

SLE

St. Joseph's Health Care Day
Programme

Lupus

- Uncommon – 1/1000 prevalence
- Autoimmune
- Named after the wolf due to the malar rash
- May be difficult to diagnose
- Spectrum of problems from mild to severe
- There may or may not be internal organ involvement



Criteria for SLE

- Duration of > 6 weeks and at least 4 of 11 criteria



SLE Criteria

- Malar rash
- Discoid or other rash
- Photosensitivity
- Oral ulcers
- Renal: Glomerulonephritis or nephrotic syndrome
- Inflammatory Arthritis (non erosive)

SLE criteria con't

- Pleuricy / Pericarditis / Serositis
- CBC: leukopenia, hemolytic anemia, thrombocytopenia
- + ANA
- + double stranded DNA
- Other autoantibodies: Smith, Ro, false + VDRL (anticardiolipin antibody)


NB

- Although Raynaud's and alopecia (hair loss) are common, they are not part of the diagnostic criteria

Raynaud's



SLE

- May be systemic (affecting more than the skin)
 - Arthritis
 - Oral ulcers
 - Kidneys
 - May be just on the skin
 - discoid
 - subacute cutaneous
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So what does the doctor order?

- Tests for diagnosis
- Tests for prognosis
- Tests to be aware of in order to determine appropriate treatment (What organ involvement is occurring?)

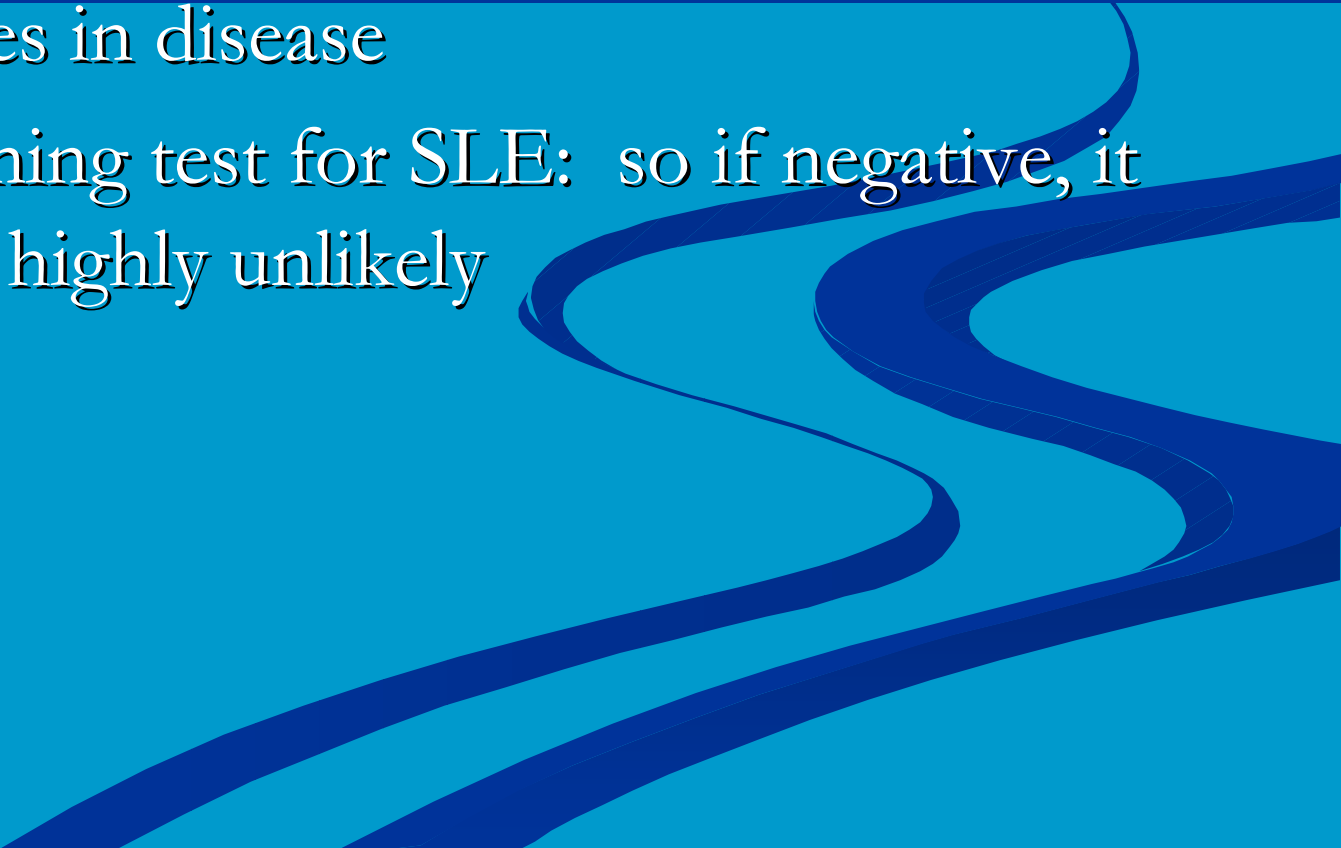
Labs

- CBC,diff, ESR (blood counts)
- Creatinine, urinalysis (kidney function)
- ANA
- Maybe ENA
- We only order an anti DNA if ANA is positive


ANA is a screening test

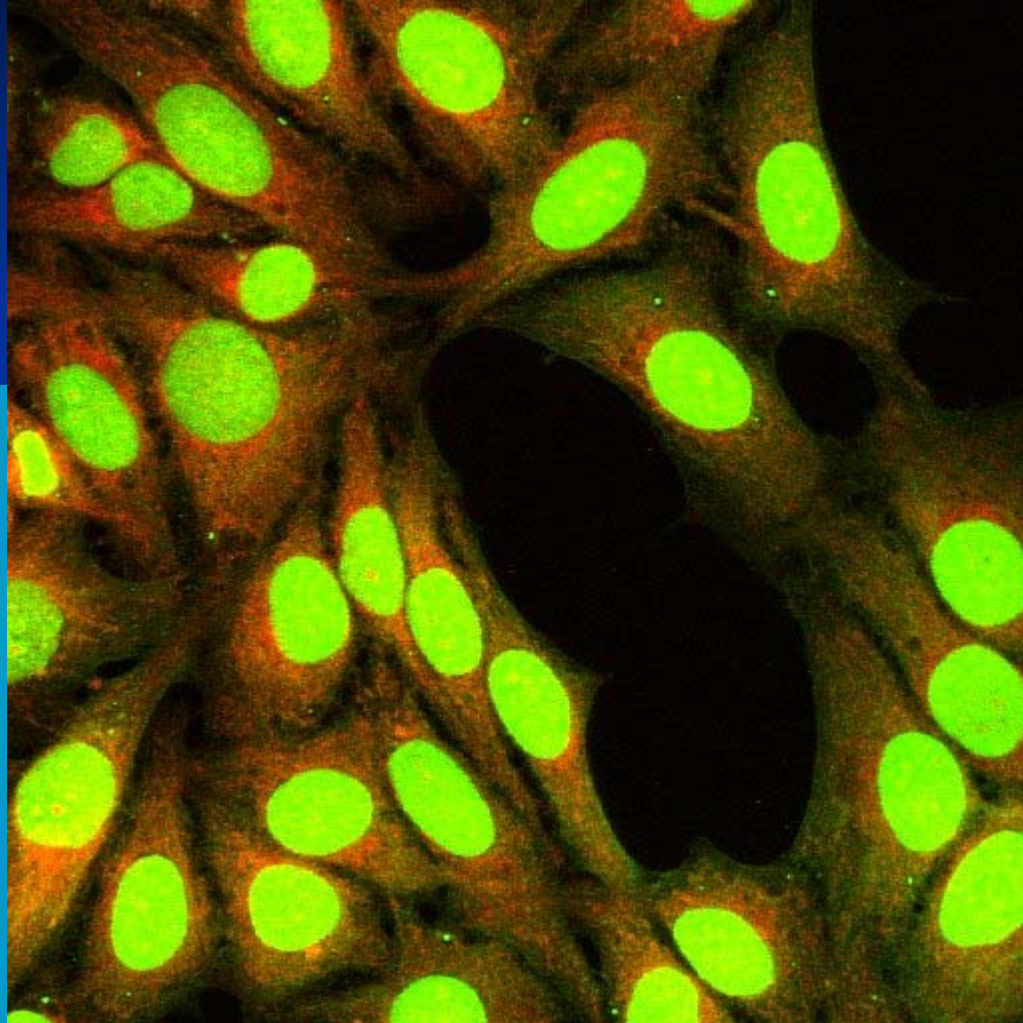
- $> 95\%$ of SLE is ANA positive
- A double stranded DNA cannot occur with a negative ANA (outside labs may do single stranded DNA)
- ANA negative SLE is often anti Ro positive
- ANA may be positive in many healthy people (2% of population)

What is ANA

- Antinuclear antibody is an autoantibody against a part of the nucleus
 - It never rules in disease
 - It is a screening test for SLE: so if negative, it makes SLE highly unlikely
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Frequent ANA patterns


- Speckled
 - Homogeneous / Diffuse
 - Nucleolar
 - Rim / Peripheral
 - Centromere
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- A decorative graphic consisting of several thick, dark blue wavy lines that flow from the bottom right towards the center of the slide, set against a lighter blue background.



Positive test

- Titres: so with a stronger positive, the dilution is larger (higher denominator)
 - Ex. 1/1280 is a strong positive
- Pattern can change depending on the dilution
 - Ex. 1/80 speckled and homogenous and 1/640 homogenous

Is there utility in following the titre?

- No
 - In general repeating the test is a waste of money
 - A positive test in past or at any time can count in the diagnostic criteria for SLE
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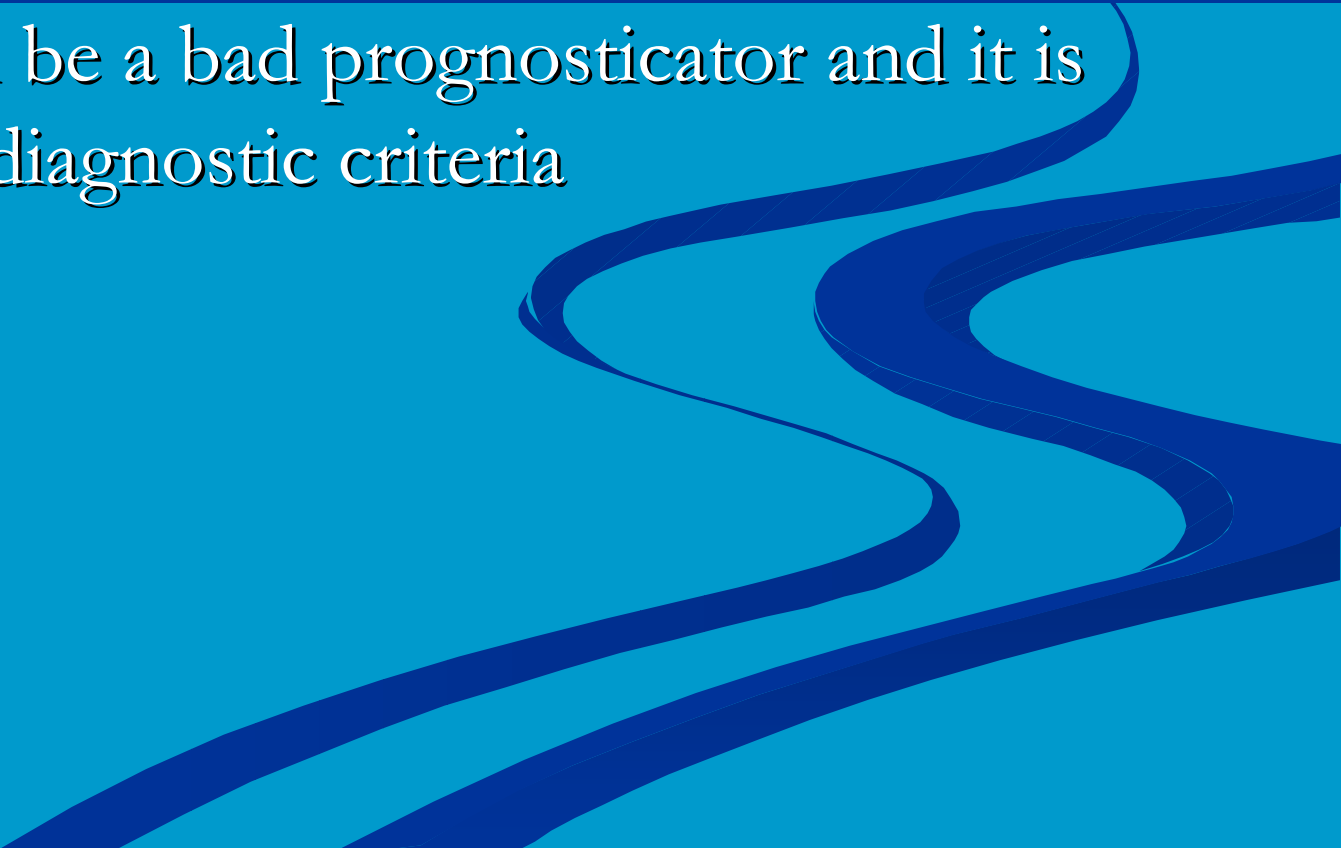
The anti DNA test

- Only order anti DNA in the presence of a positive ANA, when you are expecting SLE
- It is very specific for SLE but very insensitive (ie in most of SLE, it is negative)
- + only in approximately 20% of SLE

What is anti DNA?

- It is an auto-antibody directed against the DNA in a nucleus (thus if positive, ANA should immunofluoresce and be positive)
- Pitfalls: Outside labs often use a kit that will also be positive for single stranded DNA, which is neither sensitive nor specific

What does anti DNA correlate with?

- It is highly specific for SLE
 - It correlates with renal SLE (but not 100%)
 - Thus, it can be a bad prognosticator and it is part of the diagnostic criteria
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What is an ENA

- ENA is extractable nuclear antigens or extra-nuclear antigens
- The lab will do a screen to see if it is positive or negative
- If positive, more assays are done to determine which antibody is positive

ENA usually contains


- Anti Ro,
- Anti La
- Anti Sm (Smith – fairly sensitive for SLE)
- Anti RNP (goes with MCTD and SLE)
- Anti Scl 70 (Topoisomerase 1) – goes with diffuse scleroderma esp with interstitial lung disease
- Other: anti PM-Scl (dermatositis), anti Jo1 (polymyositis with interstitial lung disease), anti RNA polymerase

Arthritis

- May or may not be present
- Can be fixed or migratory (comes and goes)
- It usually does not cause erosions (damage on Xrays) but may rarely be deforming

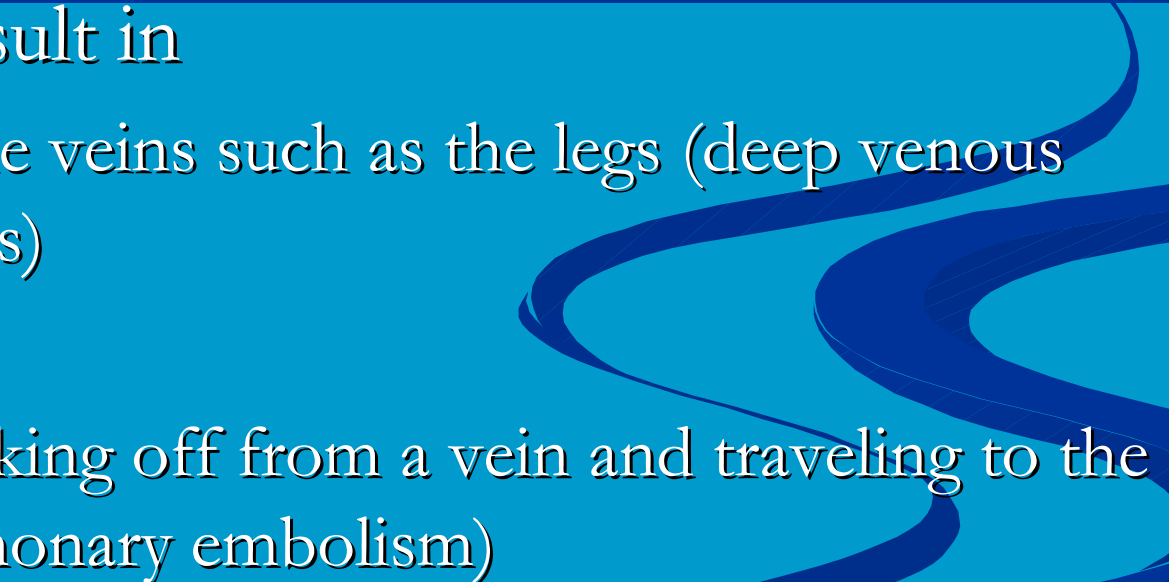
- Fibromyalgia is common in SLE
 - Widespread muscle, bone and tendon pain
 - Nonrestorative sleep
 - Tenderness in several tender points (11/18)

Lupus Rashes

- Cheeks (Malar)
 - Discoid
 - Sun exposed areas (photosensitivity)
 - Other rashes
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Clotting in Lupus

- Some people with lupus have an increased risk of blood clots (in veins or arteries)
 - This can result in
 - Clots in the veins such as the legs (deep venous thrombosis)
 - Stroke
 - Clots breaking off from a vein and traveling to the lung (pulmonary embolism)
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Antibodies and clots

- Antiphospholipid antibodies may be associated with clots
- There are several
 - False positive VDRL
 - Anticardiolipin antibody
 - Lupus anticoagulant
- There may be mottled skin (livedo reticularis), low platelets and recurrent miscarriages in people with this antibody



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Lupus and Heart Disease

- Inflammation from lupus increases the risk of heart disease (accelerated atherosclerosis) several fold
- Other risk factors should be looked for and modified
 - Smoking cessation
 - Treatment of hypertension
 - Cholesterol treatment if elevated

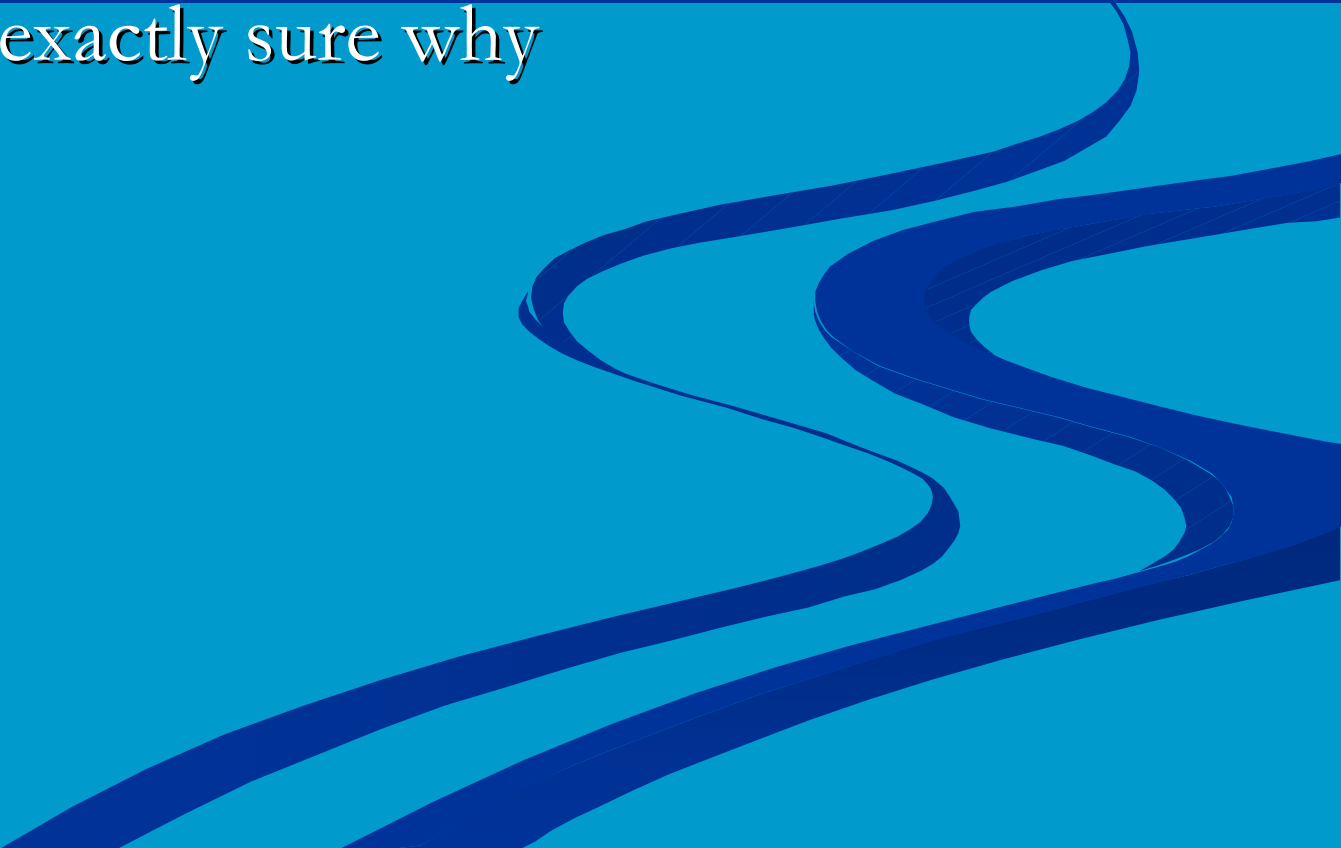
Infection in Lupus

- Infections such as mono may trigger lupus
- There is more shingles (varicella zoster) in lupus especially around the first few years of disease
- Viruses are not handled properly in lupus
 - Increased levels of antibodies to viruses in the blood (Increased B cell antibodies)
 - Decreased skin reactions to the same viruses (decreased T cell function)

CNS lupus

- Lupus can be associated with
 - Seizures
 - Psychosis
 - Strokes and TIAs
 - Brain fog
 - Depression
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SLE 'Fog'

- Many people with lupus have problems with concentration, calculation and 'zoning out'
 - We are not exactly sure why
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Depression in Lupus

- Depression and depressive symptoms are more common in those with lupus compared to age matched people
- They may be from the disease itself, from adjusting to a chronic illness, from pain, from mourning the loss of health, from family stress, job modifications or loss, etc
- It should be identified and treated if appropriate the same as how we would treat other people with depression

Fatigue

- The majority of people with lupus suffer from fatigue
- They feel exhausted after minimal activity
- It is likely multifactorial
 - Accompanies fibromyalgia
 - There are likely factors (cytokines) that are increased in lupus that account for the fatigue
 - It is not treatable by currently available medications
 - Pacing is important

Photosensitivity

- Not all people with lupus are sensitive to the sun
- Those who are may get a rash in the sun, feel sick in the sun or burn very easily
- UV light can flare lupus in animal studies
- Those who are sun sensitive should
 - Avoid the sun
 - Use strong sunscreen
 - Wear a hat with a brim and UV protective clothes

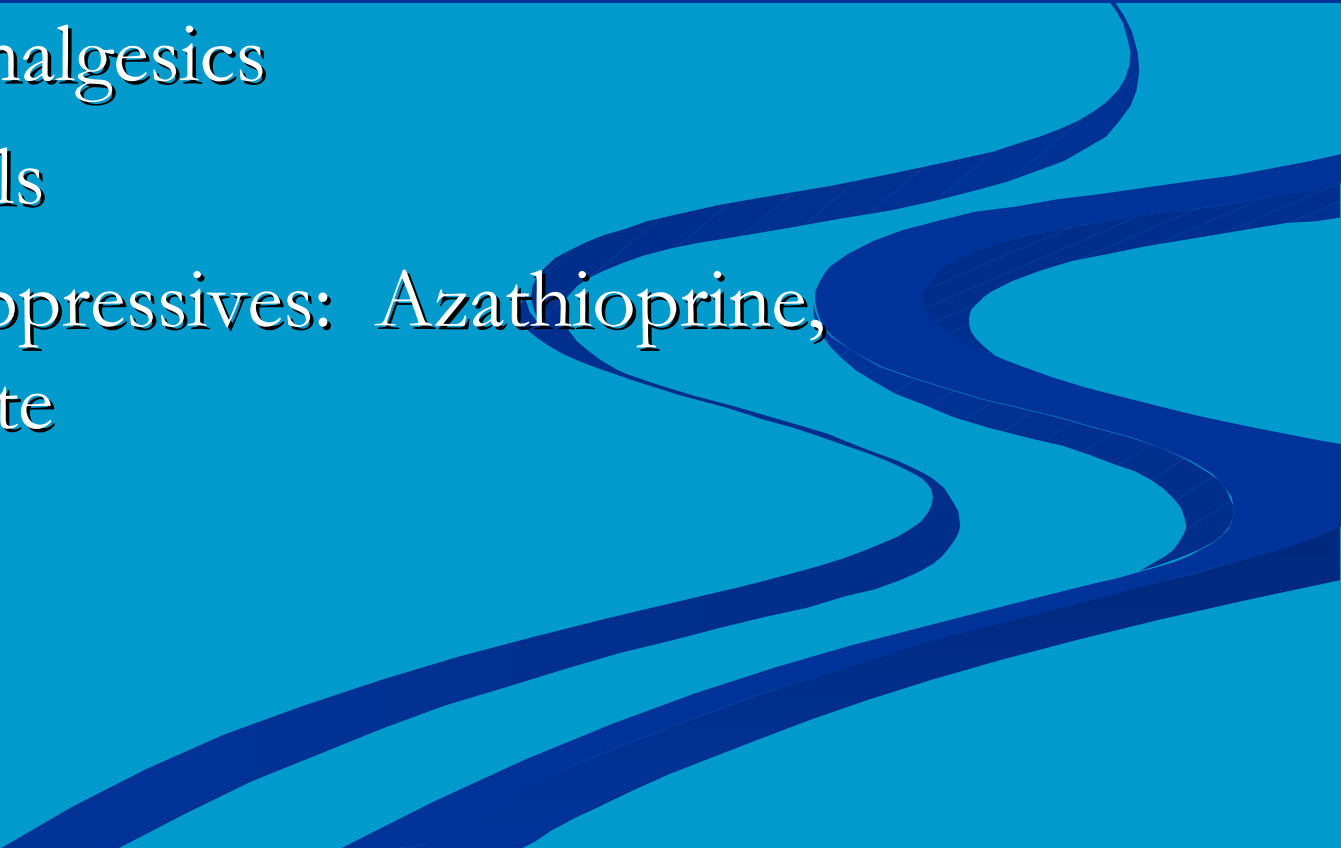
Lupus and Pregnancy

- There is an increased risk in lupus for the baby
 - Miscarriages
 - Prematurity
 - Small for dates
 - Rarely neonatal lupus or heart block
- The outcome is better if the mother is under good control just prior to and at time of conception
- The mother may have an increased risk of toxemia (high blood pressure and fluid retention) and lupus flare

Treatment

- Depends on the manifestations
- Arthritis and skin involvement and sores in mouth and pleurisy may do well with antimalarials (hydroxychloroquine/Plaquenil or chloroquine/Aralen)
- For antimalarials, visual field tests and colour vision tests are done periodically
- Only rarely will the retina get an abnormality from the antimalarials

Arthritis Treatment

- Pacing, splints
 - NSAIDs, analgesics
 - Antimalarials
 - Immunosuppressives: Azathioprine,
Methotrexate
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Prednisone

- Many people with lupus may need prednisone
- It is used often for more significant manifestations of the disease such as glomerulonephritis in the kidney, inflammation of the lungs or around the heart or lung
- It is sometimes needed to control the arthritis

Prednisone

Benefits

- Improves symptoms
- Treats the inflammation
- May improve energy
- May get the disease under control and prevent organ damage

Risks

- Half the people on prednisone lose bone mass
- Weight gain
- Distorted body image
- Breaking the head of a hip or other socket
- Cataracts, high blood pressure, diabetes

Using Prednisone

- We try to use appropriate doses and taper when the disease is suppressed
- We may use very high doses and then only low doses for long term maintenance
- It cannot be stopped quickly if using it for a long time and sometimes if you have an intermittent illness, you have to increase the dose as your gland that makes prednisone (cortisol) may be suppressed (lazy)

Immunosuppressives

- Azathioprine (Imuran)
- Cyclophosphamide (Cytosan)
- Mycophenylate (Cellcept)
- Methotrexate
- Other
 - Experimental: B cell depleting antibodies

Azathioprine

- Often used to spare prednisone
- Used for bad skin involvement when antimalarials fail
- Used to treat joints
- Used for other internal organ involvement
- Some people can't tolerate it
- May in the long term slightly increase the risk of skin cancer and blood cancers

Cyclophosphamide

- Used for serious internal organ involvement
- Usually given intravenously at first monthly
- May cause nausea, hair loss, irritation of bladder, drops in the blood counts, increased risk of infection
- Long term use may result in premature menopause, bladder cancer, blood cancers

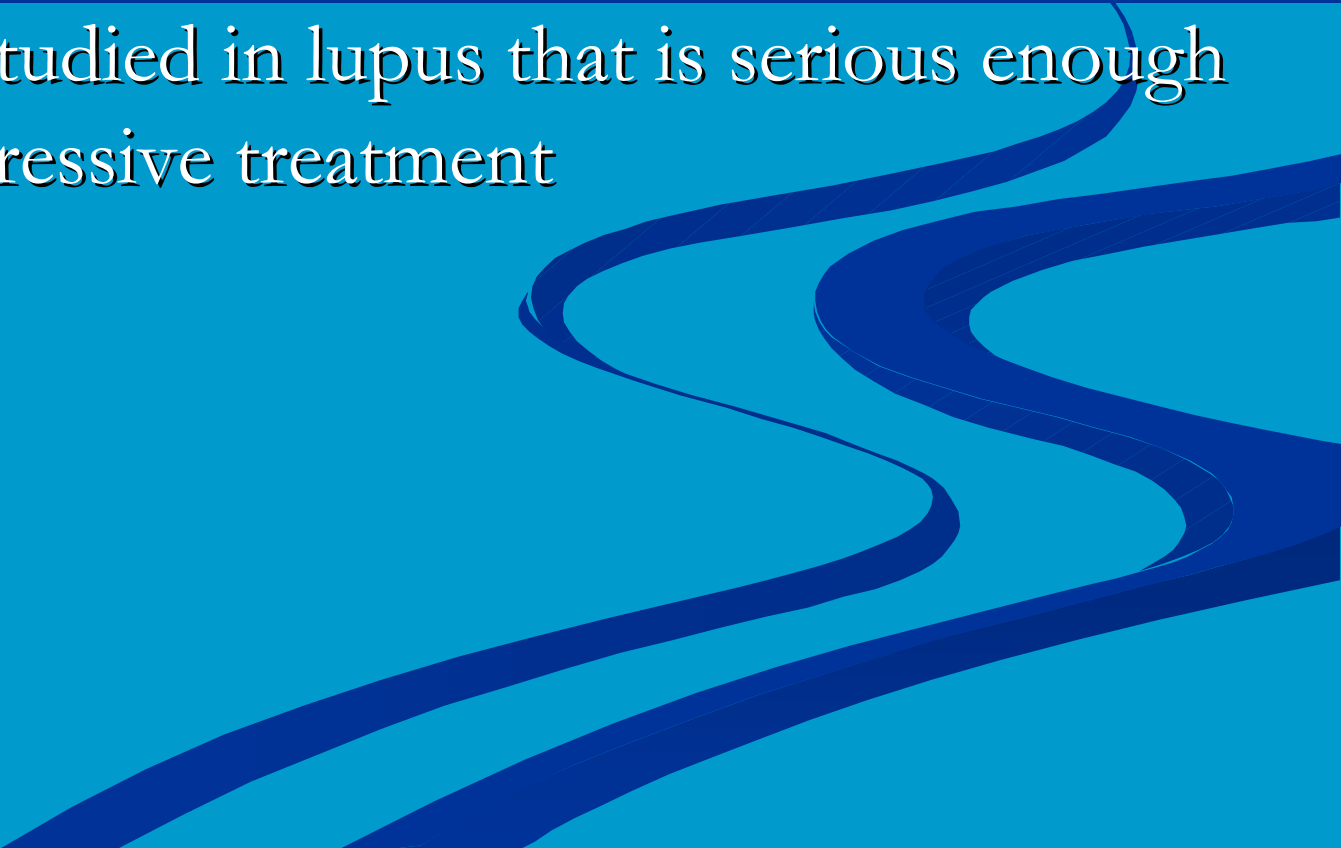
Mycophenylate

- There are trials of this drug showing it is effective in kidney lupus
- It is used to prevent rejection of an organ transplant, but adopted as it is an immunosuppressive
- We are doing a trial with it in kidney lupus
- May help for other features of lupus

Methotrexate

- This drug is widely used in rheumatoid arthritis
- We may use it in lupus for skin, joint and some internal involvement
- We were part of a lupus trial with methotrexate and it showed that it may allow for less prednisone to be used (steroid sparing)
- It may cause nausea, sores in the mouth, increased risk of infection (rare), poor wound healing, drops in the blood counts, irritation of the liver

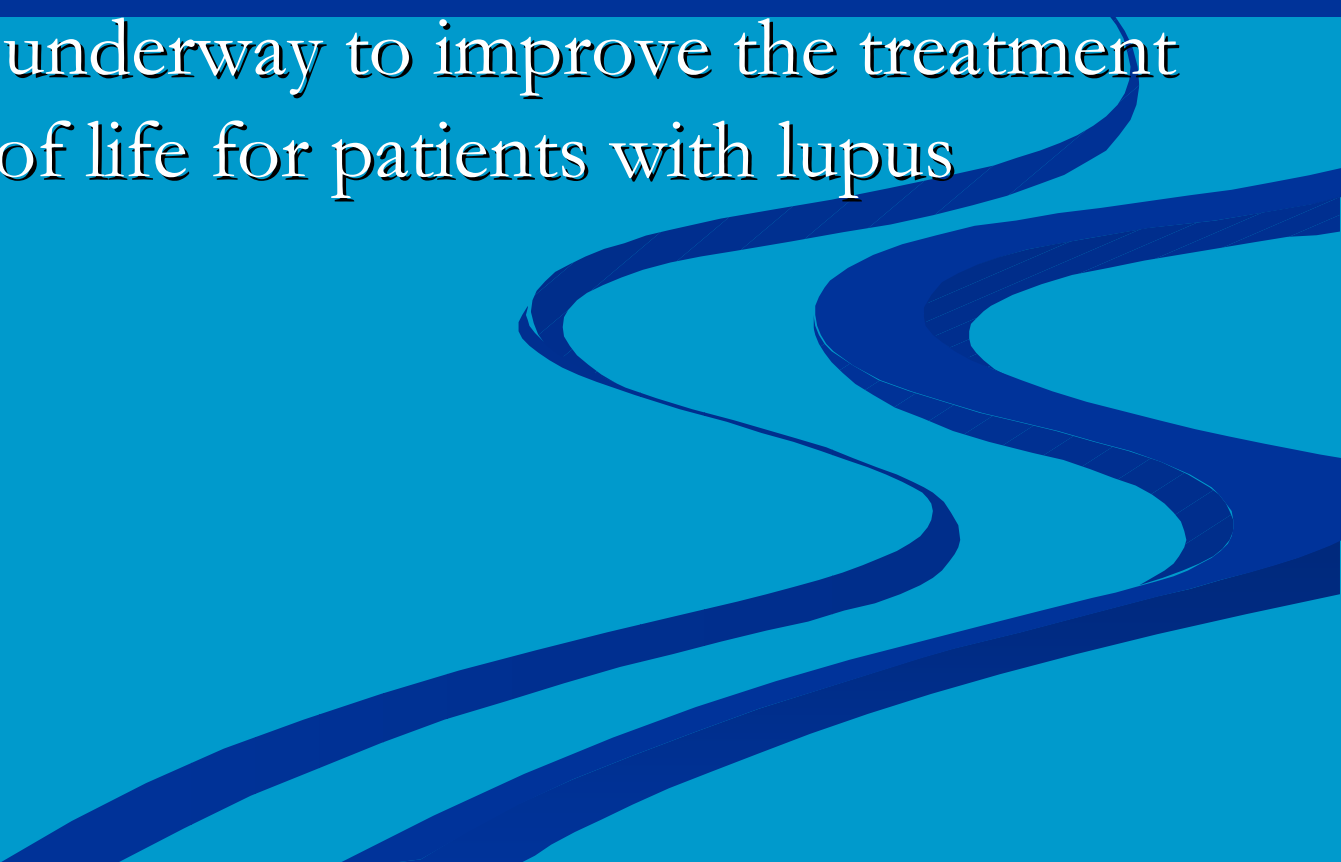
Other Drugs

- B cell depleting antibodies
 - We are doing studies on one of the these agents
 - It is being studied in lupus that is serious enough to need aggressive treatment
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Raynaud's Treatment

- Cold avoidance
- No smoking
- Vasodilators
 - Dipyrimadole calcium channel blockers
 - Nifedipine, Felodipine, Amlodipine
 - Angiotensin II Blockers
 - Losarten
- Prostacyclins (Iloprost)
- PDE5 inhibitors (Viagara)
- Sympathetic blockade – injections, surgery

Summary

- Lupus has many areas of proven treatment that is directed against organs or symptoms
 - Research is underway to improve the treatment and quality of life for patients with lupus
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