

Lupus Overlap Syndromes

Charles A. Withers, II, M.D.
CMC NorthEast Rheumatology
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Objectives

- Diagnosing autoimmune disease
- Introduce the idea of “overlap”
- Which autoimmune disease overlap?
- Review characteristics of the most common diseases that overlap with lupus
- Summarize the impact of overlap on SLE patients

What is autoimmune disease?

- Your immune system fights:
 - Viruses
 - Bacteria
 - Parasites

- Autoimmune Disease
 - Immune system targets your body
 - Antibodies vs. Autoantibodies

Causes of Autoimmune Disease

- Environmental Triggers
 - Cigarette smoke – toxins
 - Medications
 - Infections
 - Sunlight
- Genetic Factors

Making a Diagnosis

- Is *important* because...
 - Helps doctors communicate with each other
 - Helps doctors communicate with patients
 - Helps with research
 - Helps with prognosis
 - Helps with treatment choices
- Is *NOT important* because...
 - Similar medications for autoimmune disease
 - Treatment is based on symptoms more than labels

Making a Diagnosis... (cont'd)

- Requires knowledge about the cause of disease
- Pattern recognition:
 - signs and symptoms
 - Genetic markers: antibodies
- Diagnostic Criteria:
 - Good for large populations & research studies
 - Less helpful for individual patients

Making a Diagnosis... (cont'd)

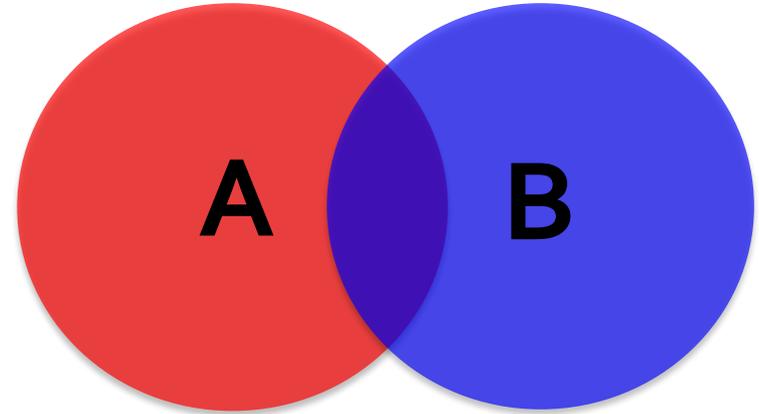
- Some patients fit into “diagnostic boxes” – they read the textbook!
- Some patients don't meet diagnostic criteria
 - Undifferentiated Connective Tissue Disease (UCTD)
 - “Incomplete Lupus”
- Some patients fit into multiple categories
 - Overlap Syndromes

Overlap Syndromes

ANIMALS

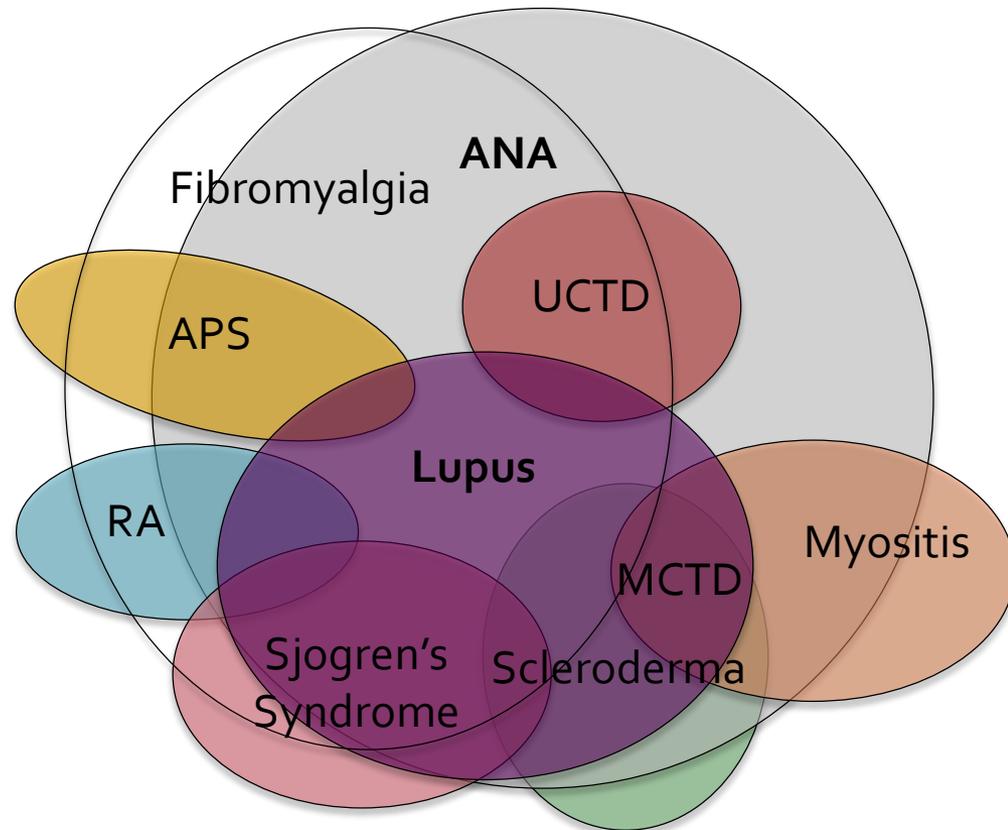
- **Group A:** animals with 2 legs
 - Humans
 - Penguins
- **Group B:** animals that can fly
 - Bees
 - Eagles
- **Overlap:** *Eagles*
 - *Eagles have 2 legs*
 - *Eagles can fly*

VENN DIAGRAM



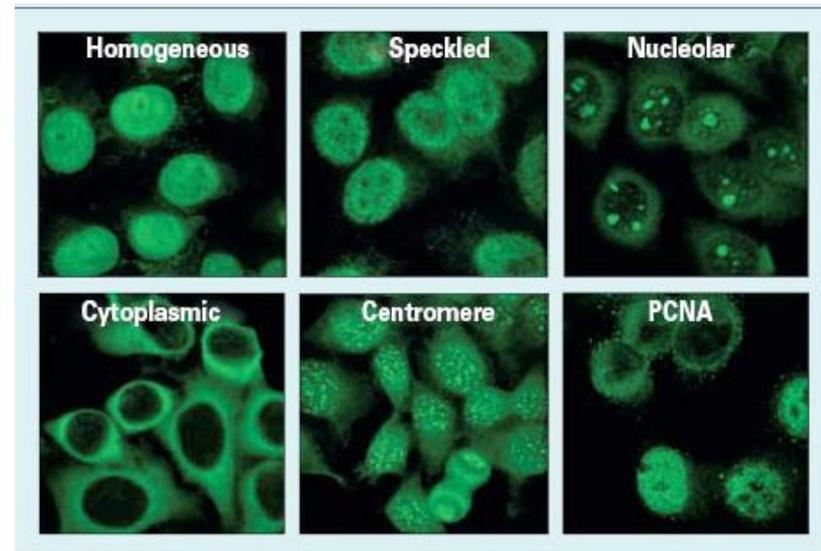
Overlapping Autoimmune Diseases

- ANA positive Disease
 - Systemic Lupus Erythematosus (95-100%)
 - Sjogren's Syndrome (40-70%)
 - Scleroderma (60-80%)
 - Rheumatoid Arthritis (50%)
 - Polymyositis/Dermatomyositis (60%)
 - Antiphospholipid Syndrome (APS)
 - Mixed Connective Tissue Disease (100%)
 - Undifferentiated Connective Tissue Disease (UCTD)
- Other organ specific autoimmune disease
- Non-inflammatory Disease: fibromyalgia



Antinuclear Antibodies (ANA)

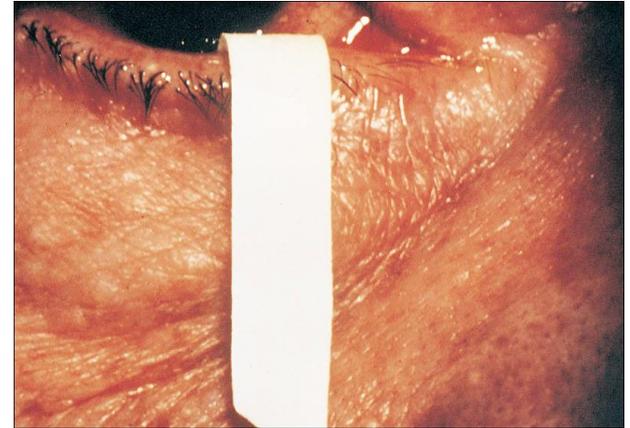
- Autoantibodies
 - Different targets (pattern)
- Extracted nuclear antibodies
 - Anti-Smith
 - Anti-SSA/SSB
 - Anti-RNP
- ANA is not a marker of disease activity
- Approximately 10-20% healthy people have a positive ANA



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Sjogren's Syndrome

- Slowly progressive, inflammatory autoimmune disease
- Primarily affects exocrine glands
 - Dry eyes
 - Dry mouth
 - Enlarged parotid glands
 - Vaginal dryness
- Non-erosive polyarthrititis
- Raynaud's phenomenon



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Sjogren's Syndrome

ACR Diagnostic Criteria

1. Symptoms of dry eyes
2. Symptoms of dry mouth
3. Positive Schirmer's or Rose Bengal Test (eye dryness)
4. Positive salivary gland biopsy
5. Abnormal salivary gland function on testing
6. Positive anti-SSA (Ro) or anti-SSB (La)

To be classified as having Sjogren's, a patient must have:

- Any 4 out of 6, including #4 or #6, or
- Any 3 of the last 4 criteria

Scleroderma (Systemic Sclerosis)

- Inflammatory disease with fibrosis
 - Skin tightening
 - Raynaud's phenomenon
 - Gastric Reflux
 - Interstitial lung disease
 - Pulmonary hypertension
 - Renal (kidney) crisis with severe hypertension
 - Labs: ANA (anti-centromere) or Scl-70

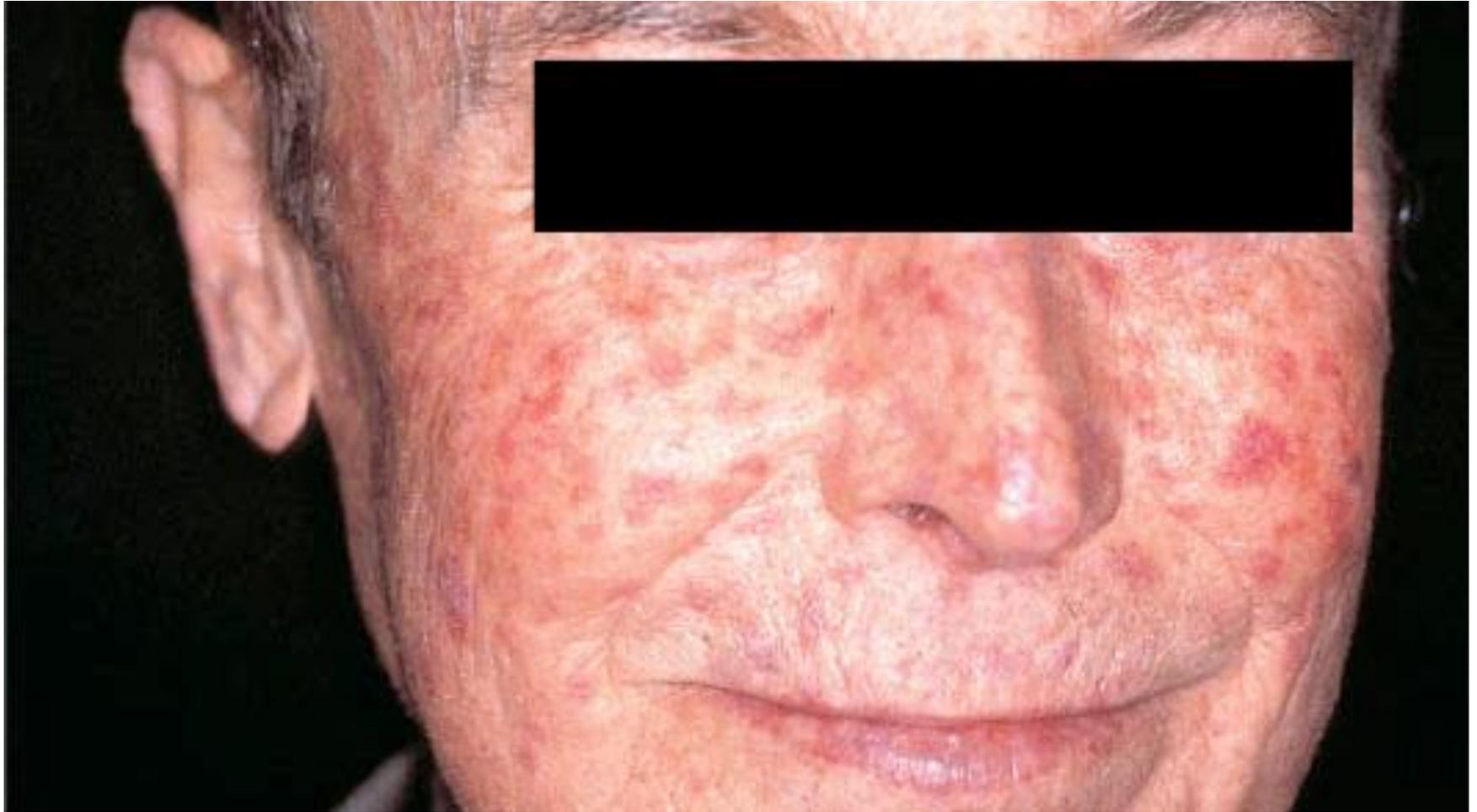
Scleroderma (Systemic Sclerosis)

RAYNAUD'S PHENOMENON



Scleroderma (Systemic Sclerosis)

TELANGIECTASIAS



Scleroderma (Systemic Sclerosis)

SKIN THICKENING AND TIGHTENING



Scleroderma (Systemic Sclerosis)

ACR CRITERIA*

Major Criteria	Minor Criteria
Proximal sclerodactyly (proximal to the MCP)	Sclerodactyly
	Digital pitting scars of fingertips Or Decreased tissue in finger pad
	Bibasilar pulmonary fibrosis

* Must have either the Major Criteria or 2 of 3 Minor Criteria

Scleroderma (Systemic Sclerosis)

LIMITED

- **C:** *Calcinosis*
- **R:** *Raynaud's*
- **E:** *Esophageal dysmotility*
- **S:** *Sclerodactyly*
- **T:** *Telangiectasias*

Positive anti-centromere

DIFFUSE

- Tight skin over hands, arms, face, torso, legs...
- Pulmonary hypertension
- Scleroderma renal crisis

Positive Scl-70

Polymyositis and Dermatomyositis

BOHAN AND PERTER CRITERIA

Individual Criteria

1. Symmetric proximal muscle weakness
2. Muscle biopsy evidence of myositis
3. Increase in serum skeletal muscle enzyme
4. Characteristic electromyographic pattern
5. Typical rash of dermatomyositis

Diagnostic Criteria

Polymyositis:

Definite: all of #1-4

Probable: any 3 of #1-4

Possible: any 2 of #1-4

Dermatomyositis:

Definite: #5 plus and 3 of #1-4

Probable: #5 plus any 2 of #1-4

Possible: #5 plus any 1 of #1-4

Rashes of Dermatomyositis

GOTTRON PAPULES



Rashes of Dermatomyositis

HELIOTROPE RASH



Rashes of Dermatomyositis

V-SHAPED RASH & SHAWL SIGN



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Mixed Connective Tissue Disease

- Overlap of lupus, scleroderma and polymyositis
 - Labs: positive RNP
 - Patient symptoms can align most with 1 disease or overlap all 3
 - Hands: puffy like early scleroderma or thickening with erythema like dermatomyositis
 - Raynaud's phenomenon
 - Malar rash
 - Lung: pulmonary hypertension
 - Muscle weakness
- Specific Disease vs. undifferentiated overlap



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Undifferentiated Connective Tissue Disease

- Patients have symptoms and lab tests that suggest a connective tissue disease but don't quite meet any specific criteria
 - UCTD is different from MCTD
 - Positive ANA and possibly other labs tests
 - Symptoms can include Raynaud's, muscle weakness, arthritis, vasculitis, rashes, lung disease, kidney disease, and fatigue
- Treat the symptoms that characterize the individual patient's disease
- Some will progress to meet classic criteria for SLE or another disease

Antiphospholipid Syndrome

SAPPORO CRITERIA*

CLINICAL CRITERIA

1. **Vascular Thrombosis:** at least 1 confirmed arterial or venous event
2. **Pregnancy Morbidity**
 - 3 or more consecutive, unexplained miscarriages before 10 weeks
 - At least 1 unexplained miscarriage after week 10
 - At least 1 premature birth before week 34 due to eclampsia, extreme pre-eclampsia, or placental insufficiency

LABORATORY CRITERIA

The presence of at least 1 of the following test on at least 2 occasions 12 weeks apart:

1. Lupus Anticoagulant
2. Anticardiolipin antibody
3. Anti- β 2-glycoprotein 1

** One clinical and 1 laboratory criteria are needed to make diagnosis*

Rheumatoid Arthritis

- Classic Symptoms
 - Morning Stiffness ≥ 1 hr
 - Symmetric, polyarticular arthritis
 - Arthritis of wrists and hands (MCPs and PIPs)
 - Rheumatoid nodules
- X-ray changes: erosions in joints



(From Clinical Slide Collection on the Rheumatic Diseases, American College of Rheumatology)



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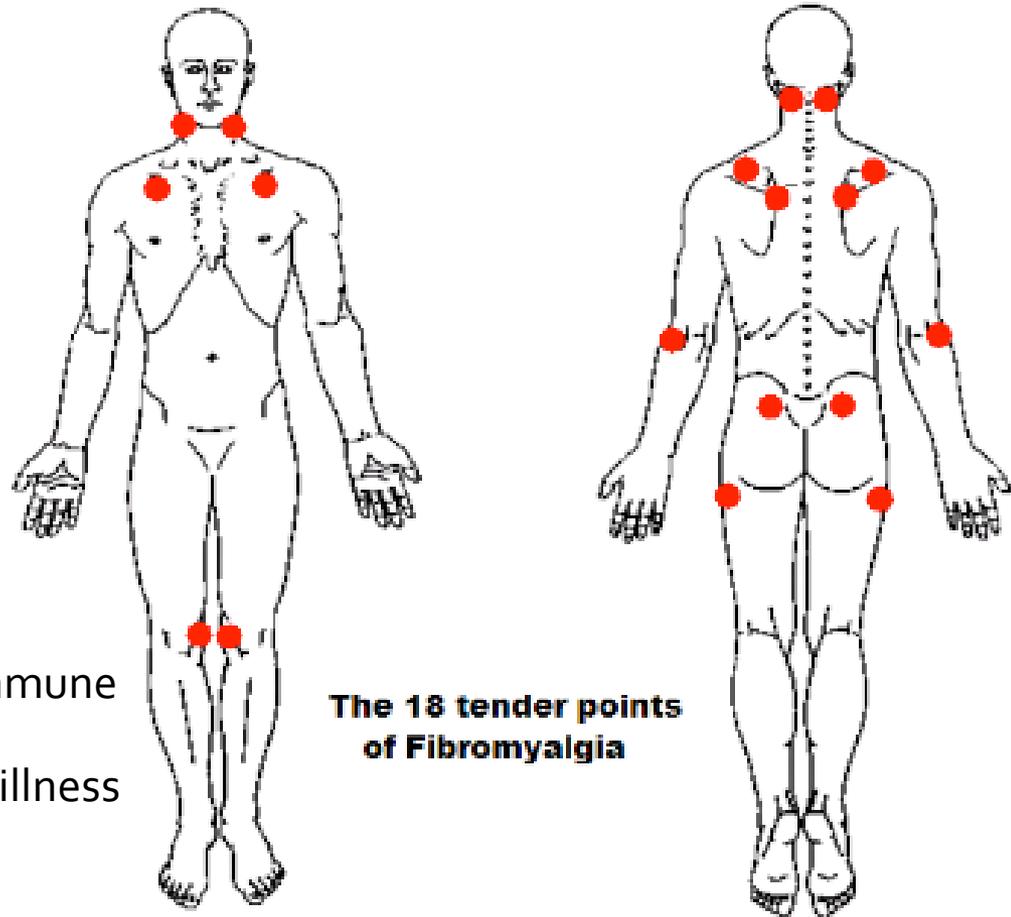
Rheumatoid Arthritis

2010 ACR/EULAR CRITERIA: *score* \geq 6

Joint Involvement	SCORE
1 large joint	0
2-10 large joints	1
1-3 small joints (with or without large joints)	2
4-10 small joints	3
>10 joints (at least 1 small joint)	5
Serology	SCORE
Negative RF and anti-CCP	0
Low-positive RF or low-positive anti-CCP	2
High positive RF or high positive anti-CCP	3
Acute Phase Reactants	SCORE
Normal CRP and ESR	0
Elevated CRP or ESR	1
Duration of Symptoms	SCORE
<6 weeks	0
\geq 6 weeks	1

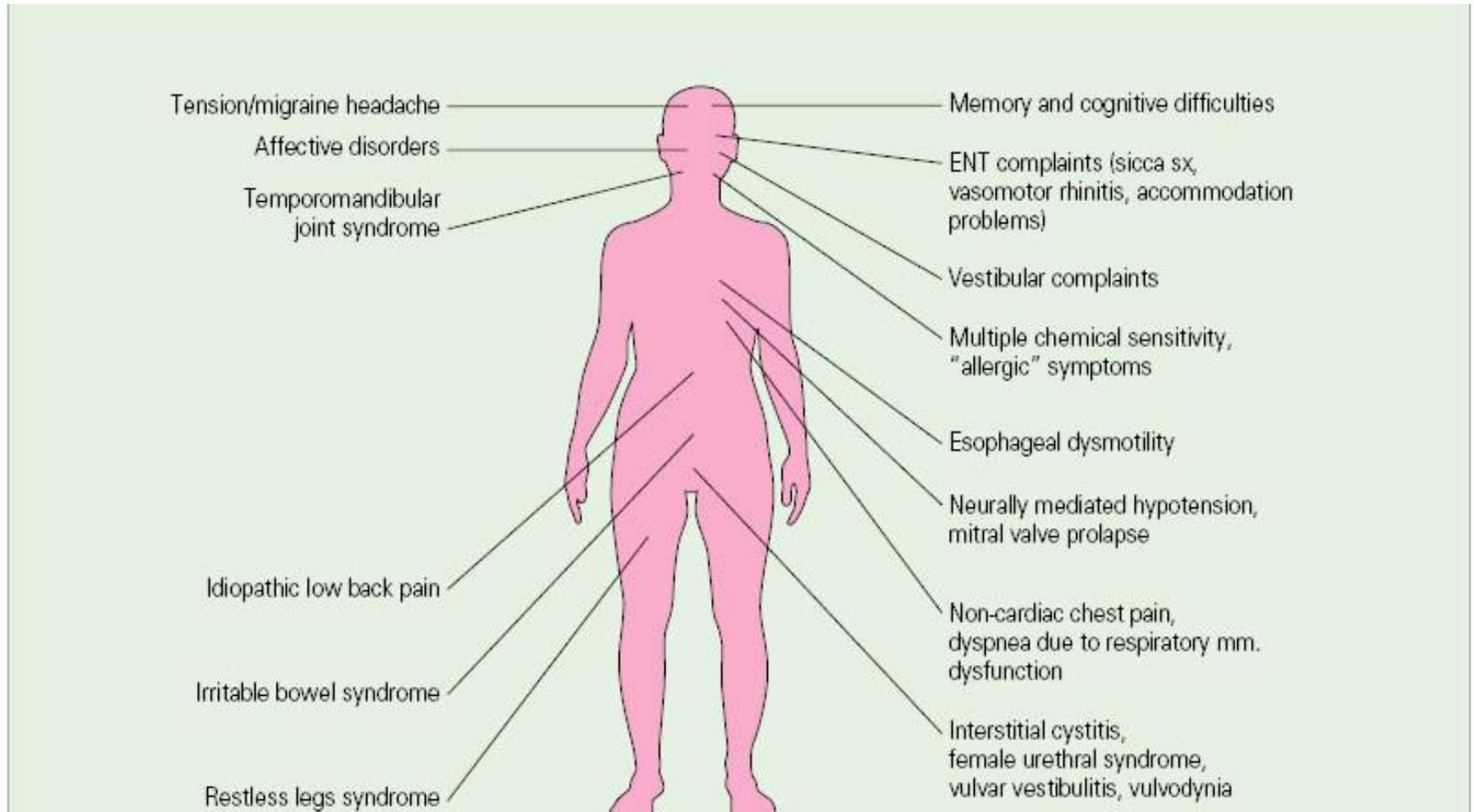
Fibromyalgia

- Widespread pain: “I hurt all over”
 - Non-inflammatory
 - “volume control” in pain processing
- Symptoms for at least 3 months
 - 11 of 18 tender points
 - Insomnia
 - fatigue
- Symptoms not better explained by another disease
 - Primary: no association with autoimmune disease
 - Secondary: associated with chronic illness
- **IMPORTANT:** *distinguish between symptoms of fibromyalgia and SLE*



Fibromyalgia

OVERLAPPING SYNDROMES



Impact of Overlap on SLE

- Increased risk for certain illnesses...
 - Antiphospholipid Syndrome: miscarriage
 - Scleroderma: pulmonary hypertension
- Monitoring: checking PFTs, Echo, etc.
- Treatment: guided toward individualized symptoms

Conclusion

- Autoimmune diseases have many different characteristics
- Positive ANA alone does not diagnosis SLE or any other disease
 - ANA can be seen in many autoimmune disease
 - ANA can be seen in healthy individuals
- Multiple connective tissue diseases can overlap with SLE
- Diagnosis can help with communication, monitoring, and treatment choices

Thank you!

- Questions?
- Comments?
- Concerns?