



# Rheumatology Pearls

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- SSM Health Rheumatology and IV Therapy
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# Learning objectives

How common are the musculoskeletal disorders

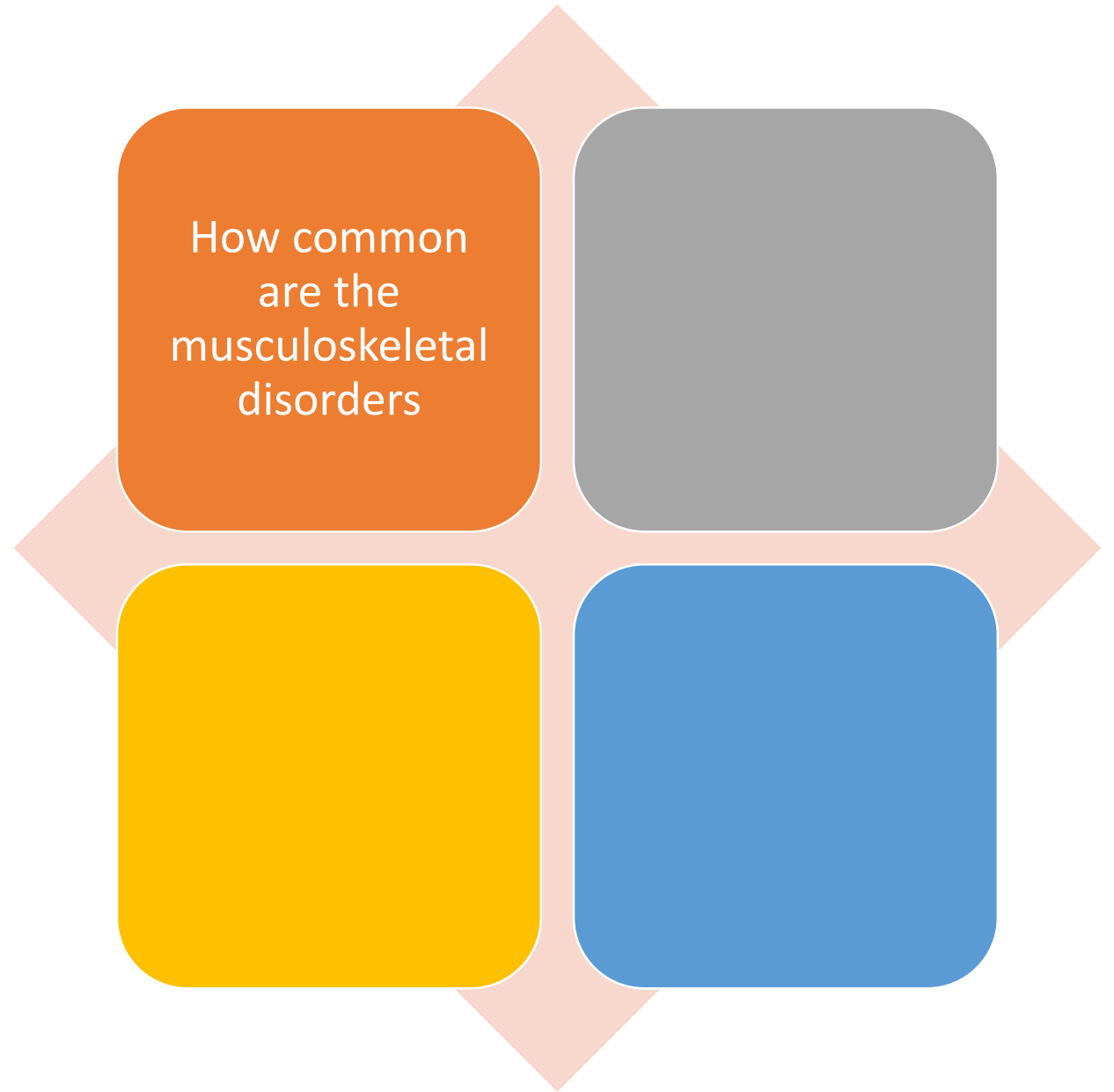
Common Laboratory Tests for Rheumatological Disorders

Recognize Seronegative Arthritis

Rheumatology at a glance : Know it when you see it

# Learning objectives

How common are the musculoskeletal disorders



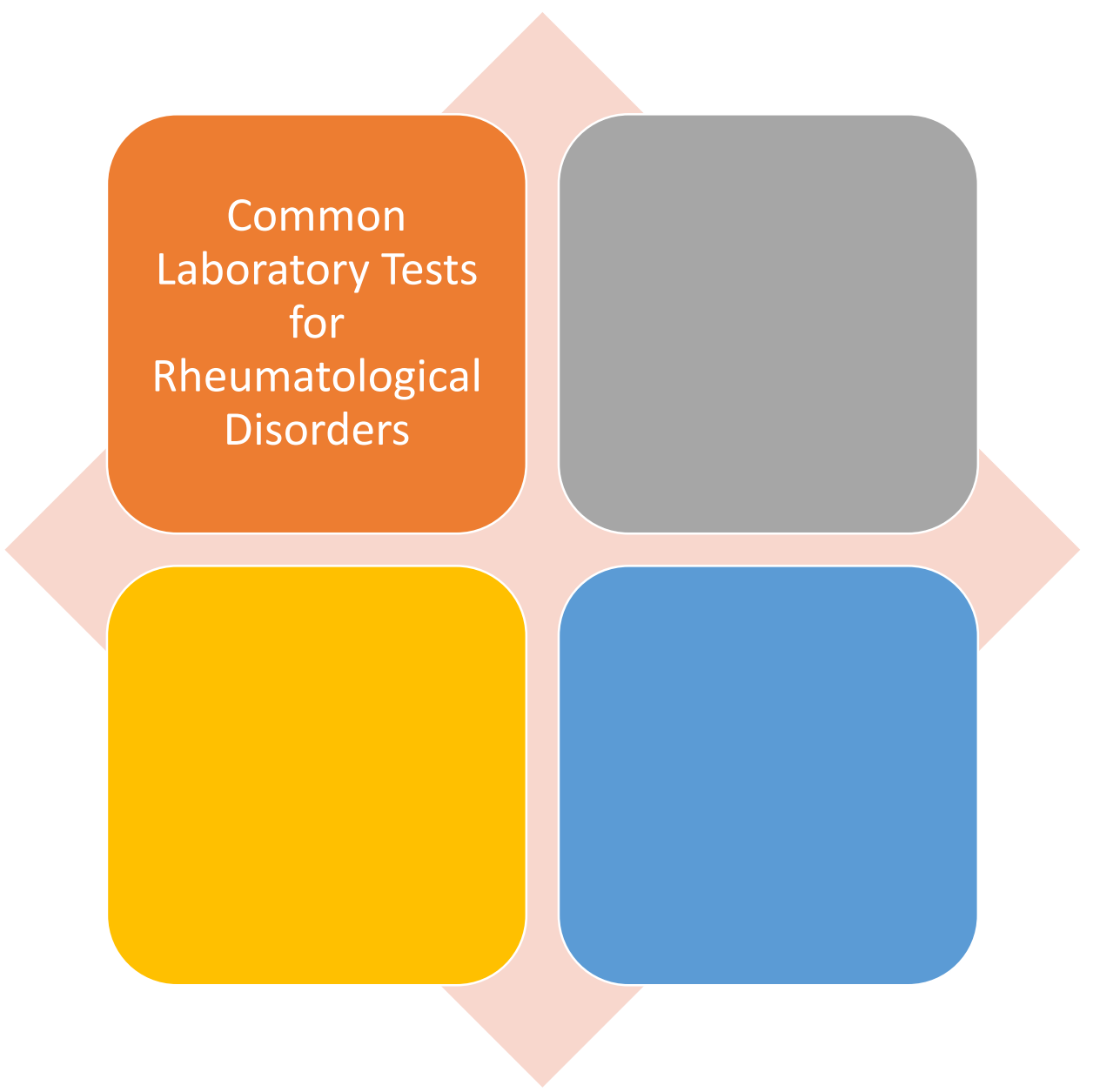
About 1 out of every 5 to 10 office visits to a primary care provider is for a musculoskeletal disorder



# Estimated Prevalence of Rheumatic/Musculo skeletal Disorders in the U.S. Population

NUMBER OF PATIENTS	PREVALENCE (ADULTS)	
All Musculoskeletal Disorders	20% to 30%	60 to 90 million*
<b>Arthropathies</b>		
Osteoarthritis	12%	27 million
Rheumatoid arthritis	1%	1.5 million
Crystalline arthritis (gout)	4%	8.3 million
Spondyloarthropathies	0.25%	0.4 to 1 million
<b>Connective Tissue Disease</b>		
Polymyalgia rheumatica	<0.01%	0.3 to 0.7 million
Systemic lupus erythematosus	<0.01%	240,000
Systemic sclerosis	<0.01%	50,000
Back/neck pain: frequent	15%	33 million
Osteoporosis (>age 50 years)	10%	9 million
Soft tissue rheumatism	3% to 5%	5 to 10 million
Fibromyalgia	2%	3 to 5 million

# Learning objectives



Common  
Laboratory Tests  
for  
Rheumatological  
Disorders

# History , Physical and Lab



History and physical examination will reveal 75% of the information required for diagnosis.



Lab is to confirm suspected diagnosis

# Laboratory Evaluation

ESR

CRP

ANA

ENA

Anti DsDNA

RF

Anti CCP

HLA B27



# ESR

Somewhat imprecise.

Affected by multiple variables:

Aging, female sex, obesity, pregnancy, and possibly race are noninflammatory conditions that can elevate the sedimentation rate.

Inexpensive and easy to perform.

Remains elevated for a longer time (decreases by 50% in 1 week) after inflammation subsides

A rough rule of thumb for the age-adjusted upper limit of normal for ESR (mm/h) is:

Male= $\text{age}/2$ ; Female= $(\text{age}+10)/2$

ESR

What causes an  
extremely high  
ESR  
100 or more?

Infection

Malignancy

Vasculitis

# CRP

CRP is produced as an acute-phase reactant by the liver in response to IL-6 and other cytokines ( inflammation)

A rough rule of thumb for the age-adjusted upper limit of normal for CRP (mg/dL) is:

Male=age/50; Female=(age+30)/50

Is more specific

It rises more quickly and falls more quickly than the ESR. Elevates within 4 hours and peaks in 24-72 hours

Note that hypergammaglobulinemia causes a persistently elevated ESR preventing it from ever becoming normal whereas CRP is not affected by immunoglobulin levels

# ANA

Screening tool for connective tissue disorders

## Techniques

- Indirect immunofluorescence (IIF)
  - HEp-2 cell line
- Solid base immunoassays (such as ELISA)
- Reported in titers (e.g., 1:80)

# When to order ANA

## Connective tissue disorder ( or Mixed)

- Fatigue, weight loss,
- Fever
- Myalgia and arthralgia
- Rash

## SLE

- CTD symptoms
- Alopecia, oral ulcers
- Malar rash, photosensitivity

## Sjogren's syndrome

- Dryness of eyes and mouth

## Scleroderma

- Raynaud's
- Skin swelling and tightness

## Drug induced Lupus (DIL)

- Hydralazine, Isoniazid, Procainamide

# Diseases associated with positive ANA

## Systemic autoimmune diseases

- SLE 99-100%
- MCTD 100%
- Scleroderma 95%
- Drug induced lupus DIL 80-95%
- Sjogren's syndrome 60%
- Rheumatoid arthritis 45%
- Raynaud's phenomenon 40%
- Polymyositis/dermatomyositis 35%

## Organ- specific autoimmune diseases

- Hashimoto thyroiditis 50%
- Grave's disease 50%
- Autoimmune hepatitis 70%
- Primary biliary cirrhosis 50 - 70%

## Infectious disease

## Malignancies

## Others

# ANA Titers as seen in healthy individuals

1:40 20% to 30%

1:80 10% to 15%

1:160 5%

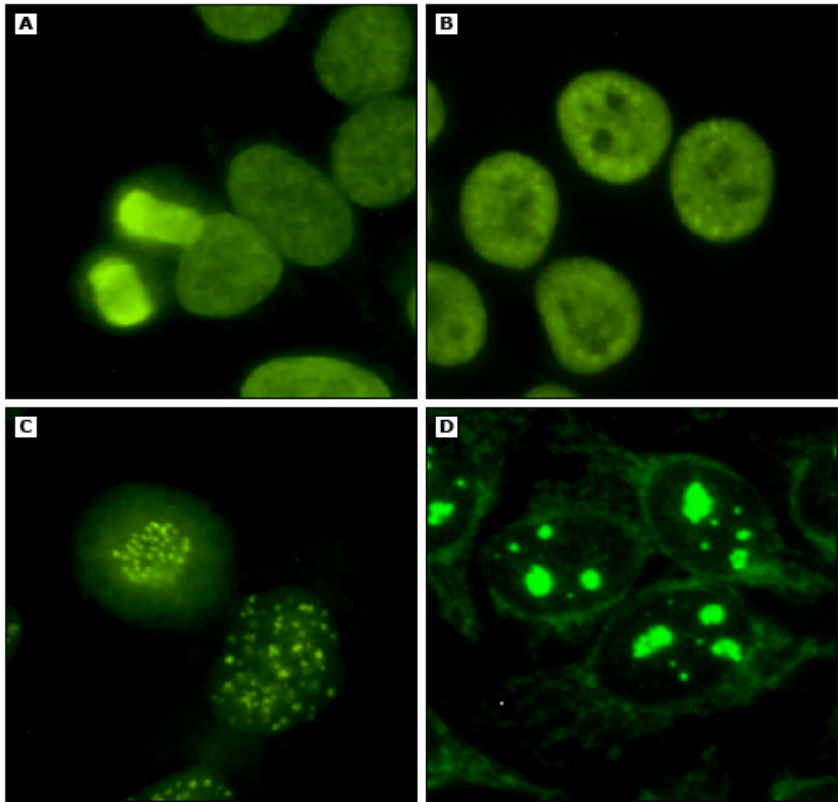
1:320 3%

Low titers in 5-25% healthy relatives of SLE

1:40 in up to 70% in age >70

# Patterns

## Four common ANA staining patterns



In the homogeneous pattern (A), the entire nucleus is diffusely stained. The chromosomes at the metaphase plate are also stained. In the speckled pattern (B), very small, uniform, fluorescent dots are seen throughout the nucleus. The centromere pattern (C) is characterized by the presence of 30 to 60 dots distributed throughout the nucleus in resting cells. The dots localize to chromosomes at the metaphase plate in dividing cells. The nucleolar staining pattern is shown in (D).

Homogeneous: SLE, Dermatomyositis.  
Histone protein, DNA, DNA-histone complexes.

Speckled: Sjogren's, SLE, MCTD  
U1 RNP, Sm, Ro and La

Centromere: Limited Scleroderma

Nucleolar: Scleroderma  
Fibrillarin, RNA polymerase I and III, Th, PM-Scl and RNA helicase.



# Significance

High titer increases likelihood of an autoimmune disease.

Once a positive ANA in an ANA associated disease, no need to repeat.

ANAs are NOT helpful to monitor disease activity.

# ENAs

## Extractable Nuclear Antigens

Anti Sm

- SLE

Anti RNP

- MCTD - SLE

Anti Ro and anti La

- Sjogren's - Lupus

Anti centromere  
and anti SCL 70

- Scleroderma

Anti Jo1

- Polymyositis

Anti ribosomal P

- SLE ( psychosis)

Ds DNA

- SLE (lupus nephritis)

Anti chromatin

- SLE, Sjogren's, Scleroderma, APS

Can a patient  
with SLE ever  
be ANA  
negative?

YES, <1%

SLE with only Anti SS-A  
(Ro)

- Not done on Hep-2 substrate
- Ab's against 52kDa SS-A/Ro ( located in cytoplasm)
- 60kDa Ss-A/Ro located in nucleus

SLE with restricted Ab's  
to cytoplasmic  
constituents (ribosomes)

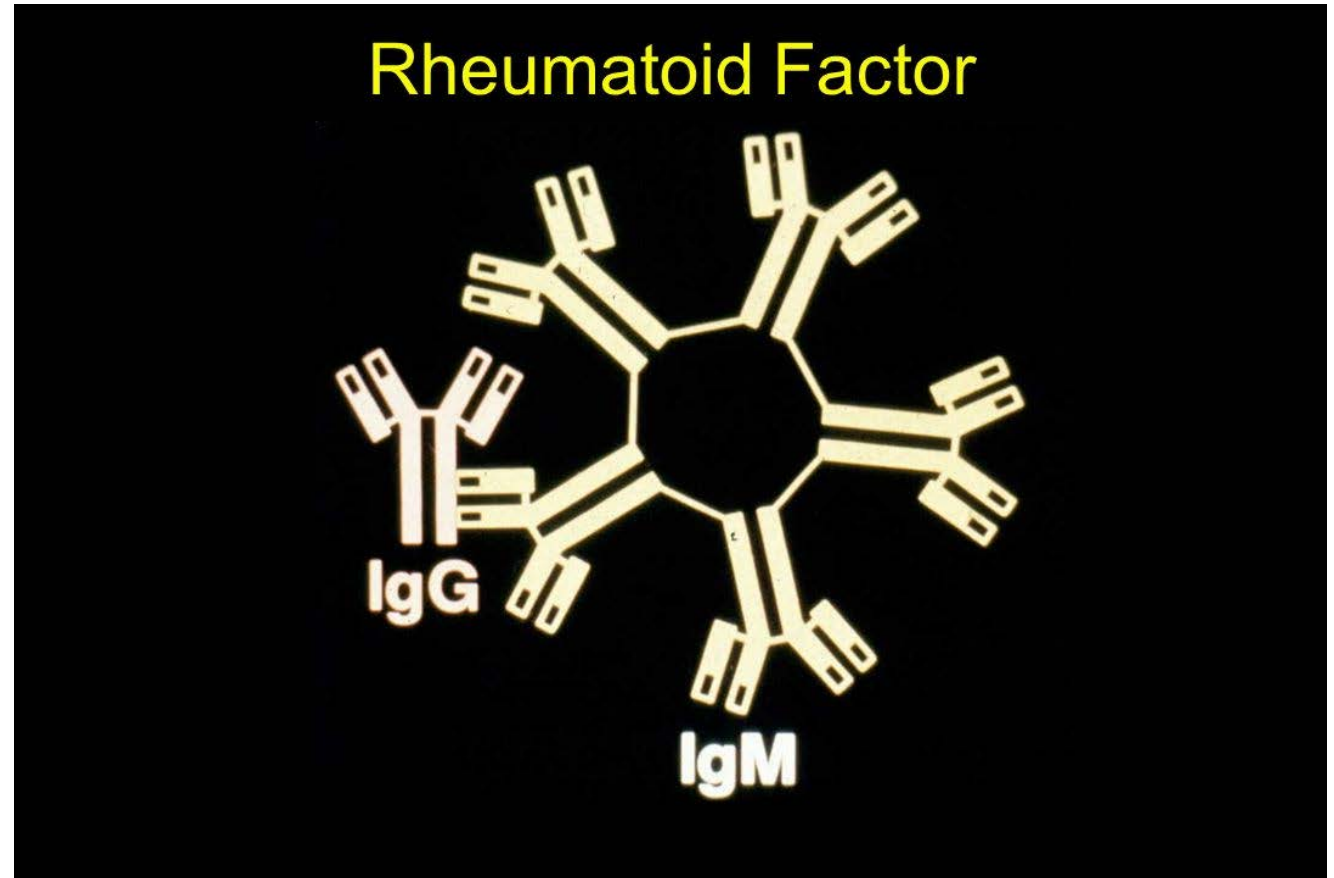
In early C2,C4 Deficiency

Severe proteinuria

ESRD on chronic dialysis

In a patient with a strong clinical suspicion for SLE and a negative ANA result by a solid phase assay, the test should be repeated using indirect immunofluorescence method with HEp-2 cells

- Antibody directed against the FC portion of IgG
  - IgG and IgM Abs are found in up to 90% of RA patients.
  - IgM is 70% sensitive and 80% specific.
  - <40% of early RA patients



# RF in non rheumatic diseases

Detectable in 1-4% of healthy individuals and up to 25% of healthy individuals above the age of 60.

Infections  
(Hepatitis C, Hep B, bacterial endocarditis, Tb)

Malignancy

Sarcoidosis, PBC, COPD, Silicosis

# RF Titers

Higher titers are more significant

High titers increase likelihood of erosive disease and extra articular manifestations

Low titers-> repeat levels in the future.

No need to repeat to monitor disease activity.

## RF in other rheumatic diseases

Primary Sjogren's syndrome 75-90%

Mixed cryoglobulinemia 90-100%

MCTD 50-60%%

SLE 20-30%

Systemic Sclerosis 20-30%



## ACPA/CCP Ab

Antibodies directed against citrullinated proteins

Sensitivity of 50-75%, specificity of 96%

High titer antibodies are associated with more aggressive disease.

New data suggests use to monitor disease activity.

# CCP Ab in non rheumatic diseases

COPD (5-6%)

Psoriatic arthritis

Autoimmune hepatitis

Pulmonary tuberculosis

NOT ELEVATED IN HEPATITIS B OR C.

# Learning objectives



Recognize  
Seronegative  
Arthritis

Seronegative  
arthritis ??

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Seronegative  
spondyloarthritis  
(spondyloarthropathy)

Ankylosing spondylitis

Psoriatic arthritis

Reactive arthritis

IBD related arthritis

Undifferentiated spondyloarthritis

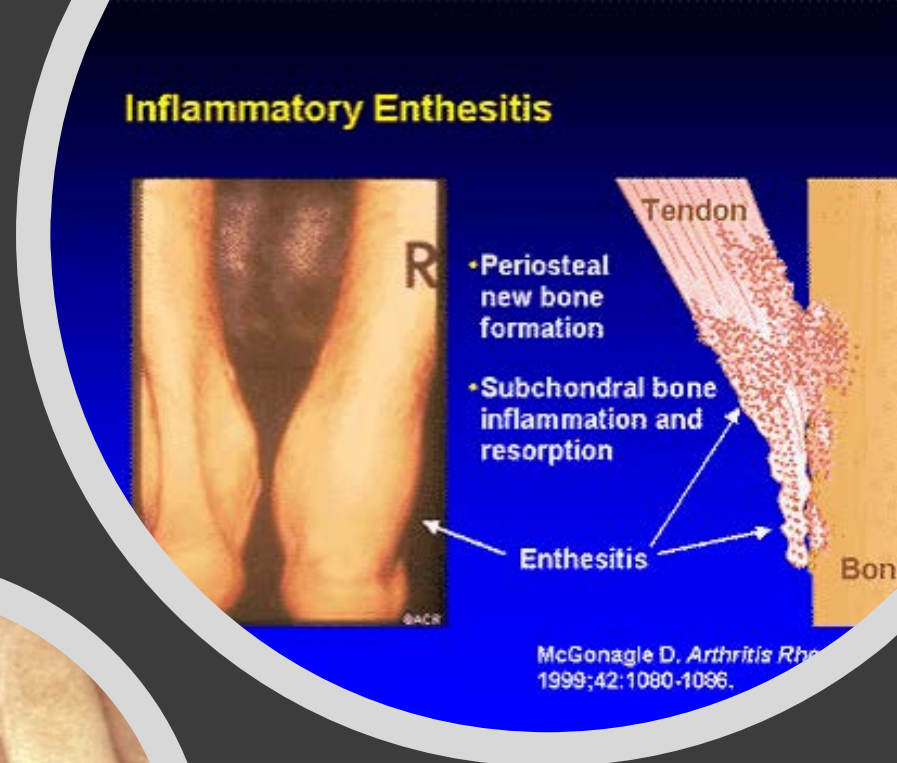
# Seronegative spondyloarthritis

- Common symptoms or findings:
- Inflammatory back pain



# Seronegative spondyloarthritis

- Common symptoms or findings:
  - Enthesitis
  - Dactylitis



# Seronegative Spondyloarthritis

Laboratory finding :

Negative  
RF

High rate  
HLA B27

- Ankylosing Spondylitis 80-90%
- Other types 50-70%
- The age-adjusted US prevalence in healthy individuals is 6.1%

Elevated  
ESR and  
CRP?

- In 30-50 % of cases



# Learning objectives

Rheumatology  
at a glance :  
Know it when  
you see it

## OSTEOARTHRITIS

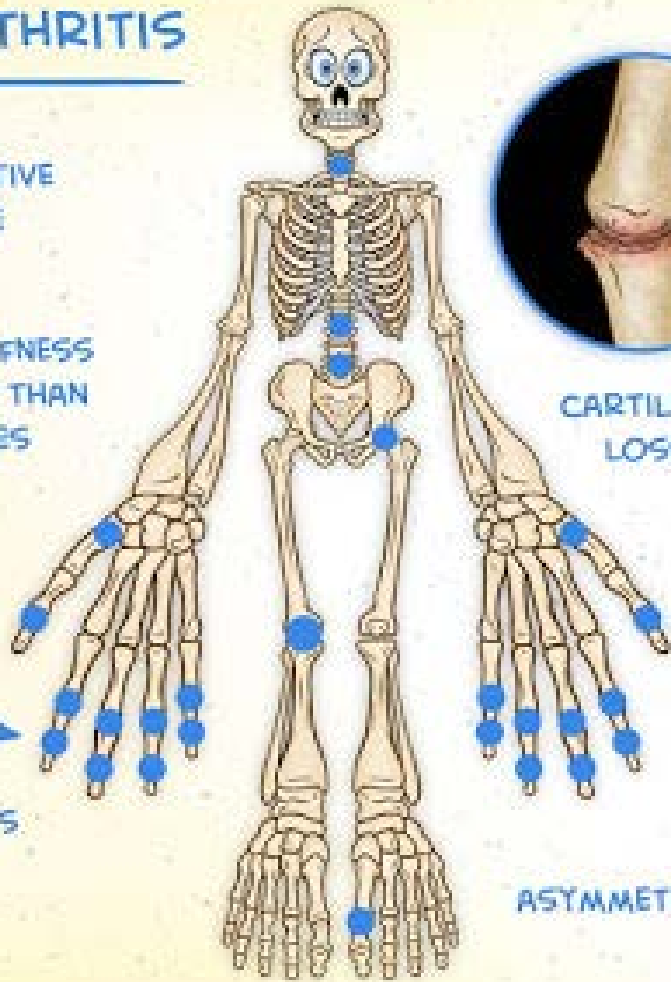
DEGENERATIVE  
DISEASE

MORNING STIFFNESS  
LASTING LESS THAN  
30 MINUTES



CARTILAGE  
LOSS

HEBERDEN'S  
NODES



ASYMMETRICAL

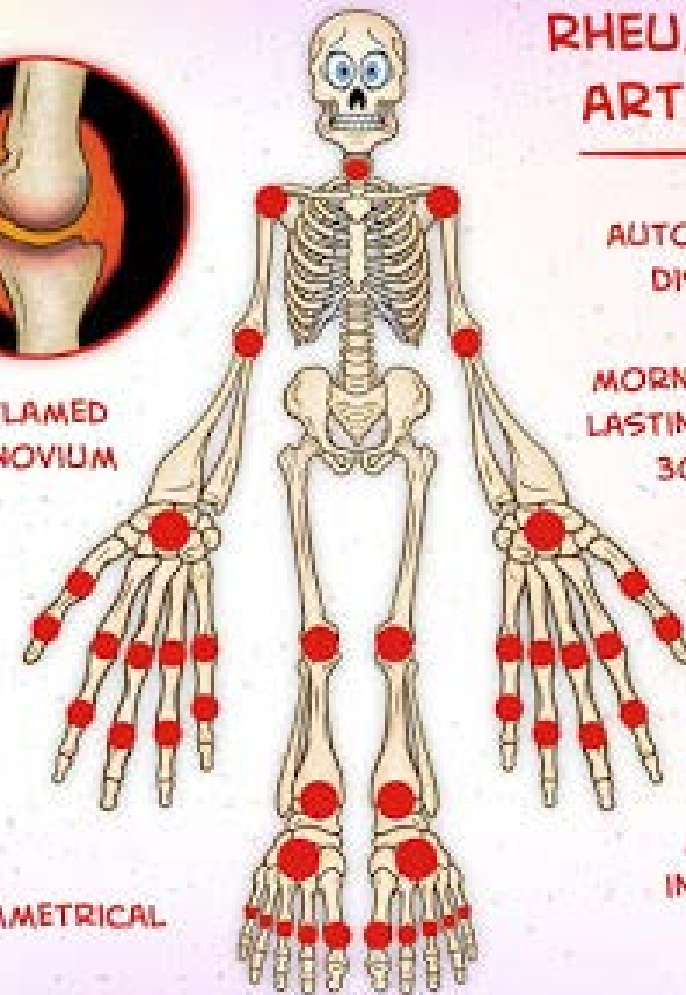
## RHEUMATOID ARTHRITIS

AUTOIMMUNE  
DISEASE

MORNING STIFFNESS  
LASTING MORE THAN  
30 MINUTES



INFLAMED  
SYNOVIUM



SYMMETRICAL

EXTRA-  
ARTICULAR  
INVOLVEMENT

# Know It When You See It

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## Osteoarthritis: Typical hand

- Hard bony enlargements
- Heberden's nodes at the DIP joints
- Bouchard's nodes at the PIP joints
- Often have "squared" first CMC joint due to osteophytes at that joint



# Know It When You See It

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## Rheumatoid arthritis

- Soft synovial swelling
- Synovitis and volar subluxation at the MCP joints
- Synovitis of the wrists
- Synovitis of the PIP joints with early swan neck deformities



# Know It When You See It

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## Rheumatoid arthritis



Rheumatoid arthritis



Image: ACR Image Bank

# Rheumatoid Arthritis: Swan Neck and Boutonnière Deformities

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- Late-stage findings indicating serious changes in the joints
- Swan neck (digits 2 to 4) PIP extension DIP flexion
- Boutonnière (digit 5) is the reverse; PIP flexion DIP extension

# Know It When You See It

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## Tendon rupture in RA

- Inability to extend fourth and fifth digits
- Due to deformity and inflammation at the wrist causing excess wear of the extensor tendons



# Know It When You See It

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## Psoriatic arthritis

- Inflammation of the DIP joints
- Sausage fingers
- Joint involvement shows radial pattern
- Nail changes
- Psoriatic patches
- Arthritis may start before the skin





# Know It When You See It

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## Psoriatic arthritis

- Sausage toes
- IP joint involvement of a toe suggests a rheumatoid variant
- Psoriatic arthritis and Reactive arthritis are the most common causes



# Know It When You See It

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## Psoriatic nails



# Psoriatic Arthritis (PsA)

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- Prevalence 0.05–0.25% of the population
- 6–41% of patients with psoriasis
- Can present after psoriasis or BEFORE
- Enthesitis and Dactylitis are common
- PsA remains under-diagnosed.

# Know It When You See It

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## Reactive arthritis

- Keratoderma blennorrhagica
- May look like psoriasis or syphilis
- Can occur in patches or as sterile pustules



# Reactive Arthritis

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Seronegative asymmetric arthritis

- Following:
  - Urethritis or cervicitis
  - Infectious diarrhea
- Often associated with:
  - Inflammatory eye disease
  - Balanitis, oral ulceration, or keratoderma
  - Enthesopathy
  - Sacroiliitis



# Know It When You See It

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Systemic lupus erythematosus

- Butterfly rash
- Involves cheeks and nose
- Patient also has rash on chin and some telangiectasia



# Know It When You See It

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## Systemic lupus erythematosus

- Interarticular dermatitis
- Also has periungual erythema
- This rash is distinct from that seen in dermatomyositis that occurs over the joints



# Know It When You See It

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## Dermatomyositis

- Scaly rash over the extensor surfaces of the interphalangeal joints





# Know It When You See It

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## Dermatomyositis

- Mantle or shawl distribution of rash



# Know It When You See It

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## Livedo reticularis

- Appears in a broad-based interrupted pattern in systemic vasculitis, including SLE or APS
- May occur as a fine, connected, lacy pattern in normals



# Know It When You See It

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## Palpable purpura

- Characteristic of dermal vasculitis in Henoch-Schönlein purpura



# Know It When You See It

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## Saddle nose deformity

- Relapsing polychondritis
- May also occur in granulomatosis with polyangiitis (Wegener's) and syphilis



# Know It When You See It

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## Relapsing polychondritis



Left: Ear changes with inflammation in the cartilage and swelling

Right: Loss of ear cartilage in late stages

# Know It When You See It

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Gout tophi in the ear a good tip-off if present

- Tophi appear rather late in gout
- Prick the tophus with a needle. Put the drop of material on a slide
- Multiple birefringent crystals will be seen on polarized microscopy

# Know It When You See It

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## Septic olecranon bursitis

- Swelling of the bursa
- Erythema and tenderness
- If it looks ugly, tap it



# Know It When You See It

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Septic prepatellar bursitis with cellulitis

- Rubor, calor, dolor over the patella and adjacent tissue
- Lack of joint involvement evident from nontender suprapatellar pouch and popliteal area
- Don't tap a normal knee through cellulitis





# Know It When You See It

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## Hypertrophic osteoarthropathy

- Clubbing with loss of nail angle
- Full syndrome includes periostitis of ends of long bones
- Associated with
  - Chest malignancies
  - Chronic lung infection
  - Other tumors



# Know It When You See It

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## Ehlers-Danlos syndrome

- A true connective-tissue disease
- Left: Hypermobility of joints. Can touch thumb to volar surface of forearm
- Right: Hyperelasticity of skin
- Associated with vascular abnormalities





Thank you

Questions?