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

	FEMALE	ALL	MALE
Risk Factors	• 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 polymorphism in the CXCR3 gene (on X chromosome) increased risk for **Lupus Serositis**

Prevalence	• Age of onset ~30-40 years
	• **Female: Male** prevalence
	  ◦ overall: 9:1
	  ◦ before puberty: 4:1
	  ◦ from age 15-50 yo: 10:1
	  ◦ post-menopause: 8:1
		• SLE, one of the strongest sex variations of autoimmune diseases
		• African American, Asian, and Hispanic ancestry: higher prevalence compared to White Americans
			• Age of onset ~50 years

Presentation	• **Mucocutaneous** complaints more likely: malar rash, oral ulcers, photosensitivity, alopecia, Raynaud's
	• Report moderate to severe **pain** more frequently
	• **Comorbidites** more common:
	  ◦ primary APS 3.5:1 (F:M)
	  ◦ secondary APS 7:1 (F:M)
	  ◦ atherosclerotic CVD
	  ◦ osteoporosis
	• **Pregnancy**:
	  ◦ higher risk of:
	  ▪ flare (recommended to wait until 6 months of controlled symptoms)
	  ▪ complications: preeclampsia, preterm delivery, loss, IUGR
		• Constitutional symptoms: fatigue, fever, joint pain
		• Malar rash, oral ulcers, alopecia, arthritis
		• No sex disparity in rate of progression from lupus nephritis to end-stage renal disease
		• SLE increases risk of:
		  ◦ antiphospholipid syndrome (APS)
		  ◦ cardiovascular diseases (CVD)
		  ◦ osteoporosis
		  ◦ malignancy
			• More **severe first presentation**
			• More likely to develop **SLE-associated**:
			  ◦ serositis (pleuritis, pericarditis, peritonitis)
			  ◦ seziures
			  ◦ vasculitis
			  ◦ venous thrombosis
			• Worse **renal** outcomes more likely:
			  ◦ lupus nephritis (LN)
			  ◦ diffuse proliferative lupus nephritis
			  ◦ thrombocytopenia
			  ◦ proteinuria
			• Organ damage more likely:
			  ◦ CVD: atrial fibrillation, valvular heart disease, aortic aneurysm/dissection, thrombotic events
			  ◦ diabetes

Pathophysiology	• Endogenous estrogen promotes plasma cell proliferation and autoantibody production	• Not completely understood
		• Hypothesis: sex hormones, environmental factors, & genetics:
		  ◦ immunomodulatory changes
		  ◦ formation of autoantibodies
			• Require a higher genetic load

Diagnostics/Screening	• Anti-Ro/SSA autoantibodies: more likely positive
	• Increased serum uric acid levels: higher risk of LN progression
		• Blood markers:
		  ◦ Positive antinuclear antibodies (ANA): anti-dsDNA, anti-Smith. anti-Ro/SSA, anti-La/SSB, anti-RNP
		  ◦ Positive antiphospholipid antibodies: anti-cardiolipin, anti-B2 glycoprotein, lupus anticoagulant
		• Other findings: cytopenia, increased serum creatinine, abnormal urinalysis, hypocomplementemia
			• Lupus Anticoagulant autoantibodies: more likely positive
			• Low complement component 3 (C3): more likely

Treatment	• Azathioprine & Mycohpenolate: lower adherence rates
	• Antimalarials & belimumab: more frequently prescribed
	• Pregnancy:
	  ◦ assess autoantibody levels
	  ◦ continue hydroxychloroquine
	  ◦ low-dose aspirin starting at 12 weeks
	  ◦ Avoid: Mycophenolate mofetil, methotrexate, leflunomide, cyclophosphamide
		• Glucocorticoids & Hydroxychloroquine: most commonly prescribed
		• Other immunosuppression medications:
		  ◦ Mycophenolate mofetil
		  ◦ Azathioprine
		  ◦ Belimumab
		  ◦ Rituximab
		  ◦ Cyclophosphamide
		  ◦ Methotrexate
		  ◦ Antimalarials
			• Cyclophosphamide: more frequently prescribed
			• Antimalarials: less frequently prescribed
			• Hydroxychloroquine: less likely to fill rx
			• Dialysis: more likely due to disease severity

Prognosis	• Higher mortality than males with SLE	• Indicators of poor prognosis: age at presentation (>< yo); low SES status; African ancestry; antiphospholipid antibodies; renal disease • Higher mortality among ethnic minorities	• Complete remission less likely ◦ especially if renal involvement • Poorer prognosis

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

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Definitions & Disclaimers

References