

# Common Rheumatic Diseases in the Alaska Native Population

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September 11, 2020

Rural Providers Webinar



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# Disclosures

- Nothing to disclose.
- Off label use of medications will be discussed.



# OUR DISEASES MAY BE INVISIBLE, BUT WE'RE NOT.



September 2020 marks the 5th Annual Rheumatic Disease Awareness Month (RDAM), a national awareness event sponsored by the American College of Rheumatology (ACR) and its public awareness campaign, Simple Tasks™. RDAM was created to raise awareness of the 100+ conditions under the umbrella of rheumatic disease. The theme for this year's RDAM focuses on amplifying the voices and experiences of people living with rheumatic disease to facilitate better public understanding of what it's like to live with one of these diseases.

ACR: [rheumatology.org](https://rheumatology.org)



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# Rheumatic Diseases Covered

- Rheumatoid arthritis
- Spondyloarthritis
  - Includes ankylosing spondylitis, psoriatic arthritis, reactive arthritis, and related conditions
- Systemic lupus erythematosus and mixed connective tissue disease
- Juvenile idiopathic arthritis



# Not covered today

- Osteoarthritis
- Gout
- Mechanical causes of joint pain
- Sjögren's syndrome
- Myositis
- Scleroderma
- Vasculitis



# Case 1

- 31 year old woman had a baby 13 months ago
- She has had joint swelling and pain for 3-4 months
- She feels stiff when she wakes up in the morning, and it takes her 4 hours to get moving well
- On physical exam, she has multiple swollen and tender joints bilaterally but not exactly symmetric (MCP, PIP, wrists, knees, ankles, MTPs)
  
- What diagnosis do you suspect?



# Rheumatoid arthritis

- Epidemiology
- Clinical Features
- Risk Factors
- Diagnosis
- Key Components of Treatment
- Primary Care Considerations



# Epidemiology of RA

- Incidence and prevalence high in several AI/AN populations
  - US population ~1%
  - Southeast AN 2.4%
- Age of onset younger
- More commonly seropositive
- More severe disease



Ferucci ED et al. Semin Arthritis Rheum 2004;34:662

Peschken CA et al. J Rheumatol 2010;37:1589



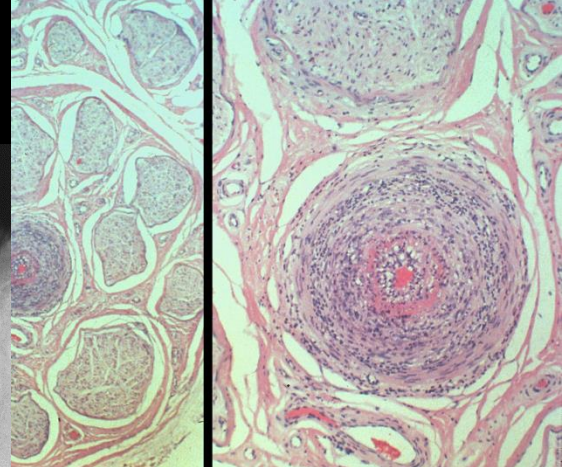
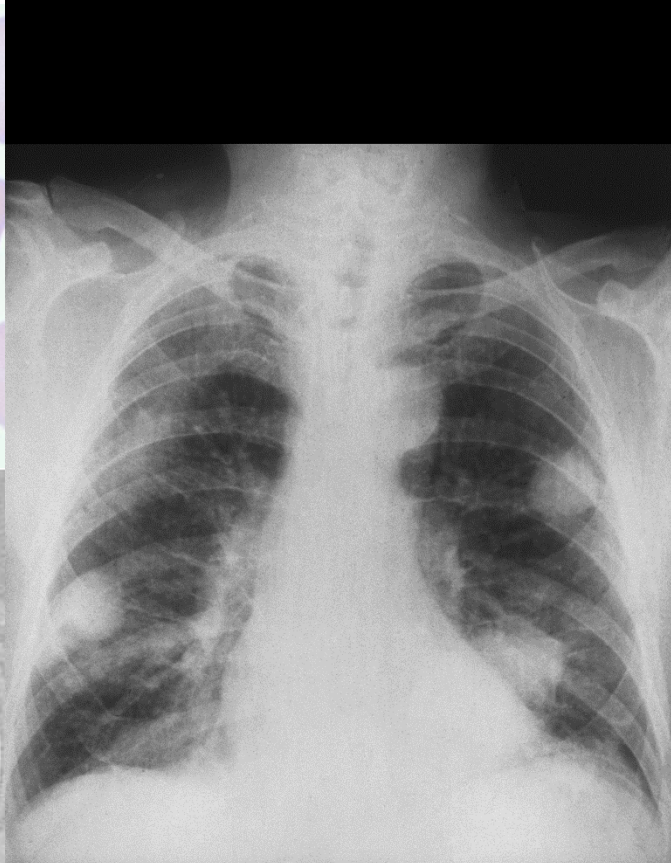
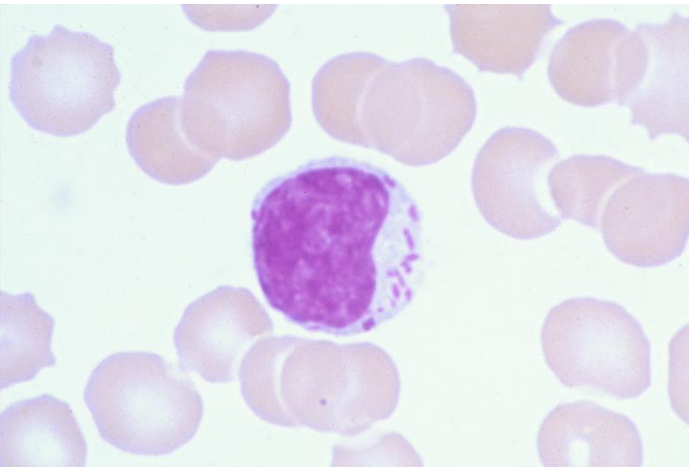
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# Clinical features of RA

- Chronic inflammatory polyarthritis that leads to joint destruction, deformity, and loss of function.
- Pathology of RA involves the synovium of multiple joints.
- Rheumatoid factor and/or cyclic citrullinated peptide (CCP) antibodies are present in ~80% of patients.





# Diagnosis of RA

- Joint exam is the most important component
  - Symmetric synovitis, especially of small joints of hands and feet
- Labs are useful in the setting of joint findings
- 1987 classification criteria designed for more longstanding disease
  - Radiographic changes, rheumatoid nodules included
- 2010 criteria revised to diagnose earlier
  - Point system, added CCP as well as inflammatory markers



# 2010 Classification Criteria for RA

- ❑ Only use these criteria for people with **at least one joint swollen** and if that joint swelling is **not already explained by another disease**
- ❑ If X-rays show **erosions typical of RA** in at least 3 separate MCP, PIP, wrist, or MTP joints, this is diagnostic of RA and the remainder of criteria are not needed.
- ❑ Score of **>=6 points/10** is needed to classify as definite RA.

## A. Joint involvement

1 large joint	0
2-10 large joints	1
1-3 small joints	2
4-10 small joints	3
>10 joints	5

## B. Serology

Negative RF/anti-CCP	0
Low-positive* RF/anti-CCP	2
High-positive* RF/anti-CCP	3

## C. Acute phase reactants

Normal CRP and ESR	0
Abnormal CRP or ESR	1

## D. Duration of symptoms

<6 weeks	0
>=6 weeks	1

Aletaha D et al. Arthritis Rheum  
2010;62:2569

\* Low-positive  $\leq 3 \times$  ULN; high-positive  $> 3 \times$  ULN

Rheumatoid Factor (RF)	Anti-Cyclic Citrullinated Peptide (CCP)
Present in ~80% of people with RA	Present in ~80% of people with RA
Included in 1987 and 2010 criteria	Included in 2010 criteria for RA
Associated with more severe RA	Associated with more severe RA
<p><b>Very non-specific</b></p> <p>Positive in Hepatitis C and many chronic infections or inflammatory conditions</p>	<p><b>Very specific for RA</b></p> <p>Occasionally found in other autoimmune diseases but usually in setting of arthritis; not in HCV</p>
PPV and NPV depend on population being tested	PPV and NPV also vary but PPV higher for CCP than RF
Not recommended for screening healthy individuals for RA	Not recommended for screening healthy individuals for RA



# Risk Factors for RA

Family history



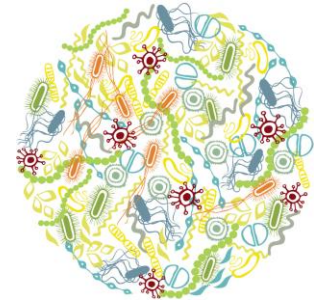
Specific genes



Smoking



Microbiome



Being female



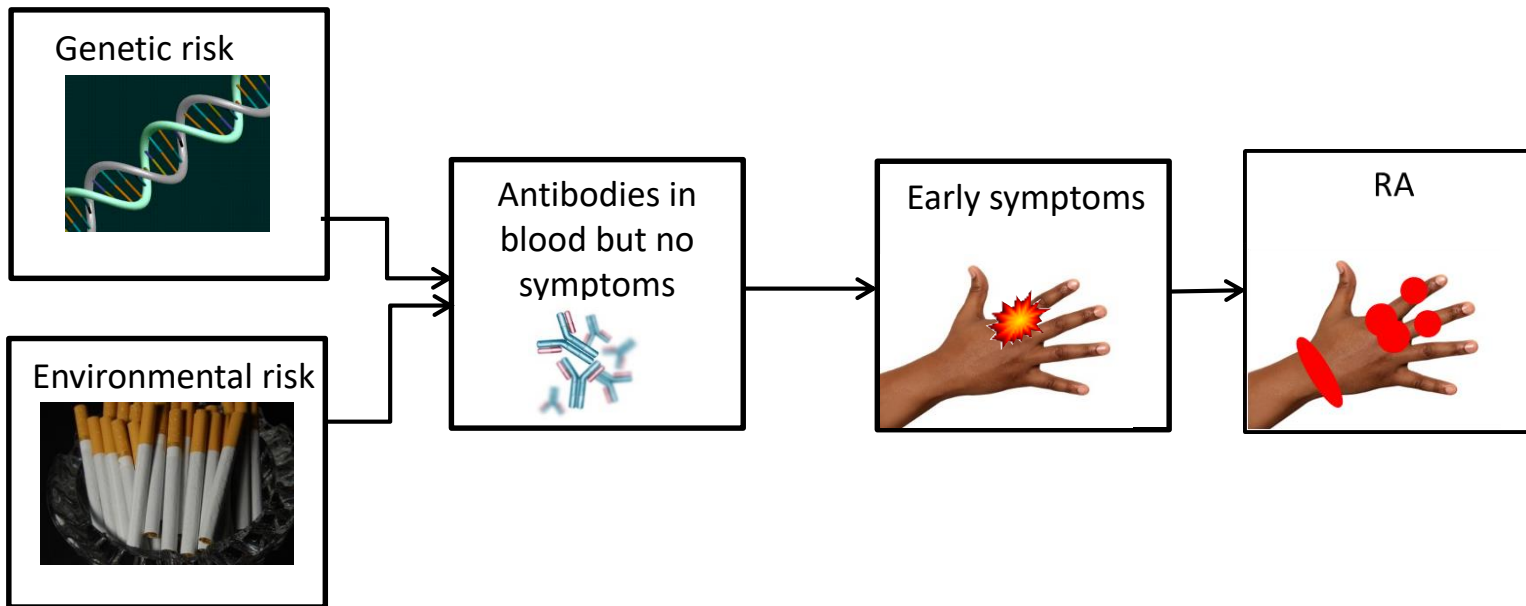
Stress



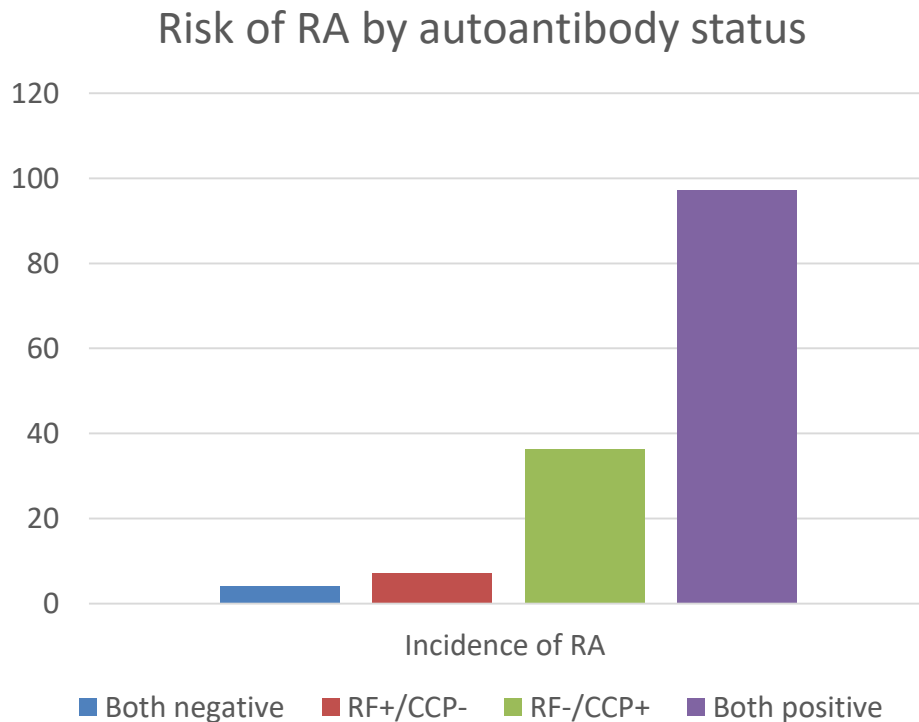
Diet



# Model of RA Development



# Development of RA in Relatives



- Study of FDRs of indigenous people with RA in Manitoba and Alaska
- People who developed RA were more likely to have positive antibodies
- RA developed 3-5 years after enrollment
  - Sooner in those with both antibodies

Tanner S et al. Arthritis Rheumatol 2019;71:1494



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# Early Referral and Treatment

- Permanent structural damage occurs early in RA
- Early DMARD intervention
  - Slows the progression of structural joint damage
  - Improves long term outcome
  - Improves patient quality of life
  - Reduces need for joint replacement
  - May decrease risk of CVD and mortality
- Recommend that if RA is suspected, rheumatology referral should be initiated without delay.

Emery P et al. Ann Rheum Dis 2002;61:290-297



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# Disease-Modifying Anti-Rheumatic Drugs (DMARDs)

## Conventional Synthetic

- Hydroxychloroquine (Plaquenil)
- Sulfasalazine
- Methotrexate
- Leflunomide (Arava)

## Targeted Synthetic

- Tofacitinib (Xeljanz)
- Upadacitinib (Rinvoq)

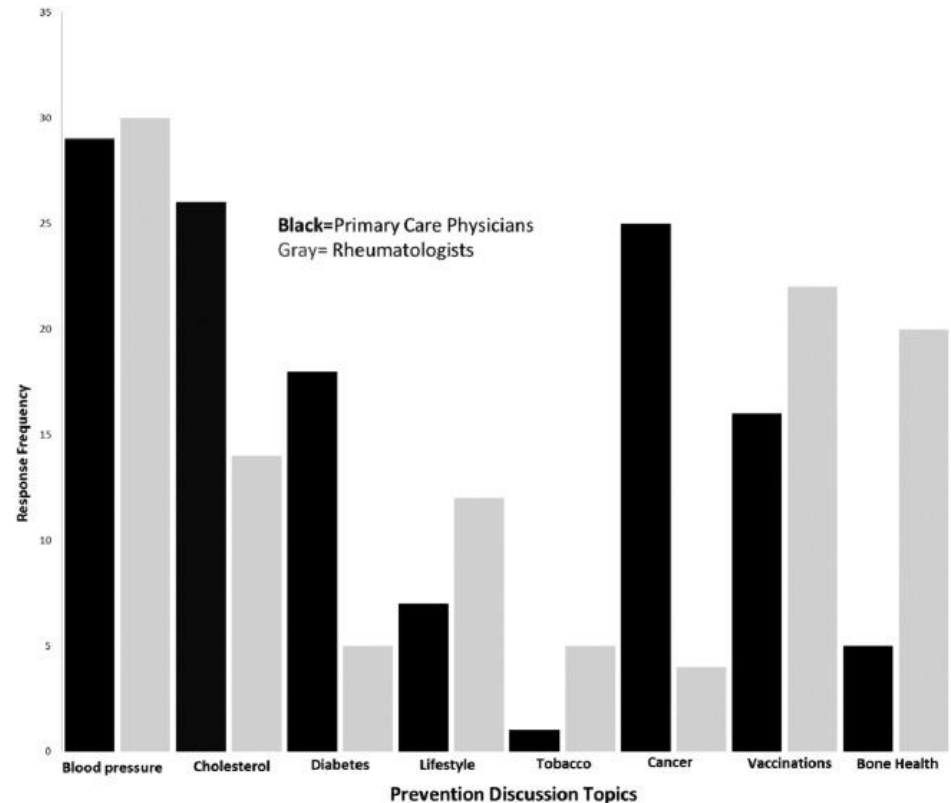
## Biologics

- Etanercept (Enbrel)
- Infliximab (Remicade)
- Adalimumab (Humira)
- Golimumab (Simponi)
- Certolizumab Pegol (Cimzia)
  
- Anakinra (Kineret)
- Rituximab (Rituxan)
- Abatacept (Orencia)
- Tocilizumab (Actemra)



# Primary Care Considerations in RA

- Medication monitoring
- Perioperative management
- Cardiovascular disease risk
  - Lipids
  - Diabetes
  - Blood pressure
  - Controlling RA
- Vaccines
- Bone health
- Tobacco cessation



Bartels CM et al. Arthritis Care & Research 2016;68:415.



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# Case 2

- 33 year old man presents with a 6 month history of lower back pain radiating to both buttocks
- He is very stiff and sore in the morning and improves after a shower and moving around.
- ROS: he was treated for iritis about 2 years ago, which resolved and has not recurred
  
- What diagnosis do you suspect?



# Spondyloarthritis

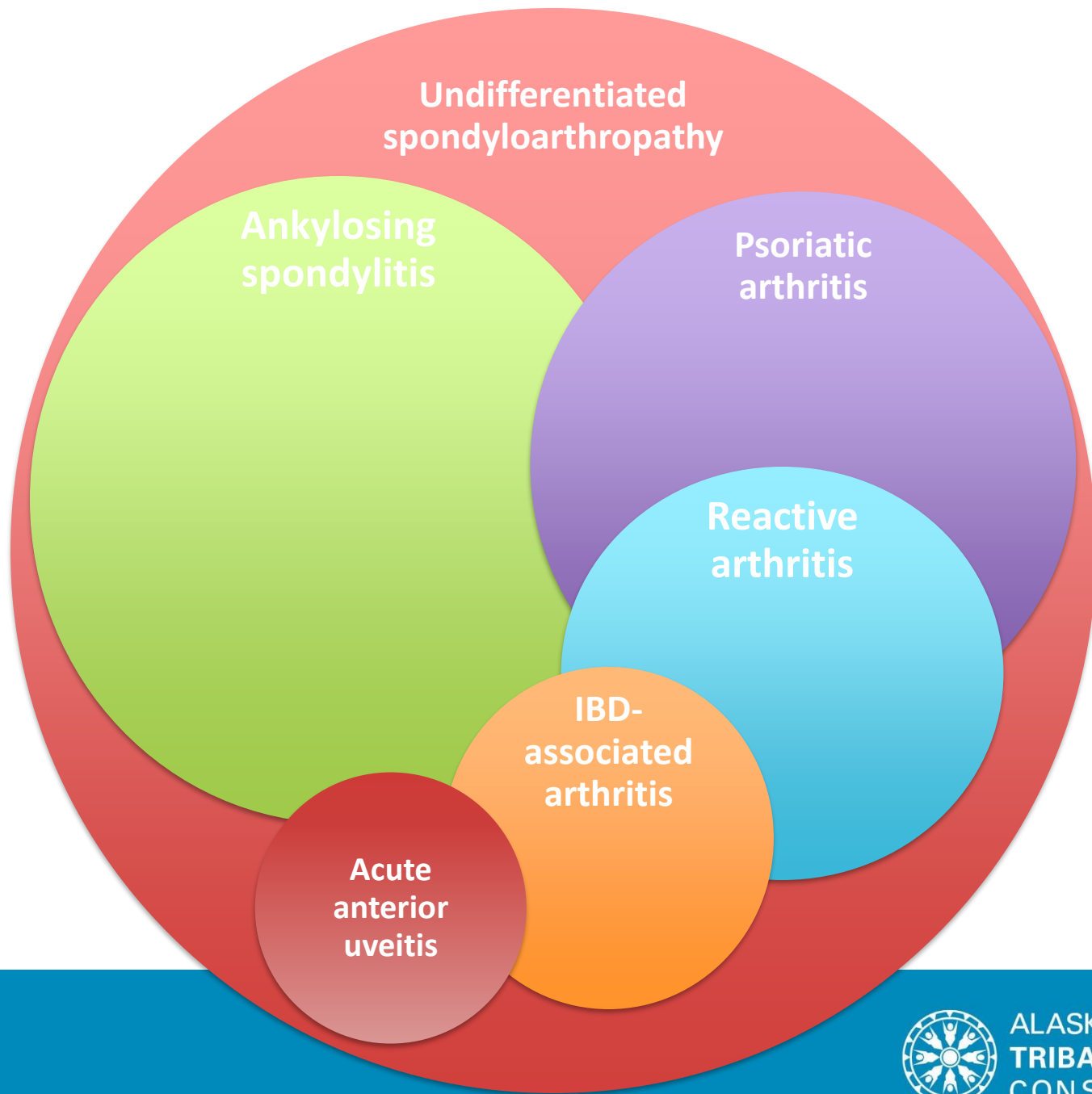
- Definition
- Epidemiology
- Clinical Features
- Management



# Spondyloarthritis

- Set of disorders linked by some common features:
  - “Seronegative”
  - Presence of HLA B27 allele
  - Sacroiliitis
- Includes the following:
  - Ankylosing spondylitis (AS)
  - Psoriatic arthritis (PsA)
  - Reactive arthritis (ReA)
  - Inflammatory bowel disease arthritis
  - Undifferentiated spondyloarthritis





**Undifferentiated  
spondyloarthropathy**

**Ankylosing  
spondylitis**

**Psoriatic  
arthritis**

**Reactive  
arthritis**

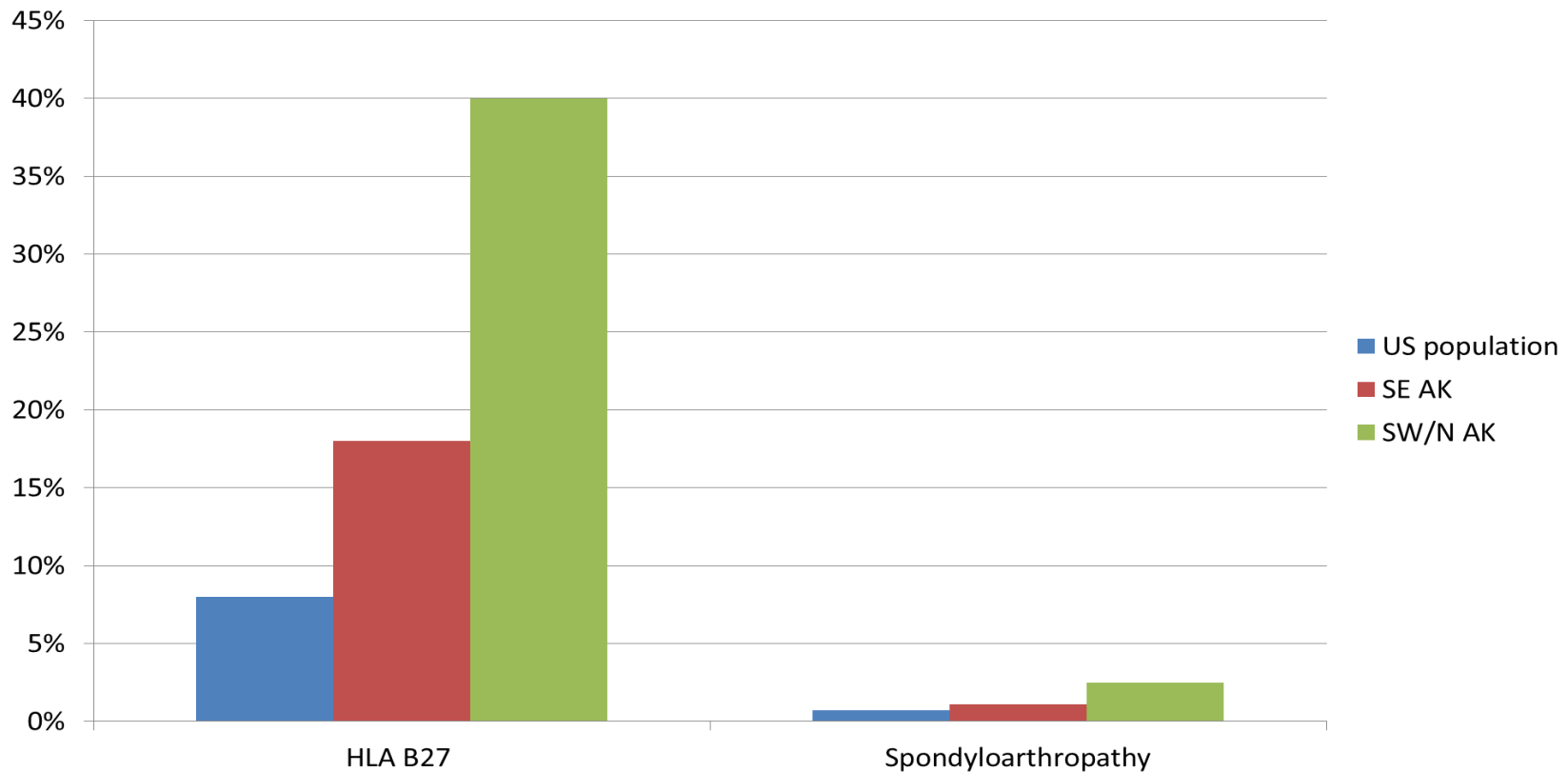
**IBD-  
associated  
arthritis**

**Acute  
anterior  
uveitis**

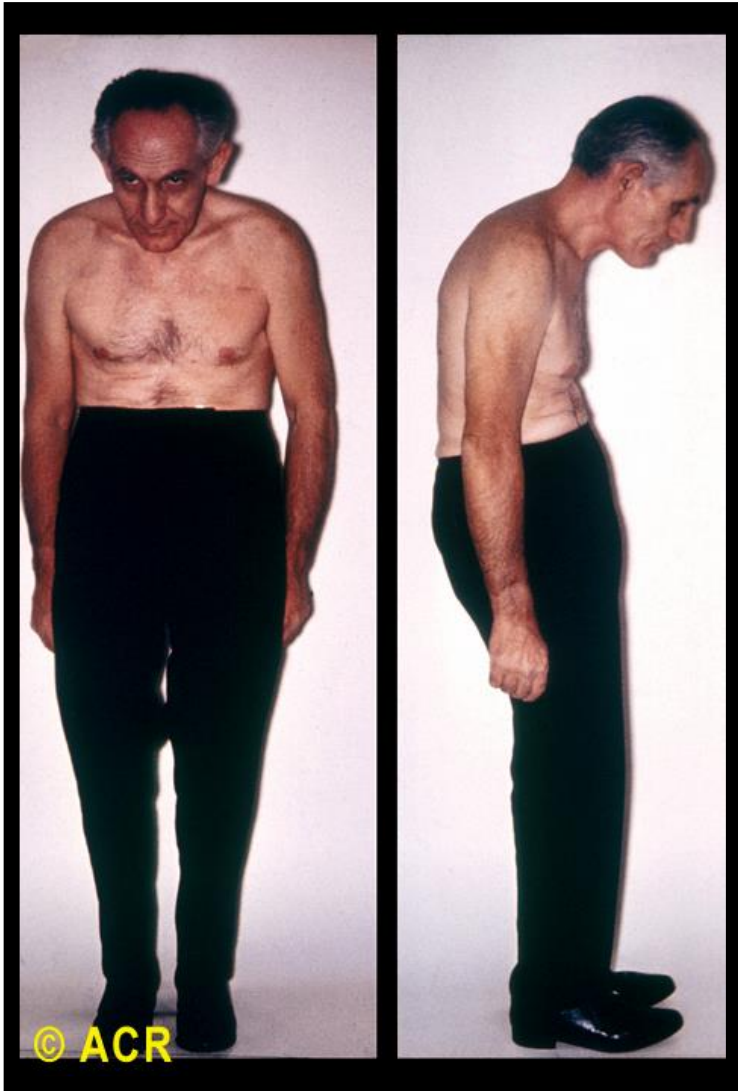


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# Spondyloarthritis in AN Population







# Ankylosing Spondylitis Features

- Inflammatory back pain
  - Worse with rest, better after activity
  - Morning stiffness
  - Age of onset <40-45
- Sacroiliitis on imaging
  - Plain film or MRI
- Other features of spondyloarthritis
  - Family history, enthesitis, HLA B27+, elevated CRP, good response to NSAIDs





# PsA Features/Diagnosis

- Inflammatory arthritis of peripheral joints or SI joints, or enthesitis
- Psoriasis
- Psoriatic nail dystrophy
- Negative Rheumatoid Factor
- Dactylitis
- Radiographic changes



# Reactive Arthritis

- Inflammatory arthritis occurring days to weeks after an infection
  - GU (*Chlamydia*) or GI (*E. coli*, *Salmonella*, *Shigella*)
- Mono- or oligoarthritis typically affecting lower extremities
- Dactylitis or enthesitis may be present
- May be extremely painful
- More common in men than women
- Often very high ESR/CRP
- Mucocutaneous involvement can occur
  - Triad of arthritis, urethritis, and conjunctivitis was formerly called Reiter syndrome



# Management of SpA

- Ankylosing spondylitis
  - NSAIDs, TNF inhibitors, other biologics
- Psoriatic arthritis
  - Methotrexate, sulfasalazine, leflunomide, apremilast, TNF inhibitors, other biologics
- Reactive arthritis
  - NSAIDs, corticosteroids, DMARDs, TNF inhibitors
  - Antibiotics do not help arthritis



# Case 3

- 28 year old woman presents with fatigue and diffuse joint pain.
- Her joint pain started about 4 months ago and has become worse.
- She has noted some new sores in her mouth and has had a rash with sun exposure recently.
- Exam shows swelling at PIP joints of hands.
- What diagnosis do you suspect?



# SLE



- Epidemiology
- Clinical Features
- Diagnosis
- Management





# Systemic Lupus Erythematosus (SLE)

- Systemic autoimmune disease
- Not organ-specific
  - Diverse presentations, evolve over time
- Hallmark is autoantibodies
- Characterized by remissions and exacerbations (“flares”)
- Prognosis varies by organ involvement and severity

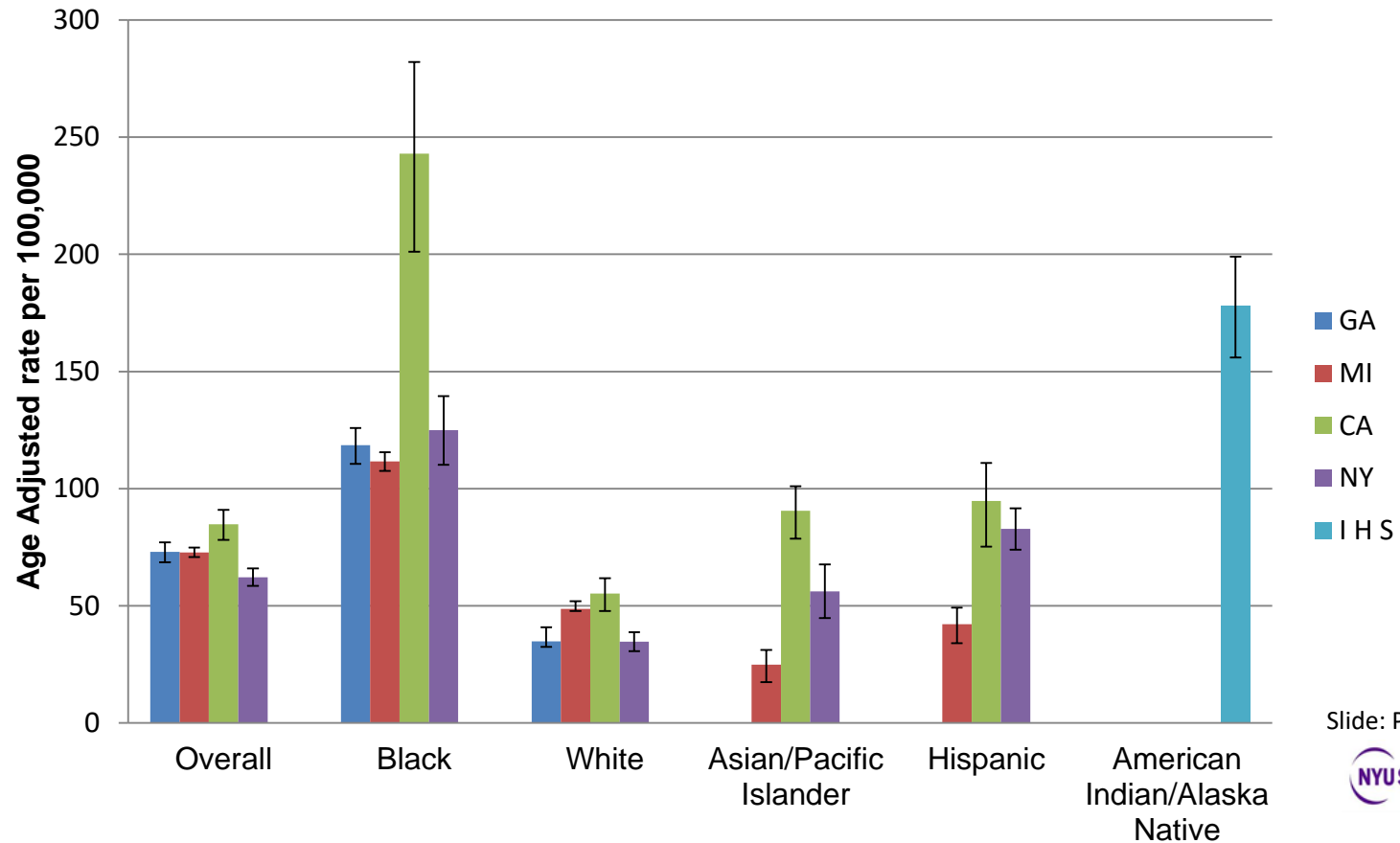


# Epidemiology of SLE

- Estimates of incidence and prevalence of SLE in the US have varied
- CDC-funded lupus registries were developed to address limitations in the literature on SLE epidemiology in the US
- Goal was to determine incidence/prevalence of SLE in populations by race/ethnicity
- Standardized data elements and methods across sites
- Included:
  - Georgia (GLR) and Michigan (MILES) 2002-2004
  - Indian Health Service (IHS), Manhattan (MLSP), California (CLSP) 2007-2009



# Overall Age Adjusted Prevalence of SLE from 5 CDC Lupus Registries as per the ACR criteria



Slide: Pete Izmirly, MD



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# Conclusions from IHS Lupus Registry

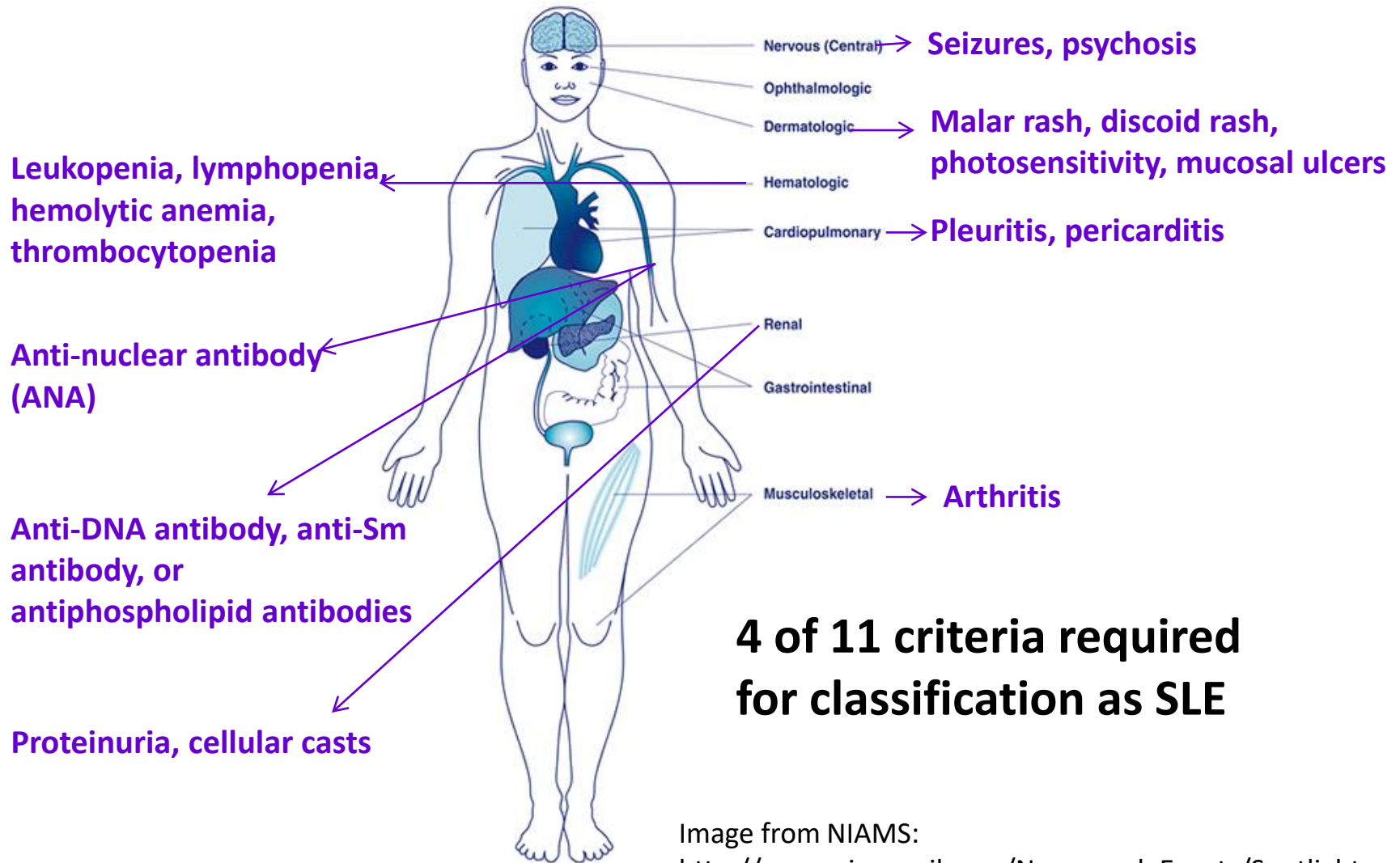
- The prevalence and incidence of SLE are high in the IHS active clinical population of AI/AN people in 3 regions.
  - **Prevalence: 178 per 100,000**
  - **Incidence: 7.4 per 100,000 person-years**
- The prevalence of SLE in AI/AN women in the population included in our registry is as high as or higher than estimates in black women.
  - **271 per 100,000**

Ferucci ED et al. Arthritis Rheumatol 2014;66:2494



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# Manifestations of SLE: ACR Criteria

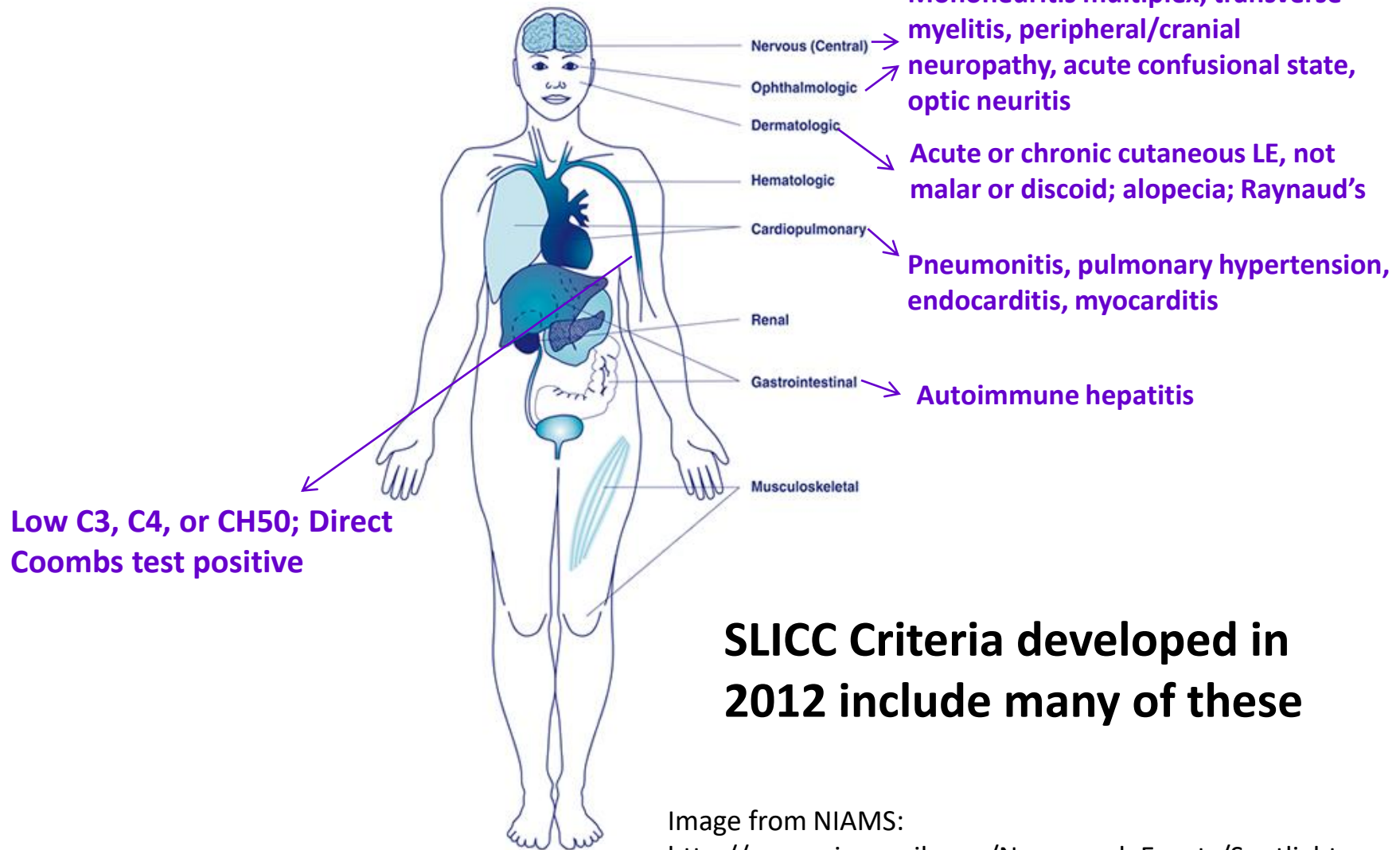


**4 of 11 criteria required for classification as SLE**

# Manifestations of SLE



# Manifestations of SLE not included in ACR Criteria



**SLICC Criteria developed in 2012 include many of these**

Image from NIAMS:

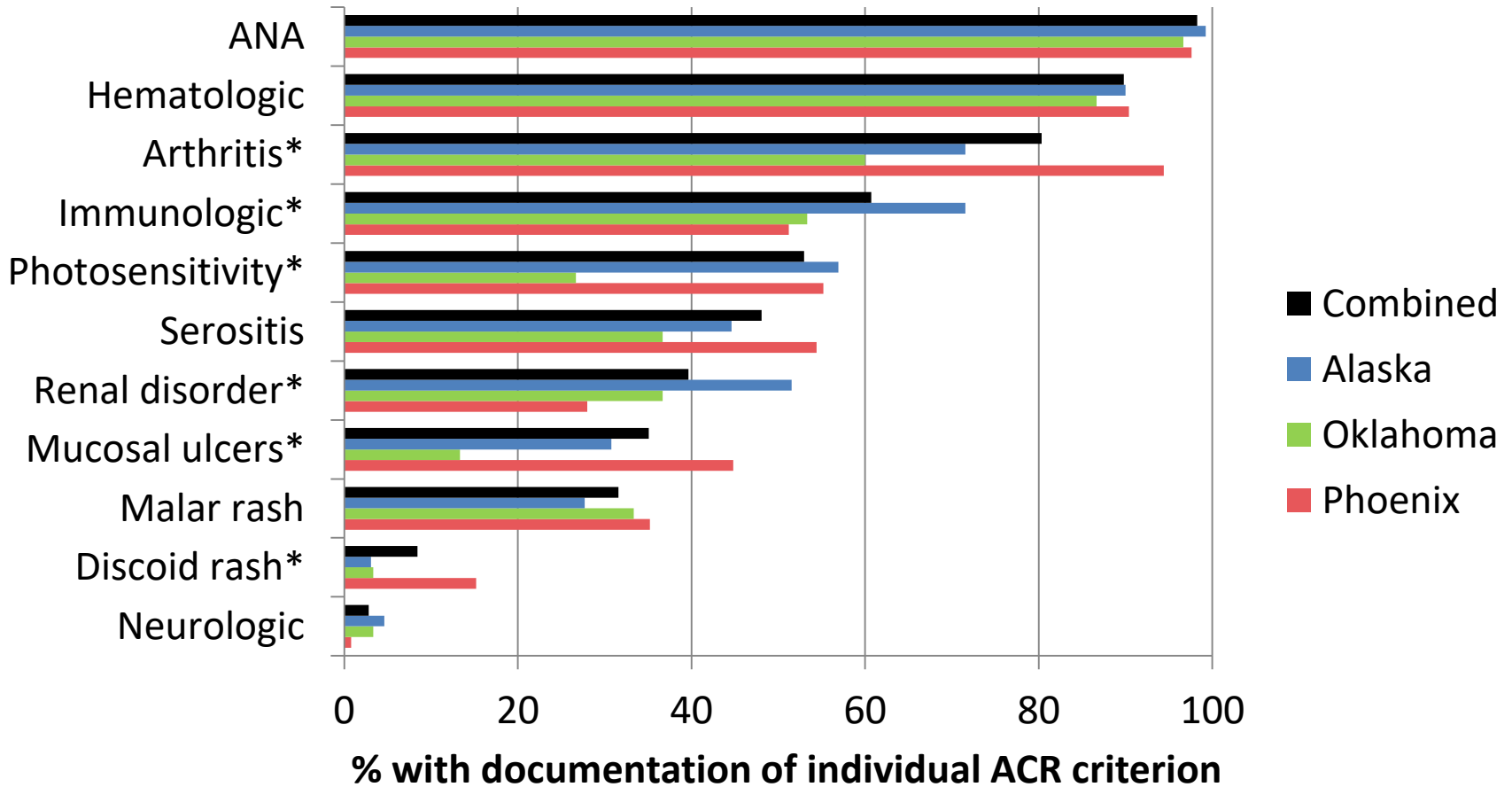
[http://www.niams.nih.gov/News\\_and\\_Events/Spotlight\\_on\\_Research/2013/novel\\_drug\\_lupus.asp](http://www.niams.nih.gov/News_and_Events/Spotlight_on_Research/2013/novel_drug_lupus.asp)

# Other Manifestations of SLE





# IHS Lupus Registry: Prevalence of Individual ACR Criteria



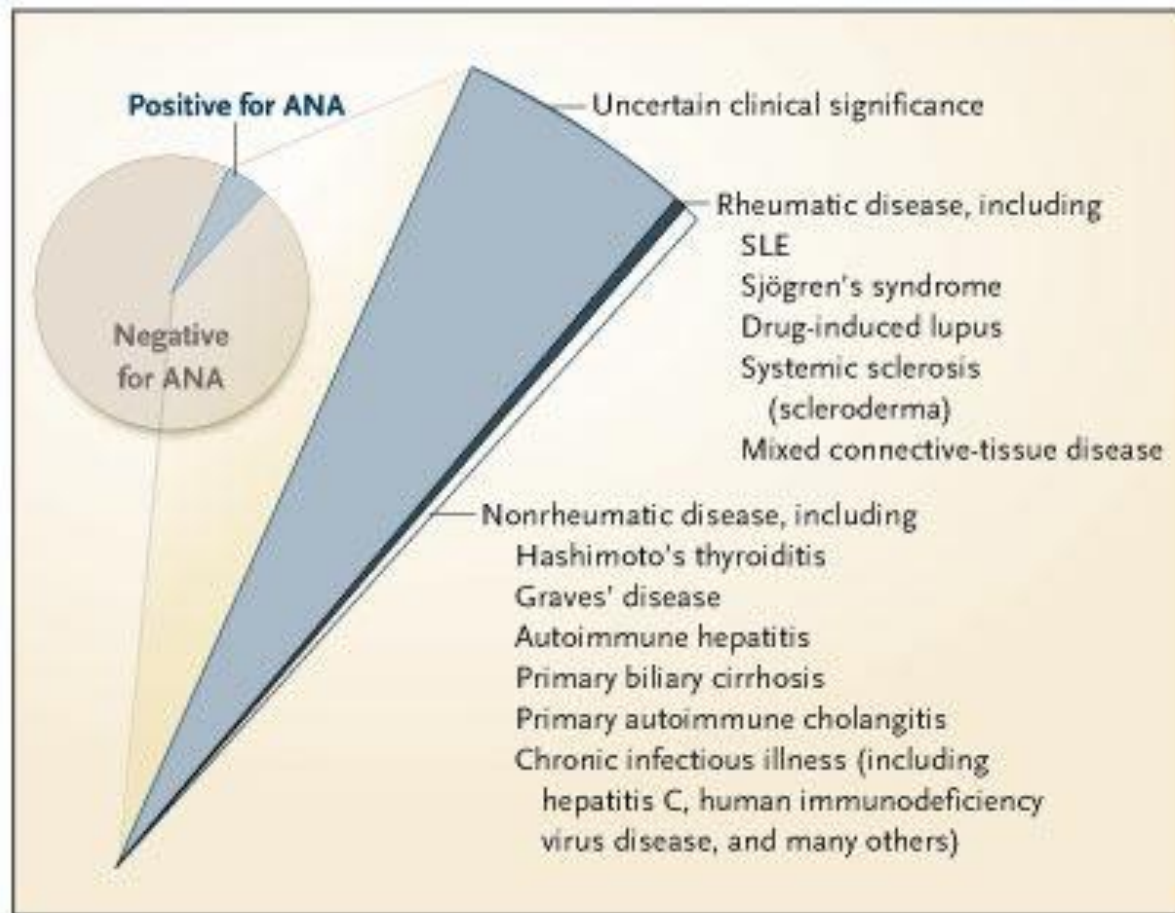
\* indicates significant differences across regions based on Chi-Square p-value < 0.05 (Fisher Exact for ACR Criteria 8 and 11)

# Clues to suspect SLE

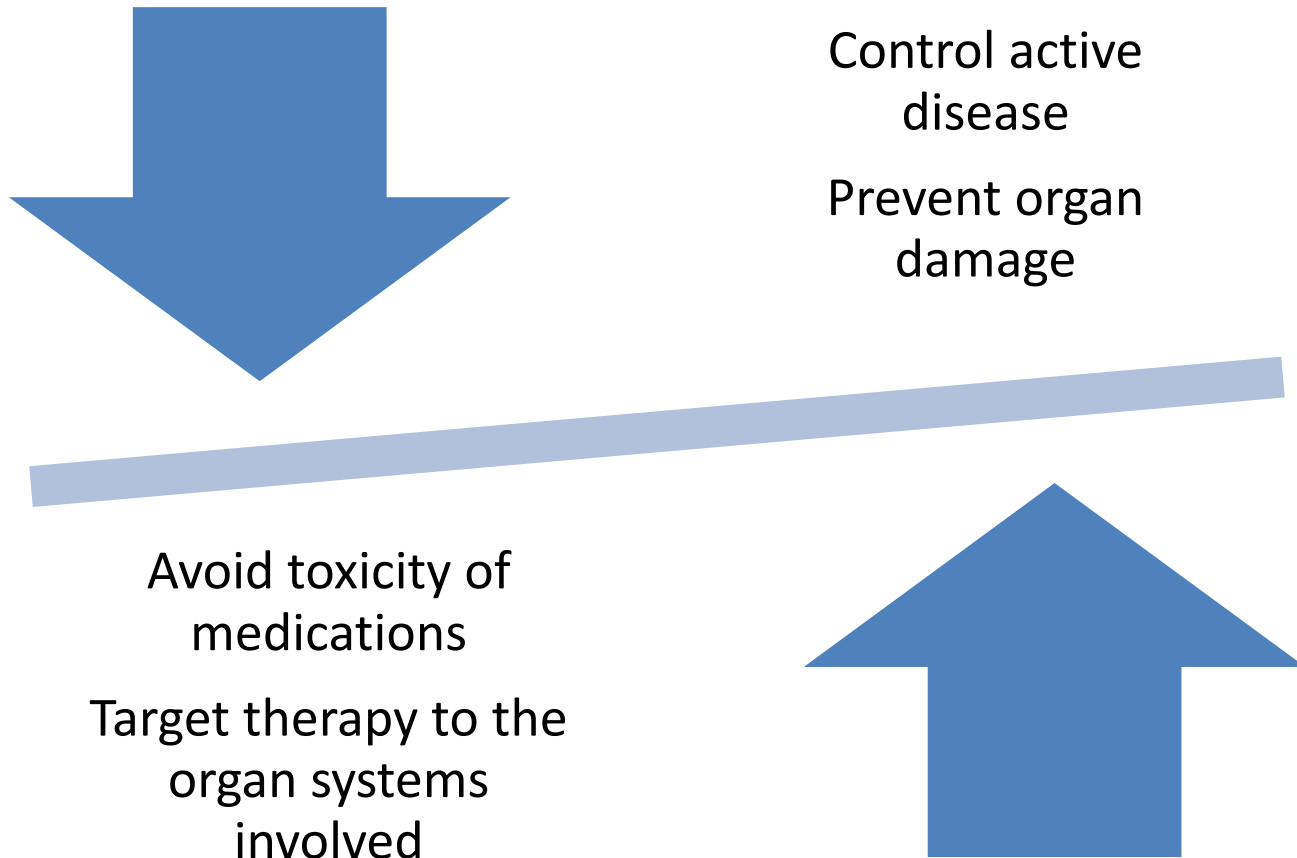
- Presentation may be with arthritis and fatigue
- DDX might include RA, other connective tissue disease, other skin diseases, fibromyalgia, and others
- Common SLE clues:
  - Rashes, alopecia, oral ulcers, serositis
  - Leukopenia, lymphopenia
  - Proteinuria, RBCs/casts in urine



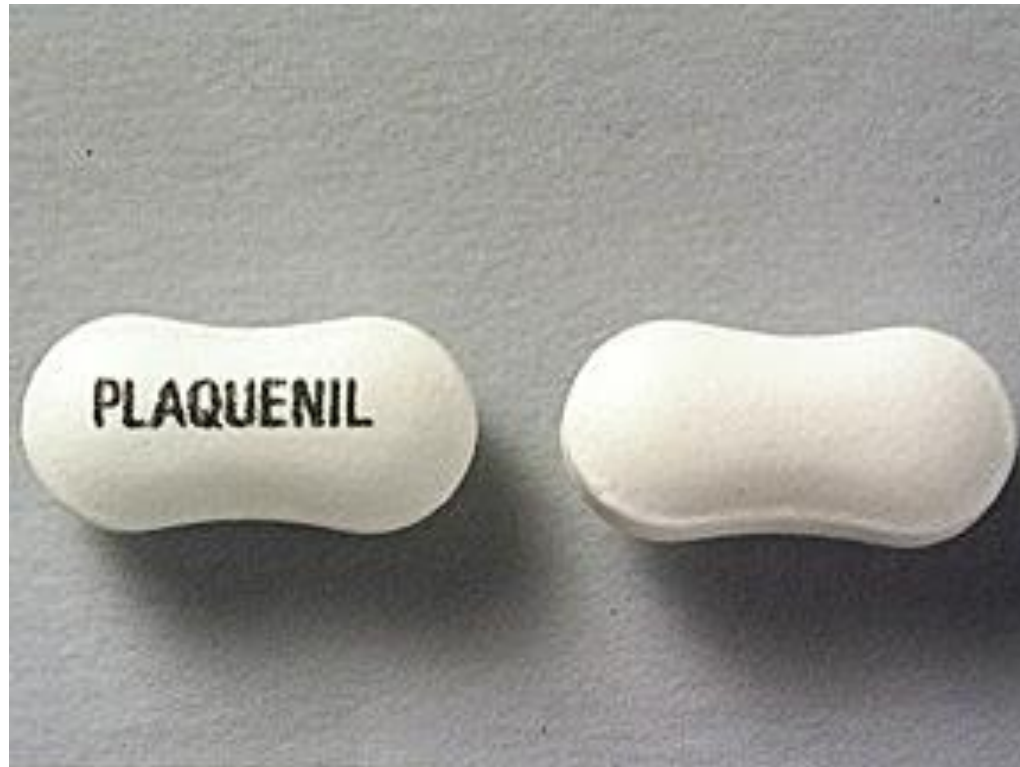
# ANA Results in a Hypothetical Population



# Goals of Therapy in SLE



# First-line therapy in SLE



Hydroxychloroquine is the most commonly prescribed anti-malarial medication.

Chloroquine is available but more toxic.

Quinacrine may be used in some cases, but availability is limited.



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# Mixed Connective Tissue Disease (MCTD)

- Defined by high titer anti-RNP antibodies and several clinical features
  - Can have features of scleroderma, Sjogren's, myositis, and/or RA
- Less common than SLE but few reports of epidemiology
- IHS Lupus Registry included data elements necessary for definition of MCTD
- Determined the age-adjusted prevalence of MCTD in AI/AN population included in IHS registry
  - 6.4 per 100,000
  - Few other studies, but Norway 3.8 per 100,000

Ferucci ED, et al. Arthritis Care Res 2017;69:1271.



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# Juvenile Idiopathic Arthritis (JIA)

- Definition
- Epidemiology



# Juvenile Idiopathic Arthritis (JIA)

- Previously called juvenile rheumatoid arthritis
- Most common form of arthritis in children
- Autoimmune but specific causes unknown
- 6 different subtypes



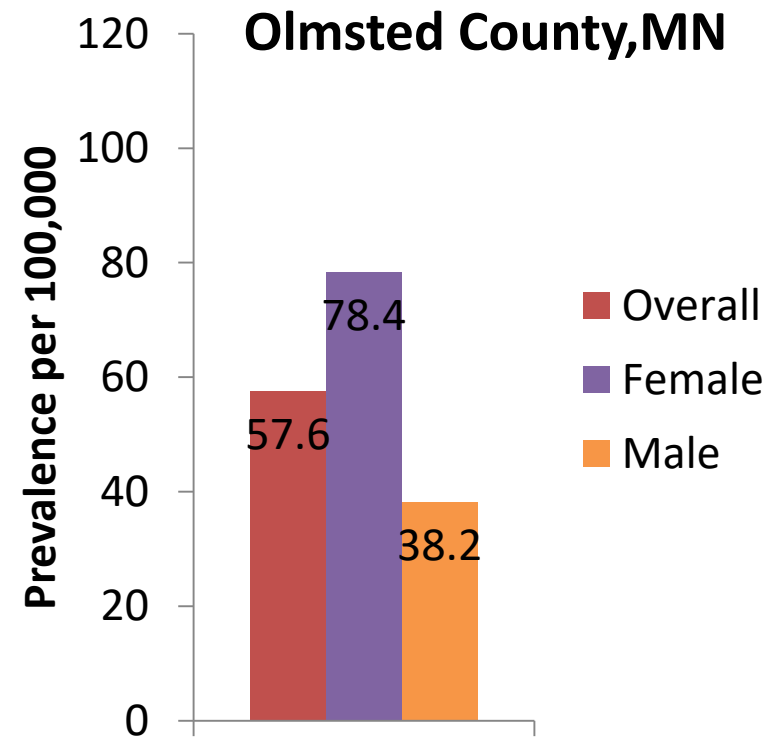
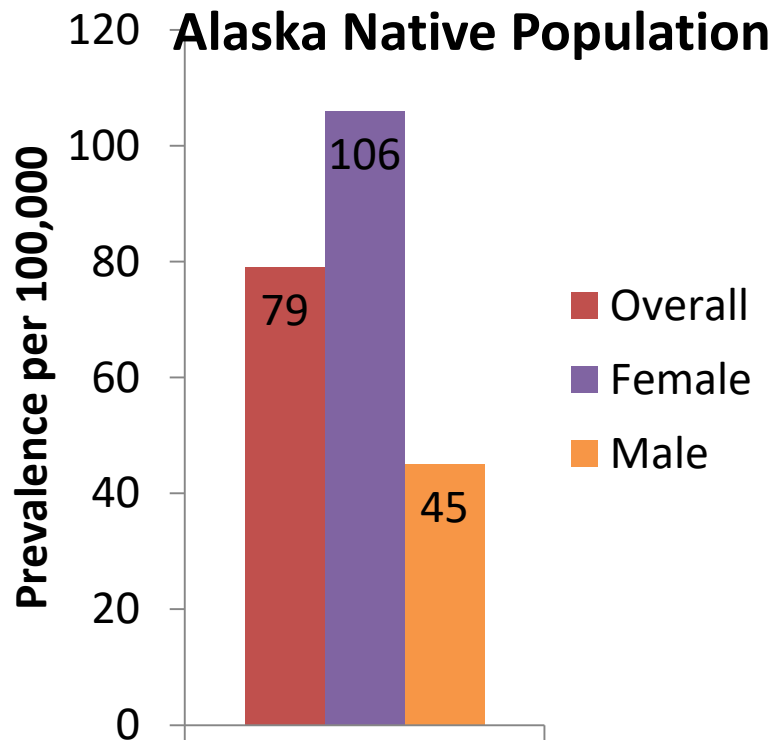
Photo: <http://emedicine.medscape.com/article/1007276-overview>



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# Juvenile Idiopathic Arthritis Prevalence

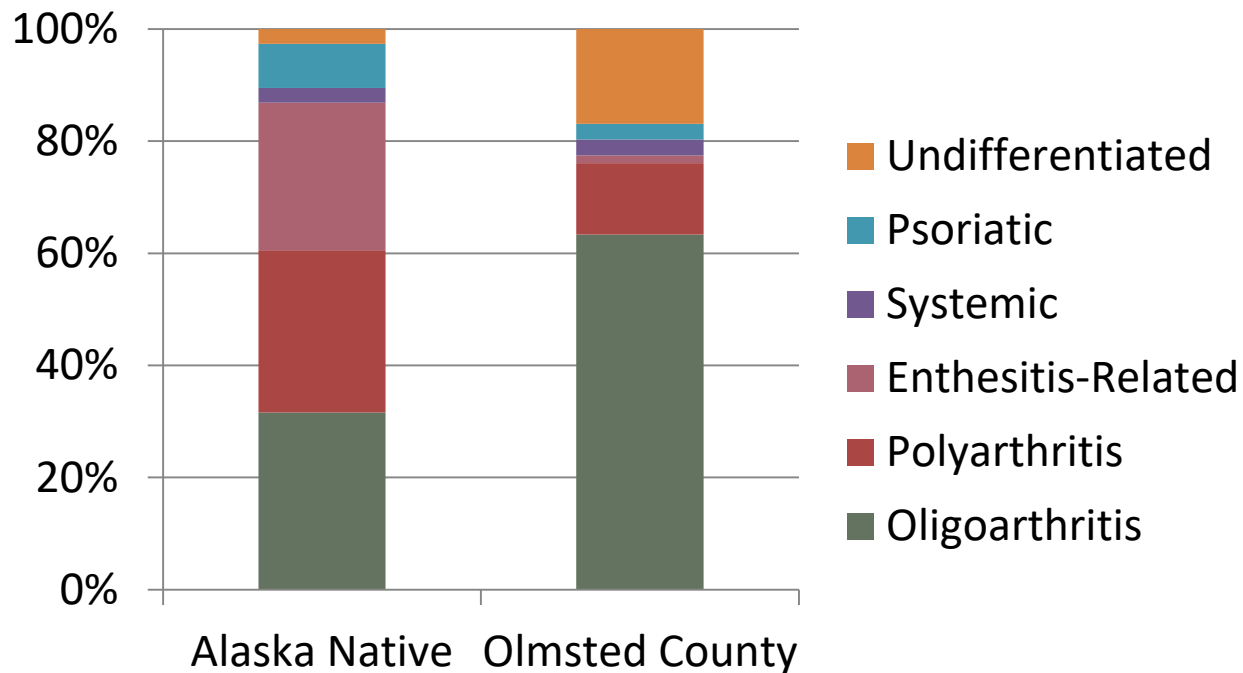


Khodra B, et al. Arthritis Care & Research 2020;72:1152



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# Juvenile Idiopathic Arthritis Subtypes



Khodra B, et al. Arthritis Care & Research 2020;72:1152

# Ongoing Research: Arthritis Epidemiology and Impact in the Alaska Native Population

- 3 specific aims:
  - **Aim 1:** Determine the prevalence of specific forms of arthritis and autoimmune diseases in Alaska Native people statewide.
  - **Aim 2:** Determine the hospitalization rates and causes of hospitalization for AI/AN compared to non-AI/AN individuals in Alaska with arthritis and autoimmune diseases.
  - **Aim 3:** Determine the rate of joint replacements (total knee and total hip) for AI/AN compared to non-AI/AN individuals statewide.

NIH NIMHD Grant# R01 MD014664



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# Patient and Caregiver Resources

- American College of Rheumatology (ACR)  
[www.rheumatology.org](http://www.rheumatology.org)
- Arthritis Foundation  
[www.arthritis.org](http://www.arthritis.org)
- **Creaky Joints**  
[www.creakyjoints.org](http://www.creakyjoints.org)



CORONAVIRUS, LIVING WITH ARTHRITIS, PATIENT PERSPECTIVES DURING COVID-19

**I Stopped Taking My Psoriatic Arthritis Biologic Because I Was Afraid of Coronavirus. Then I Had the Worst Flare of My Life.**

This mistake taught me that my psoriatic arthritis is not something to trifle with. It's a medical condition that...



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# ANMC Rheumatology

- Rheumatologists
  - David Templin, MD
  - Elizabeth Ferucci, MD
  - Sarah Doaty, MD
  - Vivek Mehta, MD
  - Javaneh Lyons, MD
  - Nick Manwaring, FNP
- Case Managers
  - Ann 729-2071
  - Kelley 729-1586
  - Han Nah 729-4773
- Schedulers
  - 729-2066 or 729-1525

Reach us on TigerText  
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Consult), by phone, on  
Cerner, etc.

Research/Epi Questions, email me:  
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