Sex and Gender Differences
Systemic Lupus Erythematosus (SLE)

SLE: a systemic autoimmune disease affecting multiple organ systems due to the production of autoantibodies and immune complex deposition.

Risk Factors & Prevalence

Mean age of onset: F ~30-40 yo; M ~50 yo

- **Female** sex
- Extra X chromosome (XXX, XXY)
- Genetic ancestry (African, Asian, Hispanic)
- Environment: UV light, viruses (e.g., EBV), silica dust, cigarette smoke
- Single nucleotide mutation in CXCR3 gene on X chromosome:
  - increased risk for **Lupus Serositis in males**

Female: Male prevalence
- **overall: 9:1**
- **before puberty: 4:1**
- **from age 15-50 yo: 10:1**
- **post-menopause: 8:1**

Clinical Presentation

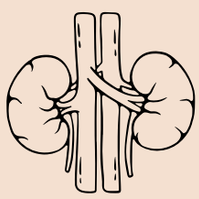
Malar rash, oral ulcers, alopecia, arthritis, constitutional symptoms (fatigue, fever, joint pain)
SLE increases risk of: antiphospholipid syndrome (APS), cardiovascular diseases (CVD), osteoporosis, malignancy
No sex disparity in rate of progression from lupus nephritis to end-stage renal disease

FEMALE

- **Mucocutaneous** complaints more likely: malar rash, oral ulcers, photosensitivity, alopecia, Raynaud's phenomenon
- Report moderate to severe **pain** more frequently
- **Comorbidities** more common:
  - primary APS 3.5:1 (F:M)
  - secondary APS 7:1 (F:M)
  - atherosclerotic CV disease
  - osteoporosis
- **Pregnancy**:
  - higher risk of:
    - flare (recommended to wait until 6 months of controlled symptoms)
    - complications: preeclampsia, preterm delivery, loss, intrauterine growth restriction

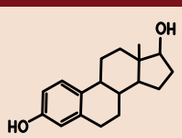
MALE

- More **severe** first presentation
- More likely to develop **SLE-associated**:
  - serositis (pleuritis, pericarditis, peritonitis)
  - seizures
  - vasculitis
  - venous thrombosis
- Worse **renal** outcomes more likely:
  - lupus nephritis (LN)
  - diffuse proliferative lupus nephritis
  - thrombocytopenia
  - proteinuria
- Organ damage more likely:
  - atrial fibrillation, valvular heart disease, aortic aneurysm/dissection, thrombotic events, and diabetes



Pathophysiology

- Not completely understood: hypothesis **sex hormones**, environmental factors, & genetics lead to
  - immunomodulatory changes and formation of autoantibodies
- **Females**: endogenous estrogen promotes plasma cell proliferation and autoantibody production
- **Males**: require a higher genetic load



Diagnostics/Screening

- Blood markers:
  - positive antinuclear antibodies (ANA): anti-dsDNA, anti-Smith, anti-Ro/SSA, anti-La/SSB, anti-RNP
    - **Females:** positive anti-Ro/SSA autoantibodies more likely
  - positive antiphospholipid antibodies: anti-cardiolipin, anti-B2 glycoprotein, lupus anticoagulant
    - **Males:** positive Lupus anticoagulant autoantibodies more likely
- Other findings: cytopenia, increased serum creatinine, abnormal urinalysis, hypocomplementemia
  - **Males:** low complement component 3 (C3) more likely
  - **Females** with increased serum uric acid levels: higher risk of lupus nephritis progression

Treatment & Prognosis

Glucocorticoids & Hydroxychloroquine: most commonly prescribed

FEMALE

- Azathioprine & Mycophenolate: lower adherence rates
- Antimalarials & Belimumab: more frequently prescribed
- Pregnancy:
  - assesss autoantibody levels
  - continue Hydroxychloroquine
  - low-dose aspirin starting at 12 weeks
  - Avoid: Mycophenolate mofetil, methotrexate, leflunomide, cyclophosphamide
- **Higher mortality** than males with SLE

MALE

- Cyclophosphamide: more frequently prescribed
- Antimalarials: less frequently prescribed
- Hydroxychloroquine: less likely to fill prescription
- Dialysis: more likely due to disease severity
- Complete remission less likely
  - especially if renal involvement
- **Poorer prognosis**

Created: 08/25/2023
Last Reviewed: 03/05/2026

To learn more or get involved, visit **amwa-doc.org/sghc** or email us at **sghc@amwa-doc.org**

Authors: Monica Ybarra, Ana Wilden, Danielle Moorer
Faculty Mentors: Dr. Sriya Ranatunga
Graphics & Editing: Sarah Osborn, MD & Sneha Chaturvedi
Updated by: Sarah Osborn, MD

SEX and GENDER HEALTH COLLABORATIVE of the American Medical Women's Association

Definitions & Disclaimers

References