Outline

- Systemic Lupus Erythematosus
- Lupus & Thyroid Disease
- Lupus and Glucocorticoids
- Metabolic Syndrome
- Diabetes mellitus
- Hyperlipidemia
- Osteoporosis & Vitamin D Deficiency
- Lupus and Pituitary
• Major mechanism: Defective immune regulation
  • Abnormal clearance of apoptotic cells, self-antigens and a break in self-tolerance
• Autoimmunity
  • The world of antibodies including ANA, anti-double-stranded DNA, immune complexes
• Women have a much higher prevalence of almost all autoimmune diseases
• SLE has a 12:1 female to male prevalence between the ages of 15 to 45 years
SLE

• Inflammation
  • Antibodies form immune complexes which activate the complement system

• Tissue Damage
  • Vasculitis, kidney problems, hematologic abnormalities, cardiovascular disease, osteoporosis, increased risk of cancer
Thyroid Disease in Lupus

• A patient with lupus is more likely to have a relative with another autoimmune disease, especially thyroid disease than SLE

• Is thyroid disease associated with SLE?
  • YES, based on small cohort studies
  • 3-24 % of patients with lupus also have autoimmune thyroid disease (AITD)
  • Up to 11-51 % of patients have thyroid antibodies
Thyroid Anatomy
Thyroid Disease in Lupus

- Hypothyroidism
  - Prevalence 5.7 % in SLE vs. 1 % in general population
  - Thyroid antibodies in 14 % of patients with SLE and in 68 % in patients with SLE and thyroid disease vs. 5-6 % in general population

- Thyrotoxicosis
  - Prevalence 1.7 % in SLE vs. 1 % in general population, not significantly different

This means that out of 300 patients with lupus 17 were hypothyroid, 5 were hyperthyroid, and 42 had thyroid antibodies.
Underactive thyroid gland

- Fatigue
- Depression
- Modest weight gain
- Cold intolerance
- Excessive sleepiness
- Dry, coarse hair and skin
- Constipation
- Decreased Concentration
- Swelling of the legs
Hyperthyroidism

Overactive thyroid gland

- Palpitations
- Excessive sweating, heat intolerance
- Tremors
- Weight loss
- Nervousness, agitation, decreased concentration
- Diarrhea
- Fatigue
- Scant menstrual flow
**Thyroid Disease**

**Table 3**  
Studies of the prevalence of hyperthyroid and hypothyroid disease in SLE

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Thyroid Antibodies in SLE

TPO Antibody Activity

• PTPN22 gene encoding tyrosine phosphatase, regulates tyrosine kinases important for T cell activation
• A polymorphism in this gene has been found in SLE, RA, Type 1 diabetes mellitus, autoimmune thyroid disease
• 16.7 % of patients with AITD and SLE had this genetic polymorphism vs. 8.5 % of patients with SLE alone
• 5q14.3–15 harbors a susceptibility gene shared by SLE and AITD
Patients with SLE have an increased risk of hematologic malignancy and possibly lung and hepatobiliary cancer.

2010 study in JCEM showed a higher number of papillary thyroid cancer in patients with lupus than in controls (5 of 153 patients, 3.2% vs. 1 of 459 patients, 0.2%).

Four of five patients with thyroid cancer and lupus had + thyroid antibodies.

25% of patients with lupus had thyroid nodules.

Mean patient age was 38 years.

Defective immune surveillance.
Thyroid disease is probably more common in SLE than the general population, especially with secondary Sjogren’s and may have a genetic basis.

Disagreement on whether both hypothyroidism and hyperthyroidism are more common.

Anti-thyroglobulin and anti-microsomal antibodies are seen at higher frequency in SLE.

Controversy whether SLE is an independent risk factor for thyroid disease or whether young to middle aged women who are most at risk for SLE are also at risk for autoimmune thyroid disease.
It is important for patients with SLE to know their family history of thyroid disease including thyroid cancer.

Know the symptoms of hypothyroidism and hyperthyroidism and bring this to your doctor’s attention.

The thyroid gland should be examined during physical exam.

Thyroid function including thyroid antibodies and thyroid ultrasound may be obtained in select cases.
Glucocorticoids are widely prescribed as part of treatment of SLE

- Anti-inflammatory properties
- Prolonged steroid use is known to cause bone loss by inhibiting bone formation and calcium absorption from the gut, enhancing bone resorption and urinary calcium loss
- Steroids may elevate blood pressure, cholesterol and blood sugar levels
- Use the lowest effective dose of steroid to optimize lupus disease control
Three of five:
1) Impaired Glucose Tolerance
2) Hypertension - Blood pressure greater than 130/85
3) High triglycerides
4) Low HDL
5) Central Obesity - Waist-hip ratio > 0.9 in men and > 0.85 in women
Prevalence of metabolic syndrome in lupus is 18% in the UK and up to 30% in the US.

Presence of hypertension is higher in lupus cohorts than controls.

Metabolic syndrome = 3 fold increase in likelihood of coronary heart disease.

Not associated with disease activity or average steroid dose.

Treatment with hydroxychloroquine was protective.
Type 1 and Type 2 diabetes mellitus can be seen but is not common in patients with lupus.

In one study, 9 of 485 patients had diabetes: 3 with Type 1 DM, 4 with Type 2 DM, and 2 with steroid induced DM.

Challenges:
- Distinguishing source of renal disease, peripheral neuropathy, and retinopathy.
- Steroids exacerbating high blood sugars.
- Increased cardiovascular risk in DM and SLE.
• Significantly elevated levels of total cholesterol and triglycerides in patients with lupus compared to controls
• Increased small and atherogenic LDL particles
• Increased risk of cardiovascular disease with mean age of 49 for first heart attack
• Diet, exercise, no smoking, and medication to lower cholesterol levels and blood pressure if necessary are ways to reduce risk
• Optimal lupus disease control with minimal dose of steroids is the goal of therapy
Osteoporosis

- Osteoporotic fractures are the most preventable form of musculoskeletal damage!
- Fracture rates are higher in lupus than expected
- 5 x higher than the general population
- 12% of women with lupus reported a broken bone
- 40% of patients mean age 44 had low bone mass at the spine and hip, 4-19% had osteoporosis
Partly due to steroid treatment AND inflammation from lupus

African American women with lupus have lower bone mass at the spine than Caucasian women even though white ethnicity is a known risk factor for osteoporosis.
Osteopenia in SLE (disease severity and steroids)

Lower Bone Mass in African American Women

Risk factors for bone loss in lupus

- Older age at diagnosis **
- Longer duration of SLE
- Longer duration of steroid use
- Post-menopausal status (low estrogen)
- Vitamin D deficiency
- Ethnicity
- Impaired mobility **
- Low Body Mass Index
- Increased inflammatory markers
Vitamin D is important for a healthy immune system

- Vitamin D deficiency is common in SLE partly due to avoidance of sun exposure
- Low vitamin D is a risk factor for low bone mass at the spine
- Supplementation with vitamin D
  - 800 to 1,000 International Units of D3 daily
  - A total daily calcium intake of 1500 mg
Vertebral Fracture

In a study of 107 women with lupus, at least 1 vertebral fracture was detected in 20% of patients.

Bone Mineral Density – DXA Scan

Spine  Hip  Distal forearm
In addition to vitamin D, calcium and weight bearing exercise:

- Hormone replacement therapy only in select cases as possibility of lupus flare and thrombosis, cannot be used in patients with anti-phospholipid antibodies
- Bisphosphonates; fetal abnormalities in animal studies, cannot be used in young women who desire pregnancy or in severe renal disease
- Anabolic bone treatment; Forteo injections
- Novel therapies
Prolonged glucocorticoid use can suppress pituitary function, it is important to always taper steroids over time

In patients with SLE prior to steroid treatment, a study showed normal pituitary function and reserve

Response to hormonal stimulation was higher in patients with lupus for TSH, LH, and FSH but normal for prolactin, growth hormone, and cortisol

This suggests a predilection for hypothyroidism and hypogonadism (low testosterone)
Pituitary Hormones

Take Home Points on Bone Health in Lupus

• Patients with lupus are at risk for bone loss from chronic inflammation and steroid use in addition to other risk factors for osteoporosis (e.g. smoking, alcohol, menopause, low weight)

• It is important to diagnose and treat osteopenia and osteoporosis in this patient population by measuring bone mineral density with DXA scan

• Vitamin D deficiency is common and should be treated with vitamin D3 and calcium supplementation daily to maintain serum D level greater than 32 ng/mL

• Assessment of fracture risk should include lateral x-ray of the spine as part of osteoporosis evaluation


