolone daily for three days; use of prednisone for maintenance therapy should be limited to 10 mg or less daily

Immunosuppressives Methotrexate or azathioprine can be used as steroid-sparing drugs; methotrexate not during pregnancy

Avascular necrosis (14% cases) commonly at hip joints, early detection requires MRI. Core decompression of bone is an effective treatment in early stages of the disease
>20mg/day >1 month prednisone / Raynauds / vasculitis

Osteoporosis (64%) lumbar spine osteoporosis is associated with high dose, long-term prednisone. Calcium, vitamin D, calcitonin and bisphosphonates are effective treatments (even in premenopausal women with osteoporosis)

SKIN

1. Sunscreen Blocks both UVA and UVB radiation

2. Antimalarials Use of combination antimalarial therapy (hydroxychloroquine and quinacrine) or chloroquine, which has more risk of retinopathy, is sometimes necessary

If antimalarials not tolerated:

Dapsone G6PD status should be checked

Retinoids avoid in pregnancy

3. Corticosteroids Try topical steroids first. Systemic steroids may be necessary as part of initial therapy for severe discoid lupus or for lupus vasculitis; intradermal corticosteroids are helpful for individual discoid lesions, especially in the scalp

If very severe, requiring >10mg/day steroids, consider adding:

Immunosuppressives Methotrexate or azathioprine is used as steroid-sparing drug

Thalidomide One of the most effective drugs for treatment of discoid lupus, but teratogenicity and neuropathy will limit its acceptance and use

RENAL

corticosteroids / immunosuppressives

MILD (mesangial GN, focal proliferative GN) may take a single therapy

SEVERE (diffuse proliferative GN, severe proteinuria) should take both

PREDNISONE
Corticosteroids: start high, then decrease dose by 10% at reg intervals to wean off completely if poss. Use clinical signs as a guide. If long-term high-doses are required, consider oral immunosuppressives.
AZATHIOPRINE / CYCLOPHOSPHAMIDE / antimalarials
Intermittent regime for immunosuppressives. Treat with minimal dose that controls tissue inflammation.

CNS

Psychosis / Seizures - anti-psychotics / anticonvulsants & corticosteroids
Must exclude other conditions: tumours / infection / toxic metabolic states. Severe states can be treated with methyprednisalone pulse therapy or IV immunosuppressives

CARDIOVASCULAR

Accelerated atherosclerosis (6-10%) due to disease (↑ homocysteine) and steroid SE's (HT, weight gain, cholesterol)
Lifestyle changes and pharmacologic management.

Thrombosis resulting from production of antiphospholipid Abs (incl. lupus anticoagulant and anticardiolipin Ab), seen in 50% cases.
Responsible for thrombosis, recurrent miscarriage & thrombocytopenia.
Warfarin (INR 3-4) if history of thrombosis
Heparin & low dose aspirin if recurrent miscarriage
(neither if thrombocytopenia also present)

HAEMATOLOGICAL

hemolytic anaemia prednisone for severe acute states
leucopenia usually not severe enough for treatment
thrombocytopenia usually not severe enough for treatment
if <50 000 x10^9/L, give high dose IV prednisone then start treatment regime.

PREGNANCY ISSUES

Contraindicated if on WARFARIN or IMMUNOSUPPRESSIVES (cyclophosphasmide). Miscarriage more likely if antiphospholipid syndrome. Postpartum flares frequent. Elective caesarean advised.

Miscarriage Early losses usually due to active SLE or unknown factors
2nd or 3rd -trimester losses usually due to antiphospholipid antibody syndrome
Heparin & low dose aspirin

Congenital heart block Mother usually has both anti-Rh_o and anti-La antibodies. Most babies survive, but some have important morbidity (early detection possible).

Premature birth Risk factors: active SLE, daily prednisone >20 mg, renal disease and hypertension (↑ risk of premature rupture of the membranes) Pre-eclampsia may be difficult to differentiate from SLE renal flare.

DIAGNOSIS AND MANAGEMENT ALGORITHM of SLE

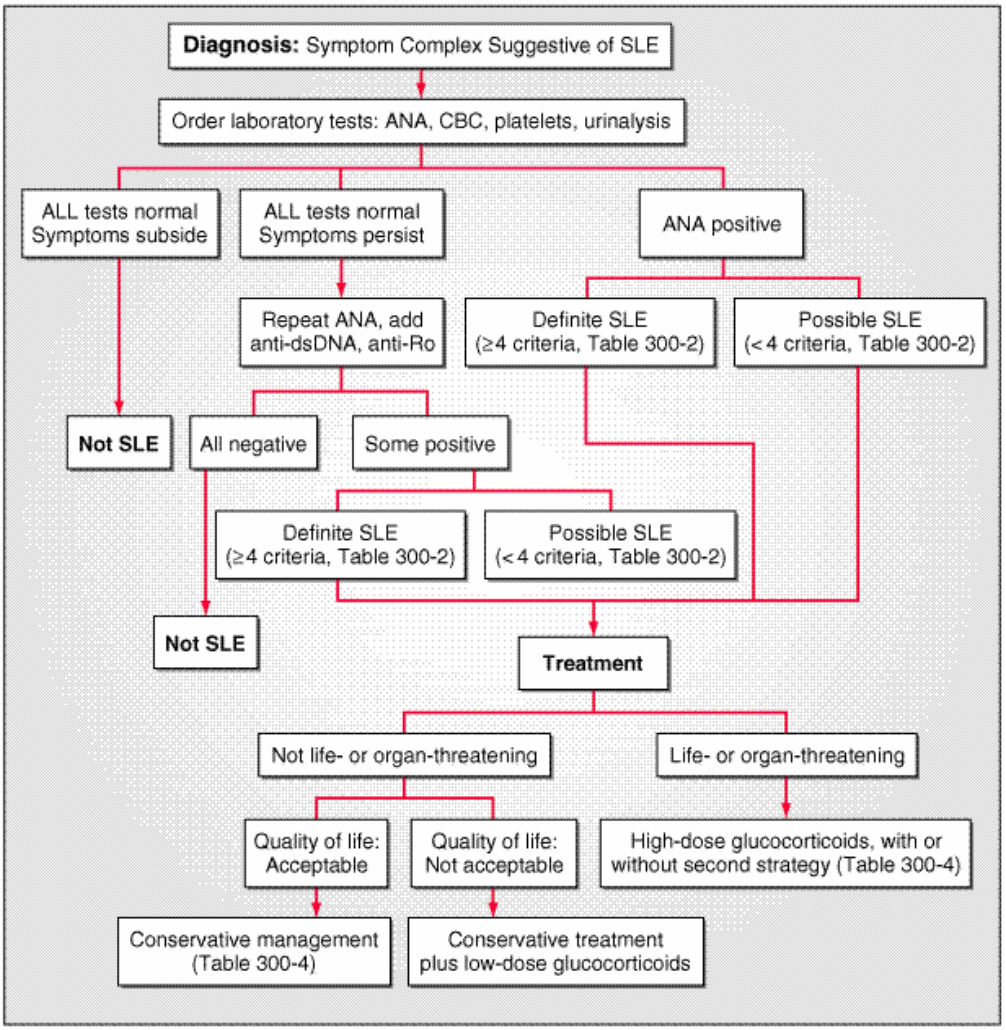

Table 300–4. Medications for the Management of SLE

Medication	Dose Range	Drug Interactions	Serious or Common Adverse Effects
NSAIDs, salicylates (Ecotrin[a] and St. Joseph's aspirin[a] approved by FDA for use in SLE)	Doses toward upper limit of recommended range usually required	A2R/ACE inhibitors, glucocorticoids, fluconazole, methotrexate, thiazides	NSAIDs: Higher incidence of aseptic meningitis, transaminitis, decreased renal function, vasculitis of skin Salicylates: ototoxicity, tinnitus Both: GI events and symptoms, allergic reactions, dermatitis, dizziness, acute renal failure, edema, hypertension
Topical glucocorticoids	Mid-potency for face; mid to high potency other areas	None known	Atrophy of skin, contact dermatitis, folliculitis, hypopigmentation, infection
Topical sunscreens	SPF 15 at least; 30+ preferred	None known	Contact dermatitis
Hydroxychloroquine[a] (quinacrine can be added or substituted)	200–400 mg qd (100 mg qd)	None known	Retinal damage, agranulocytosis, aplastic anemia, ataxia, cardiomyopathy, dizziness, myopathy, ototoxicity, peripheral neuropathy, pigmentation of skin, seizures, thrombocytopenia Quinacrine usually causes diffuse yellow skin coloration
DHEA (dehydroepiandrosterone)	200 mg qd	Unclear	Acne, menstrual irregularities, high serum levels of testosterone
Methotrexate (for dermatitis, arthritis)	10–25 mg once a week, with folic acid; decrease dose if CrCl < 60 mL/min	Acitretin, leflunomide, NSAIDs and salicylates, penicillins, probenecid, sulfonamides, trimethoprim	Anemia, bone marrow suppression, leukopenia, thrombocytopenia, hepatotoxicity, nephrotoxicity, infections, neurotoxicity, pulmonary fibrosis, pneumonitis, severe dermatitis, seizures
Glucocorticoids, oral[a] (several specific brands are approved by FDA for use in SLE)	Prednisone, prednisolone: 0.5–1 mg/kg per day for severe SLE 0.07–0.3 mg/kg per day or qod for milder disease	A2R/ACE antagonists, antiarrhythmics class III, [b]cyclosporine, NSAIDs and salicylates, phenothiazines, phenytoins, quinolones, rifampin, risperidone, thiazides, sulfonylureas, warfarin	Infection, VZV infection, hypertension, hyperglycemia, hypokalemia, acne, allergic reactions, anxiety, aseptic necrosis of bone, Cushingoid changes, CHF, fragile skin, insomnia, menstrual irregularities, mood swings, osteoporosis, psychosis
Methylprednisolone sodium succinate, intravenous[a] (approved for lupus nephritis)	For severe disease, 1 g IV qd x 3 days	As for oral glucocorticoids	As for oral glucocorticoids (if used repeatedly); anaphylaxis
Cyclophosphamide[b] Intravenous Oral	0.7–2.5 mg/kg q month x 6; consider mesna administration with dose 1.5–3 mg/kg per day Decrease dose for CrCl < 25 mL/min	Allopurinol, bone marrow suppressants, colony-stimulating factors, doxorubicin, rituximab, succinylcholine, zidovudine	Infection, VZV infection, bone marrow suppression, leukopenia, anemia, thrombocytopenia, hemorrhagic cystitis (less with IV), carcinoma of the bladder, alopecia, nausea, diarrhea, malaise, malignancy, sterility
Mycophenolate mofetil [b] (approved for lupus nephritis)	2–3 g/d PO	Acyclovir, antacids, azathioprine, bile acid–binding resins, ganciclovir, iron salts, probenecid, oral contraceptives	Infection, leukopenia, anemia, thrombocytopenia, lymphoma, lymphoproliferative disorders, malignancy Alopecia, cough, diarrhea, fever, GI symptoms, headache, hypertension, hypercholesterolemia, hypokalemia, insomnia peripheral edema, transaminitis, tremor, rash
Azathioprine[b]	2–3 mg/kg per day PO; decrease frequency of dose if CrCl < 50 mL/min	ACE inhibitors, allopurinol, bone marrow suppressants, interferons, mycophenolate mofetil, rituximab, warfarin, zidovudine	Infection, VZV infection, bone marrow suppression, leukopenia, anemia, thrombocytopenia, pancreatitis, hepatotoxicity, malignancy, alopecia, fever, flulike illness, GI symptoms

[a]Indicates medication is approved for use in SLE by the U.S. Food and Drug Administration.
[b]Indicates the medication has been used with glucocorticoids in the trials showing efficacy.
Note: NSAIDs, nonsteroidal anti-inflammatory drugs; FDA, U.S. Food and Drug Administration; A2R, angiotensin 2 receptor; ACE, angiotensin-converting enzyme; GI, gastrointestinal; SPF, sun protection factor; CrCl, creatinine clearance; VZV, varicella-zoster virus; CHF, congestive heart failure.