RHEUMATOLOGY REVIEW AND UPDATE

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Session Objectives

- Recognize the distinguishing features between inflammatory and non-inflammatory forms of arthritis.
- Discuss the most common disease modifying anti-rheumatic drugs and the monitoring required with these treatments.
- Identify the typical skin rashes associated with conditions such as lupus, dermatomyositis, and vasculitis.
- Explain the significance of the most common rheumatology laboratory tests and findings.

Disclosures

- There is no commercial support associated with this educational activity.
- The speaker has no financial relationships with commercial agencies to disclose.
- The use of any trade names is solely for familiarity of the audience.

Rheumatology

Specialty who manages the non-surgical treatment of musculoskeletal disease, systemic autoimmune conditions, and vasculitides.

Rheumatic Diseases

Rheumatoid Arthritis and its varients:
Palindromic Rheumatism
Felty's Syndrome
Polymyalgia rheumatica

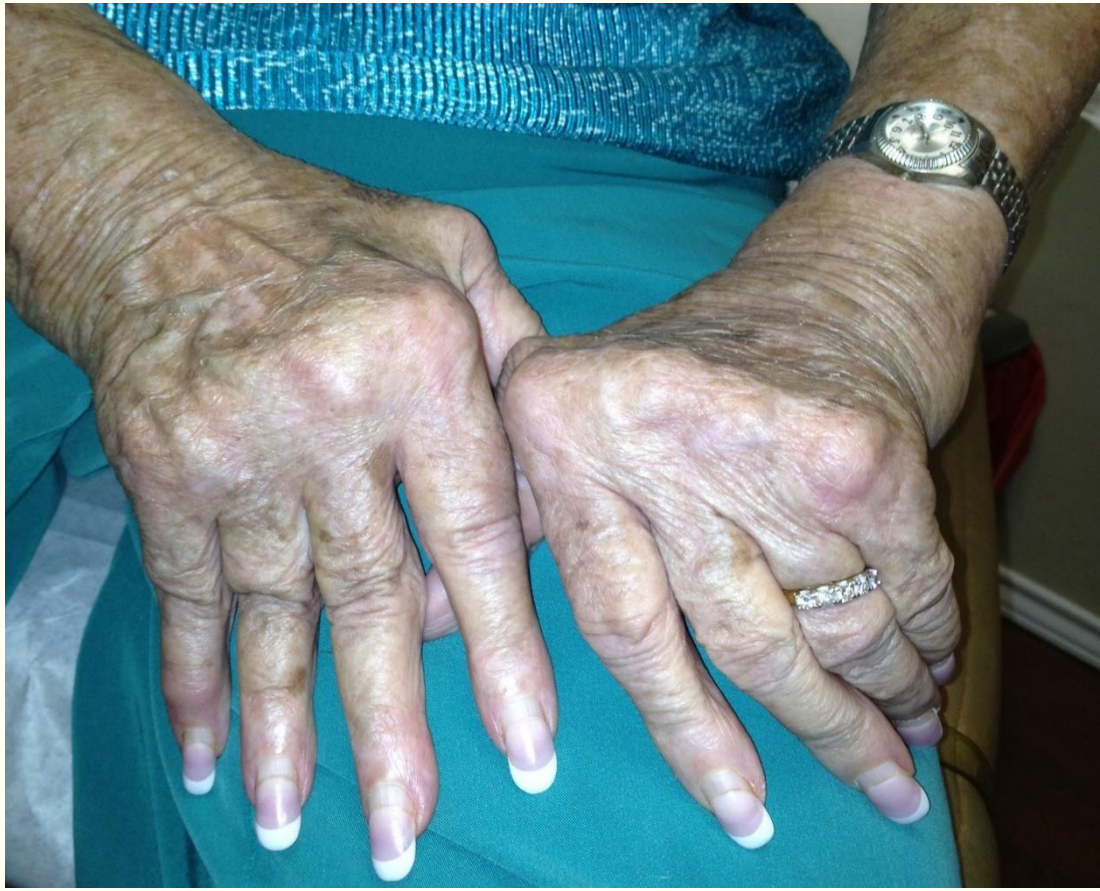
Connective Tissue Diseases:
Systemic Lupus Erythematosus
Sjogren's syndrome
Scleroderma
Polymyositis
Dermatomyositis

Vasculitis:
Giant Cell Arteritis
Takayasu's arteritis
Polyarteritis nodosa
Wegener's granulomatosis
Microscopic polyangiitis
Leukocytoclastic
Henoch-Schonlein purpura
Cryoglobulinemia

Seronegative Arthropathies:
Ankylosing spondylitis
Psoriatic Arthropathy
Reactive Arthritis
IBD associated arthropathies

Mechanical/Degenerative:
Osteoarthritis
Degenerative Disc Disease
Spondylolisthesis

THE ARTHRITIDES



Pathophysiology

Non-inflammatory

- Usually result from breakdown of cartilage and secondary mechanical disruption of the joint

Inflammatory

- Results from aggregation of inflammatory cells and their products in the joint space and synovium

(Goroll & Mulley, 2009)

Distinguishing Features

Non-inflammatory

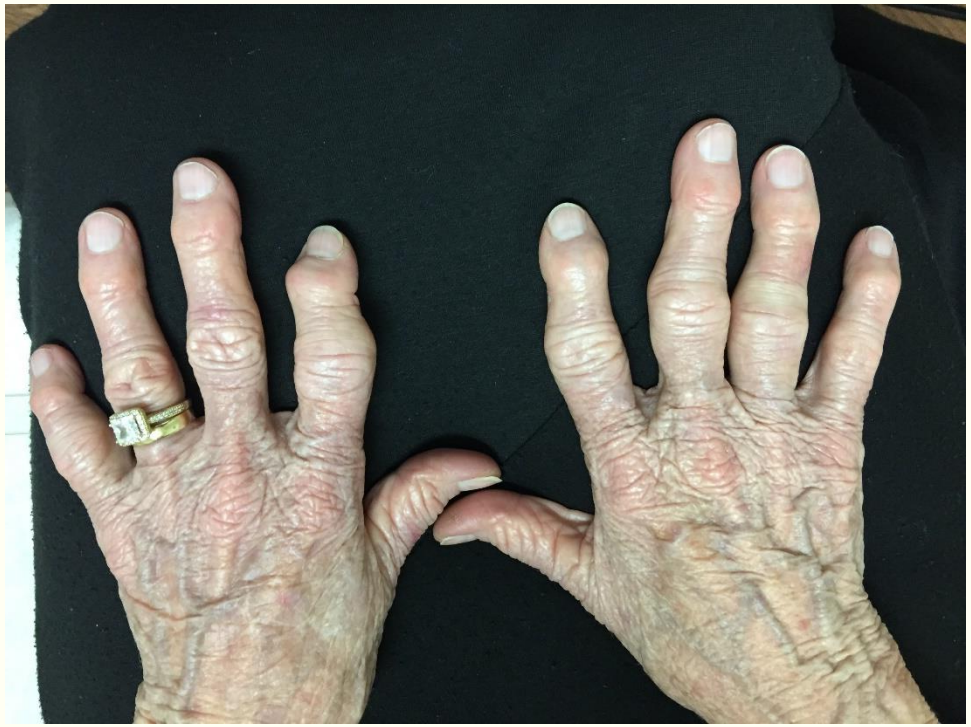
- Asymmetric
- Morning stiffness 30 minutes or less
- Not usually warm and erythematous
- Improved with rest

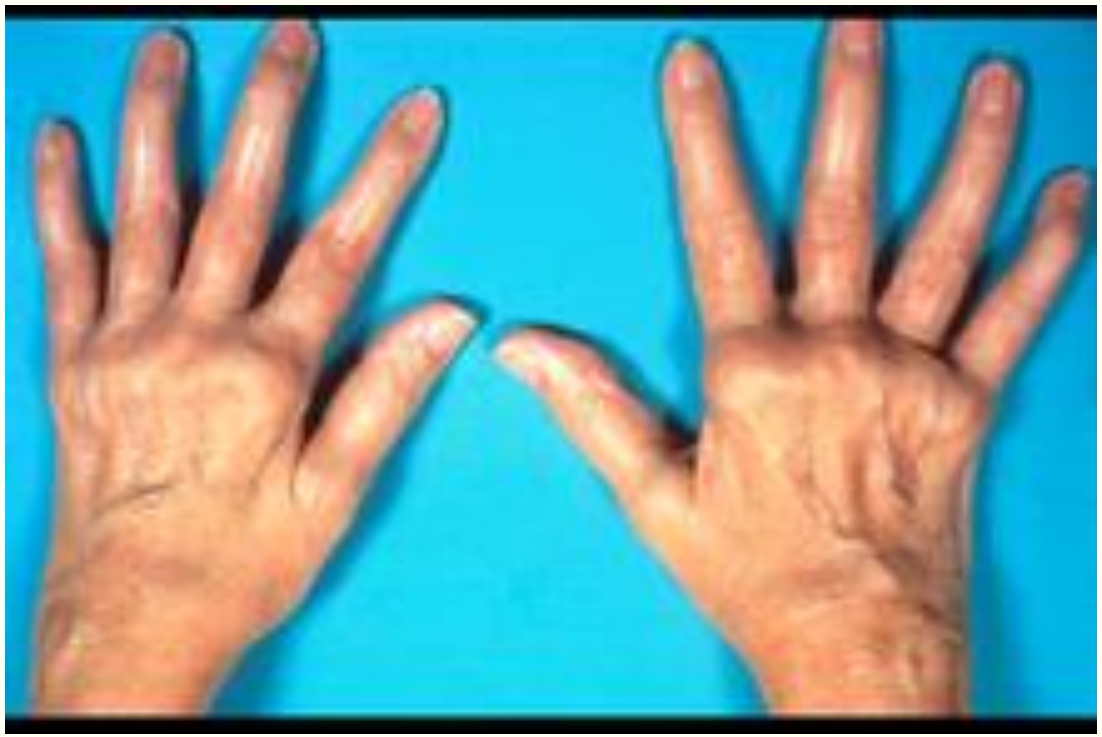
Inflammatory

- Symmetric
- Morning stiffness greater than 30 minutes
- Usually warm and erythematous
- Extra-articular features

(Pujalte & Albano-Aluquin, 2015)

Look at the Joints Affected

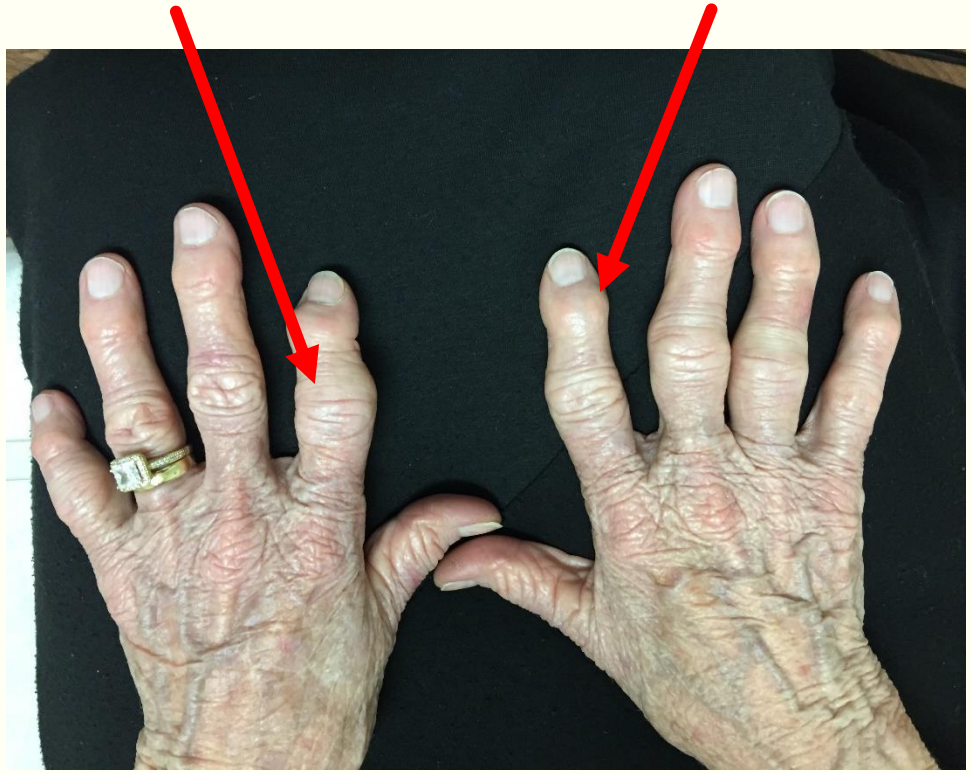


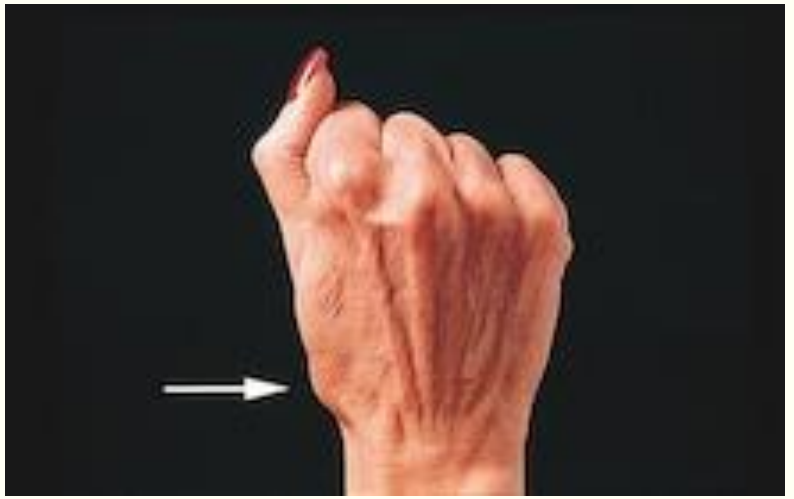


Osteoarthritis

PIP joints

DIP joints

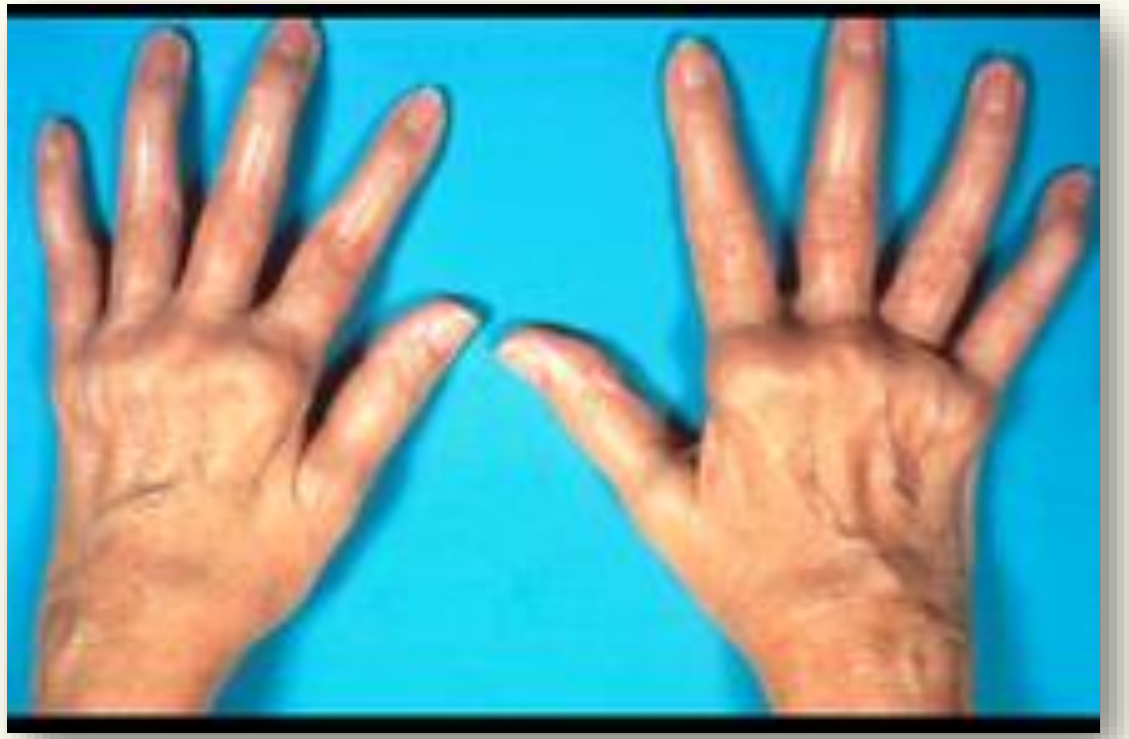


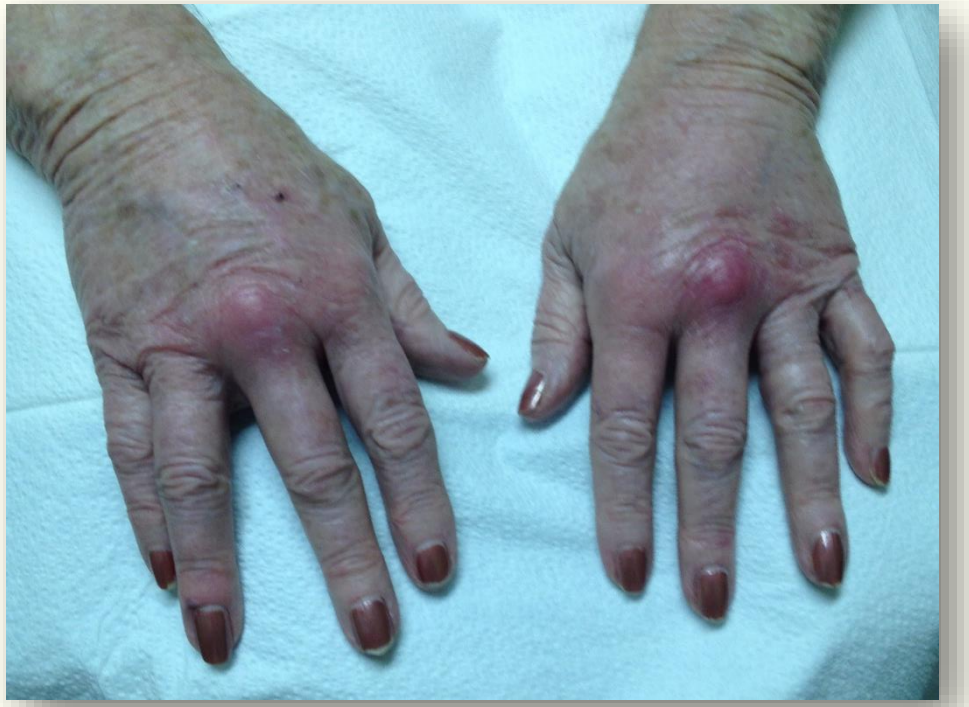


CMC joint involvement is common

Rheumatoid/Inflammatory Arthritis

MCP joint involvement





Symmetrical Presentation

OSTEOARTHRITIS

Osteoarthritis

- Non-inflammatory condition (although there are inflammatory types of OA)
- Also called “degenerative joint disease”
- Accounts for 30% of visits to PCPs
- Most common cause of disability in persons over 65

(Goroll & Mulley, 2009, p. 1093)

OA - Presentation

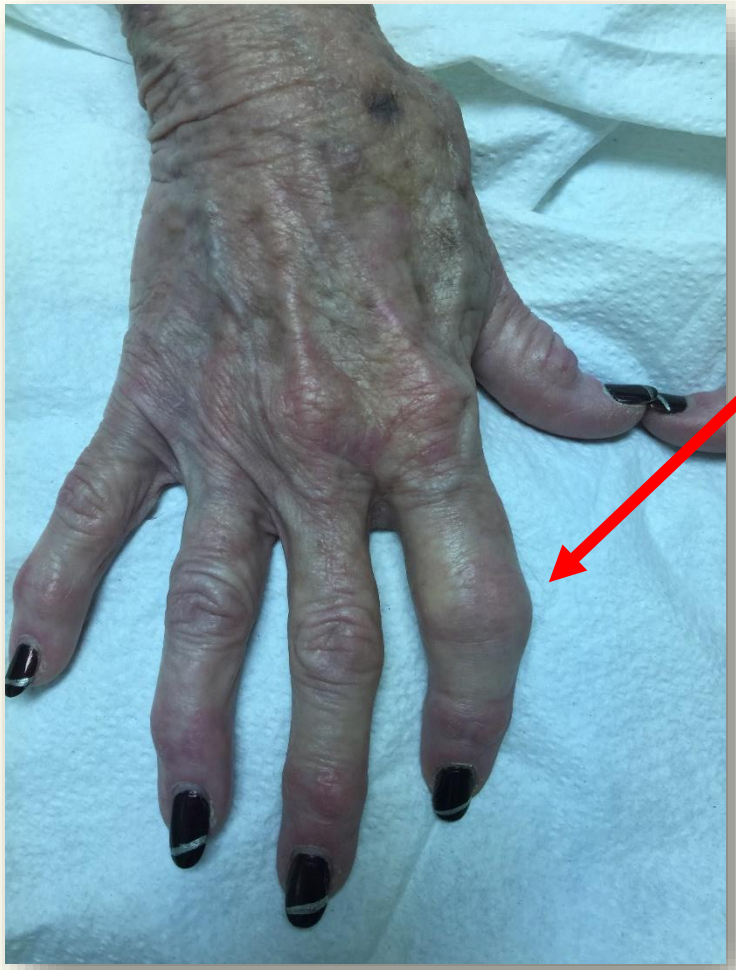
- Joint pain and stiffness
- Commonly distal fingers, thumb CMC, neck, lower back, knees, and hips
- May have mild swelling
- Crepitation often present
- May have bone cysts

(National Institutes of Health, 2016)

OA - Presentation

- Age of onset, sequence of joint involvement, and disease progression varies from person to person
- Can be asymptomatic (incidental finding on exam or x-ray) to rapidly progressive and disabling

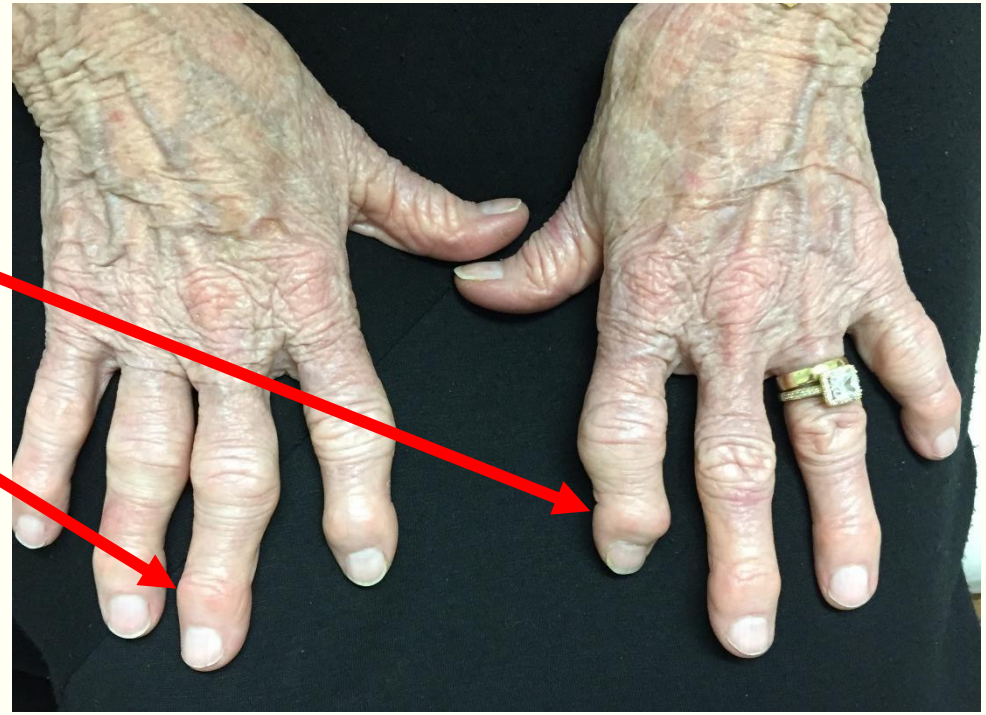
OA - Hands



- **Bouchard's nodes**
  - Bony enlargement at the PIP joints
  - Gradual development
  - May or may not be painful

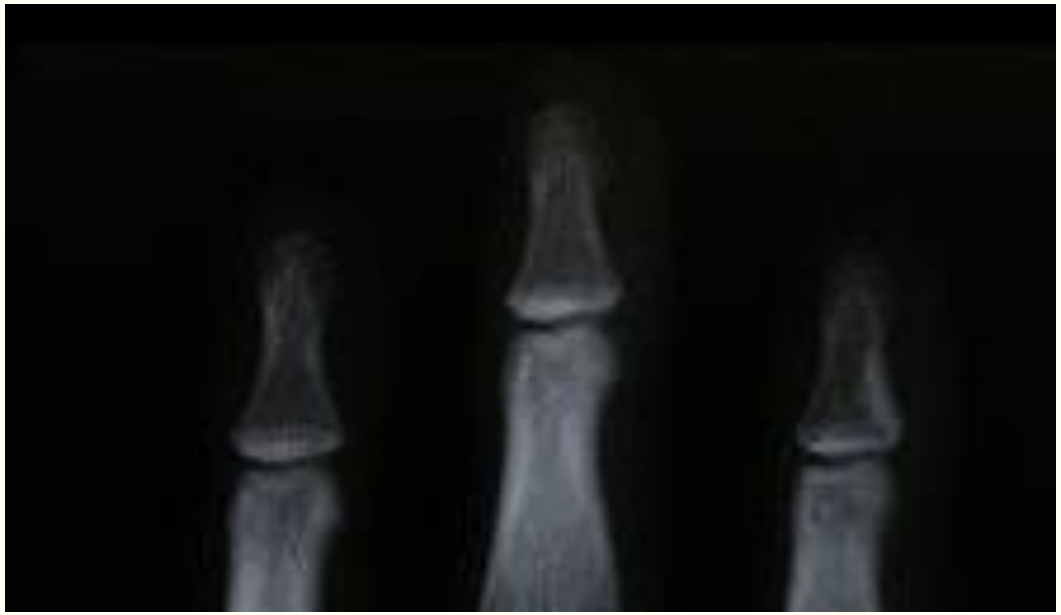
OA - Hands

- Heberden's nodes
  - Bony enlargement at the DIP joints
  - Loss of flexibility
  - Deviation

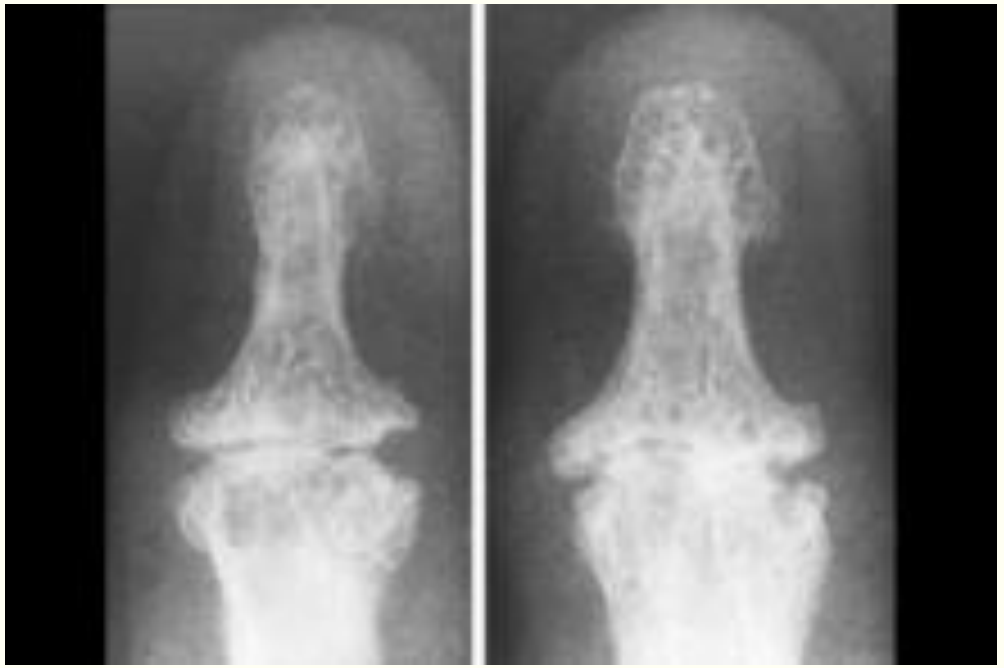


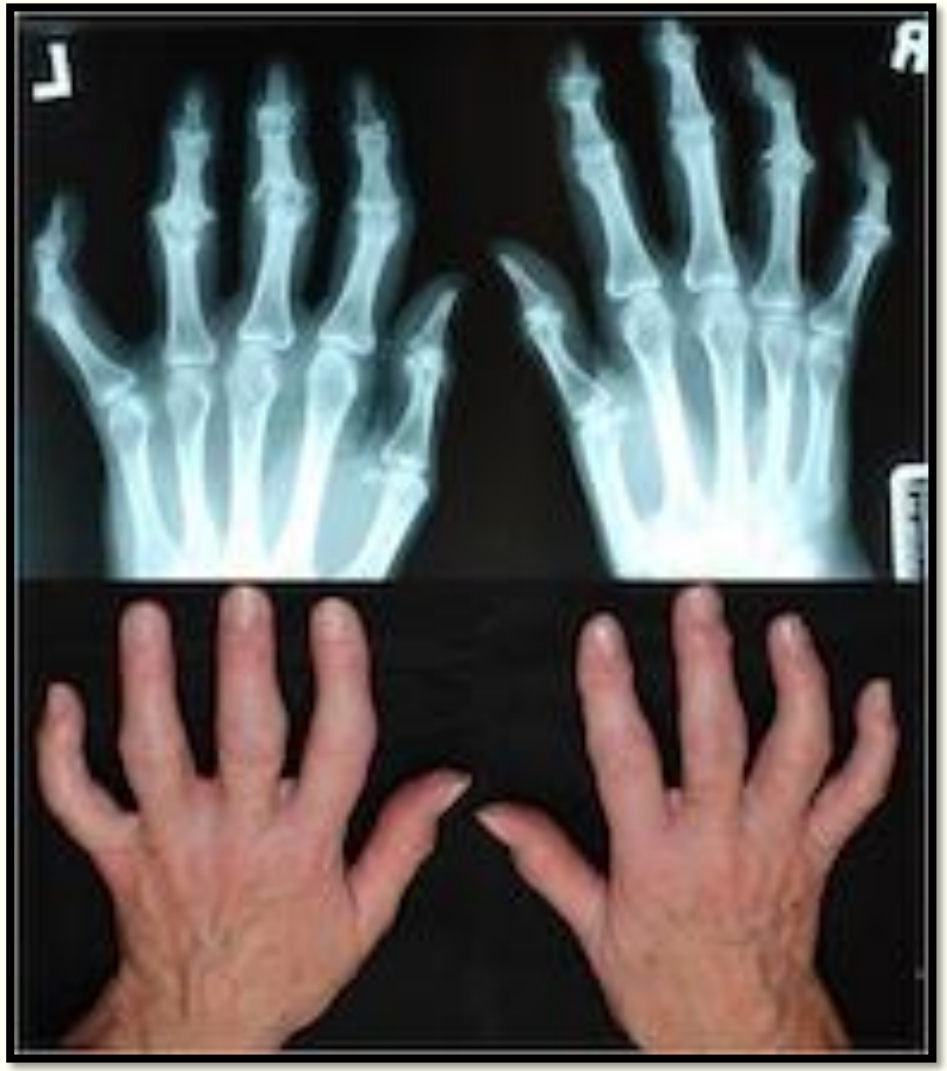
DIP Joints

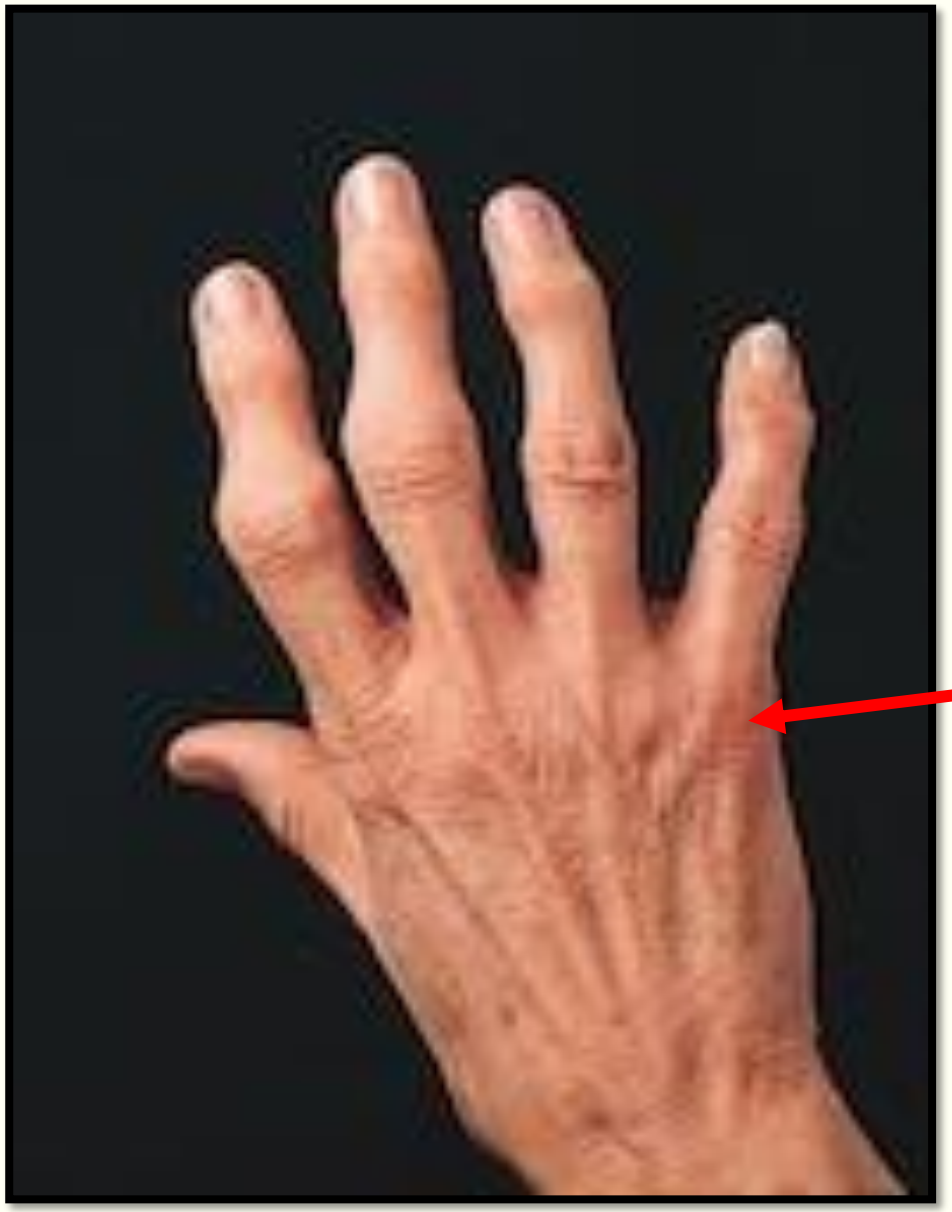
Normal



Sclerosis

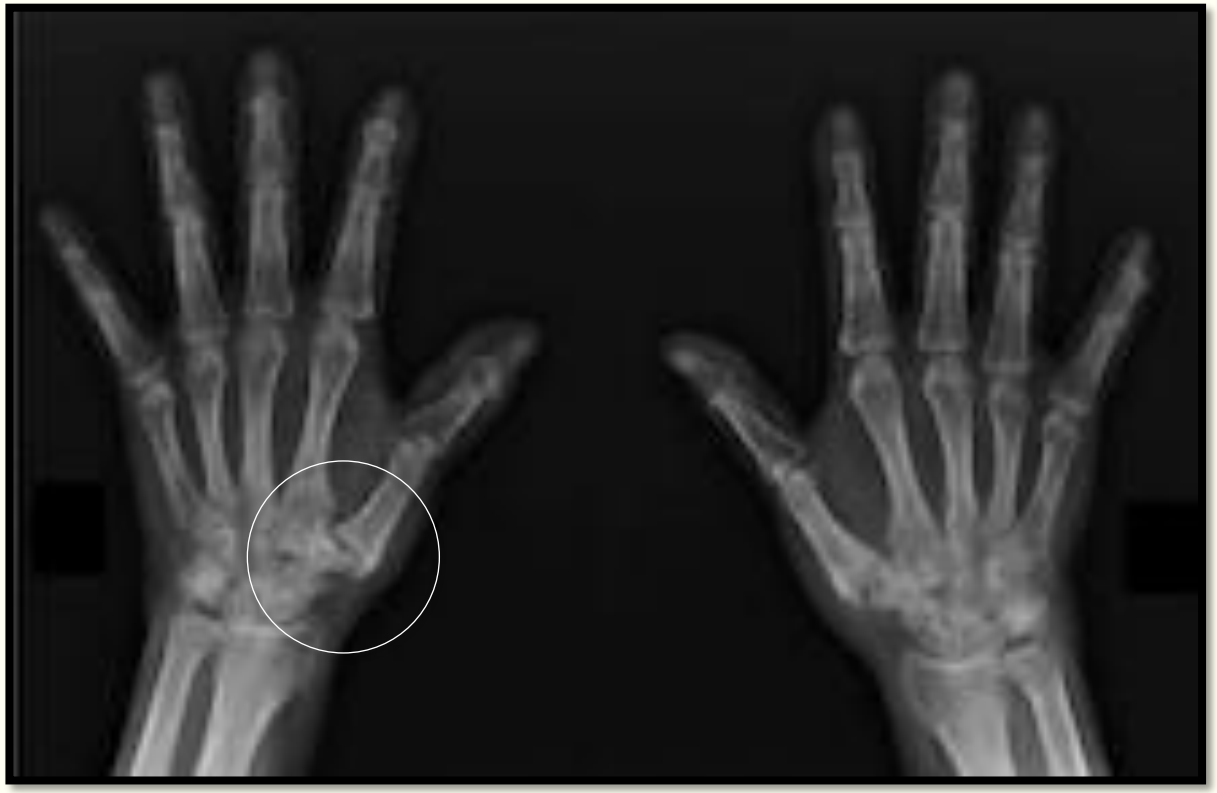


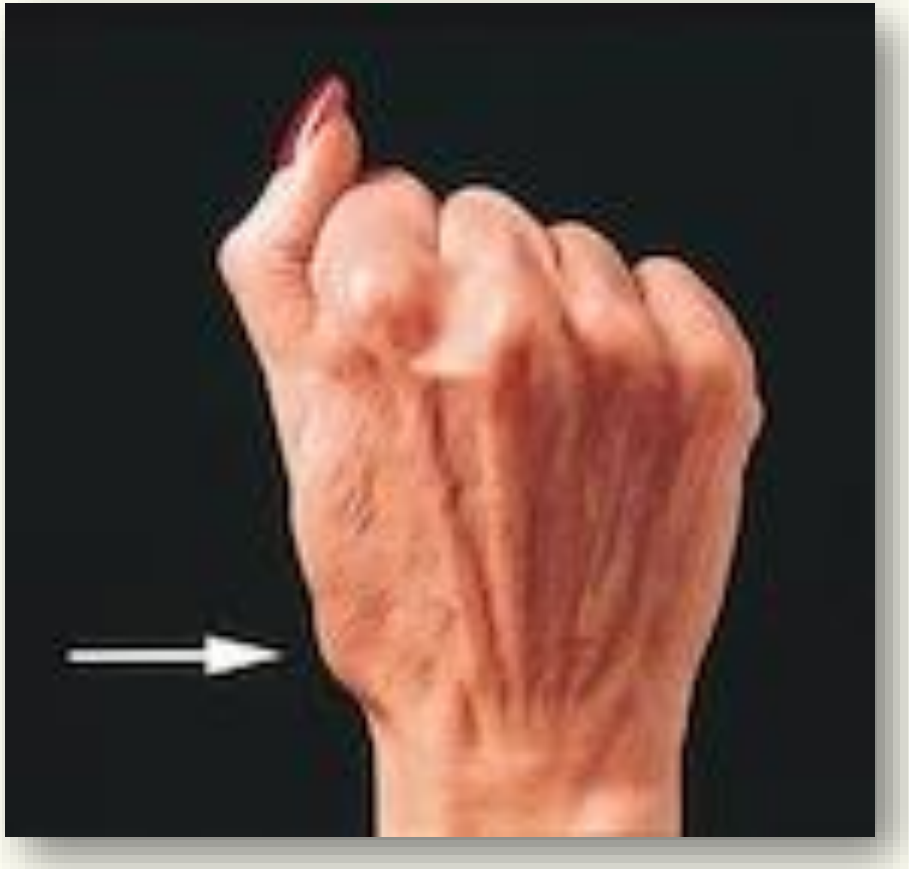




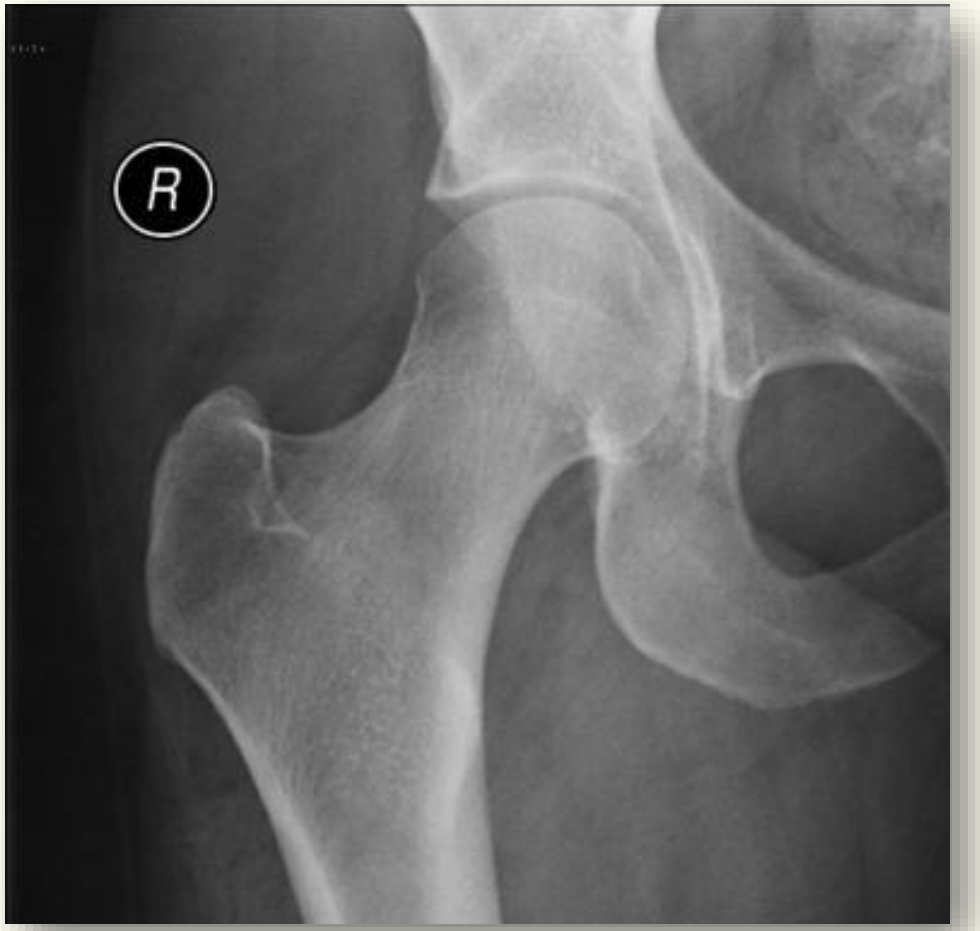
Note:
Normal
MCPs

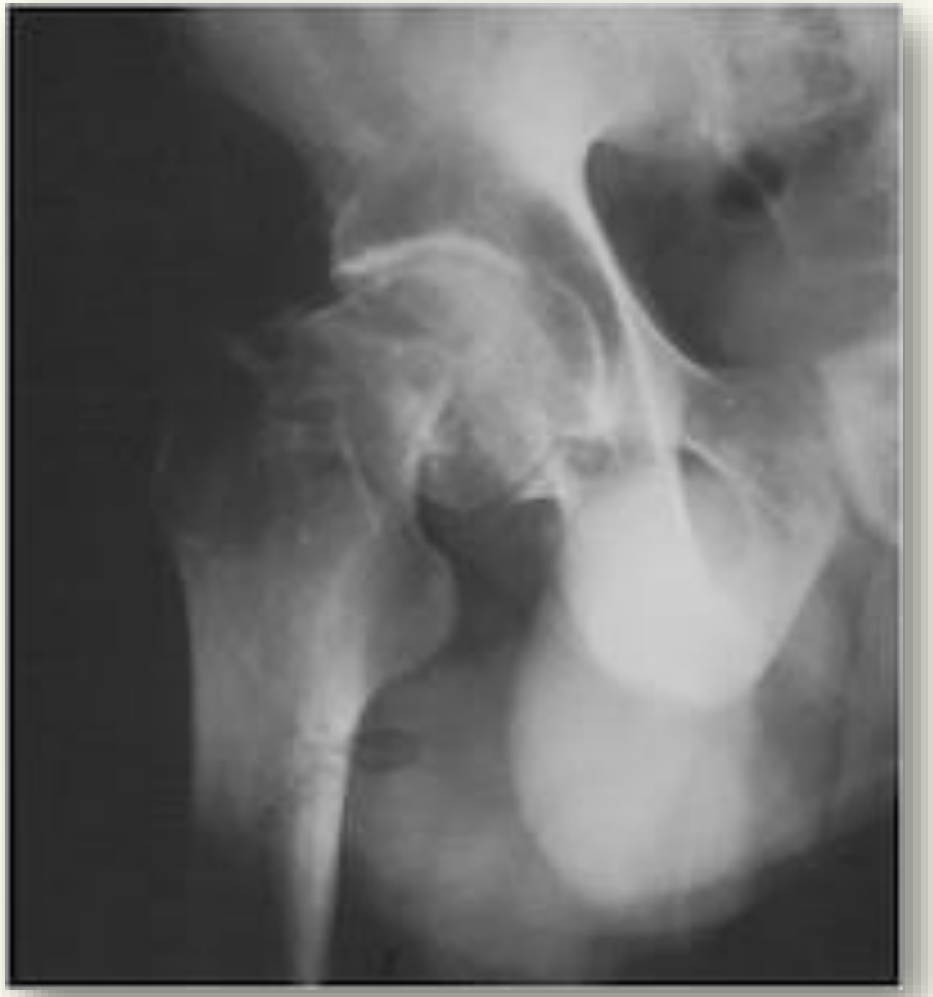
OA – CMC Joint



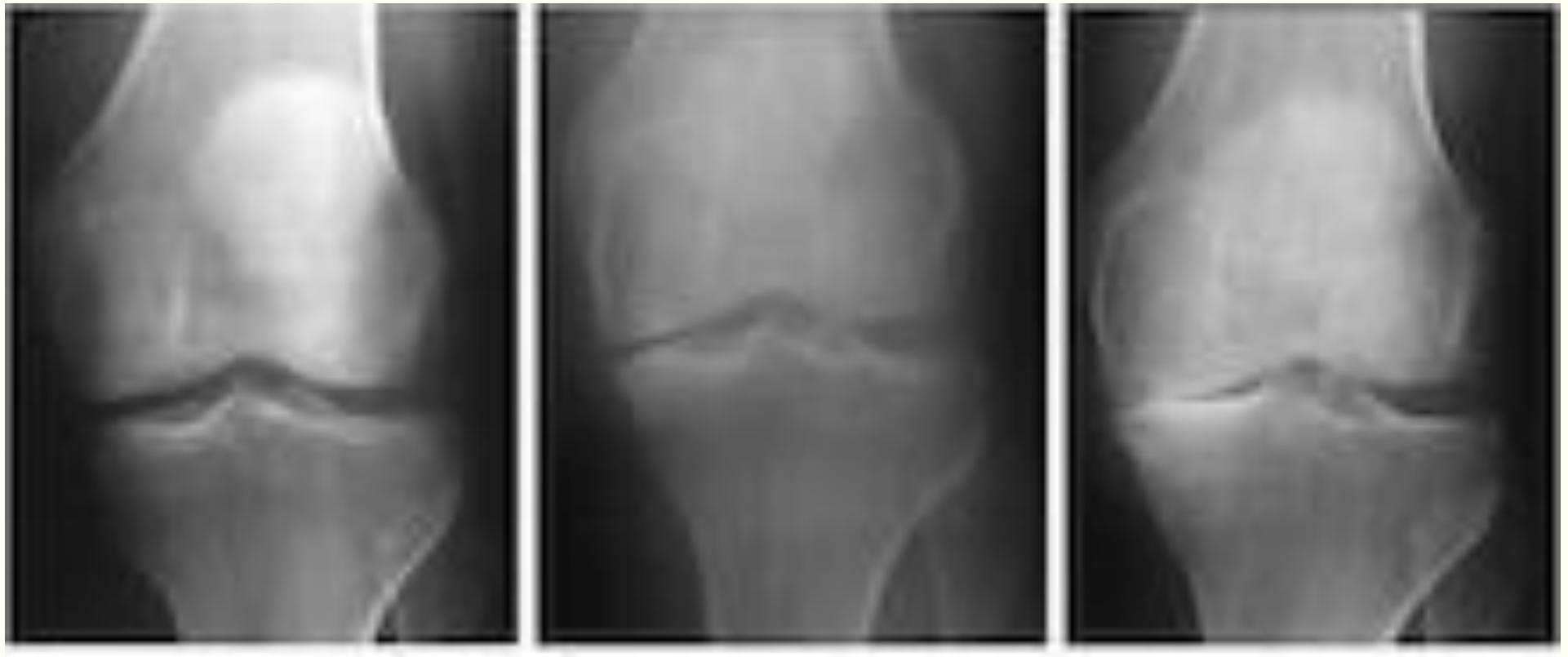


OA – Hip Joints





Progression of Knee OA

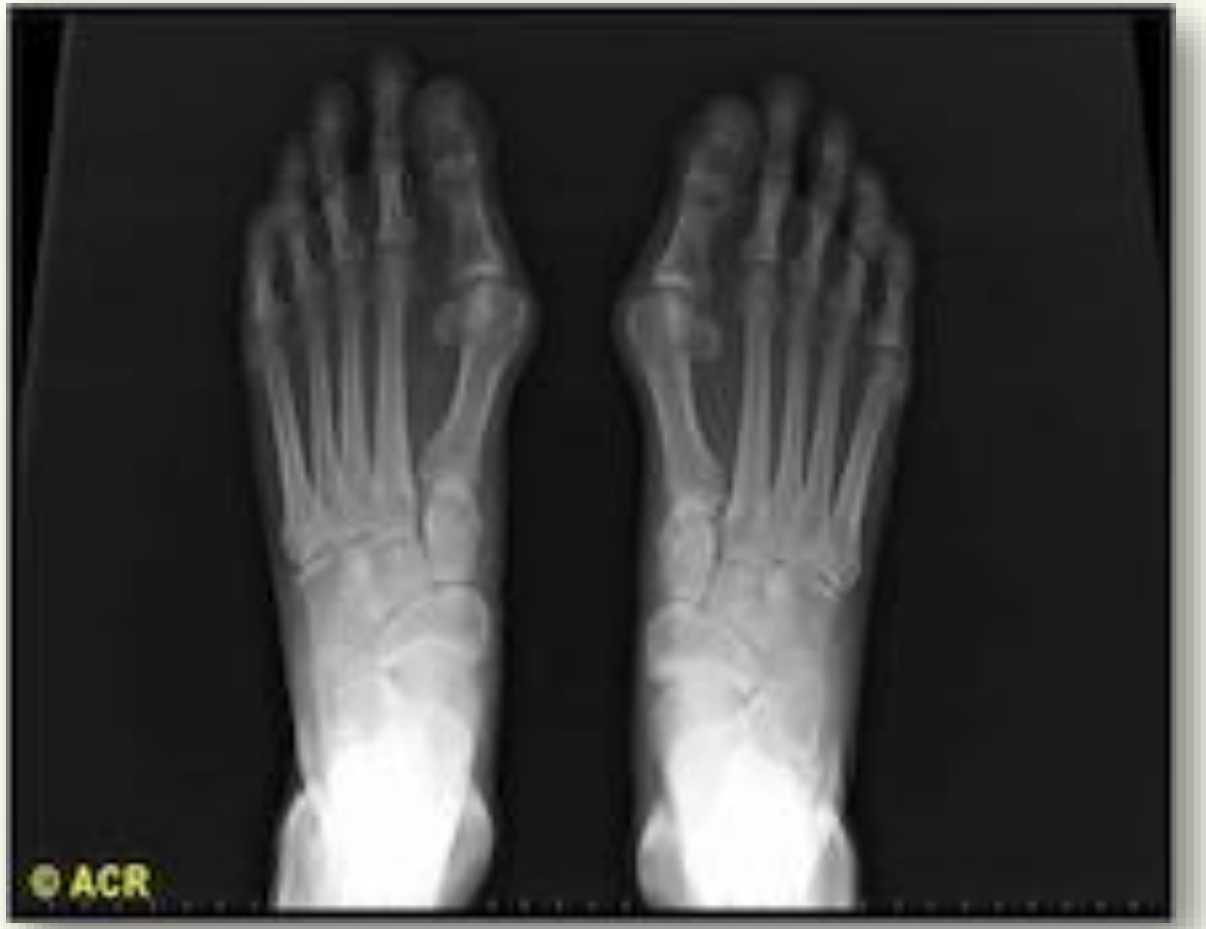


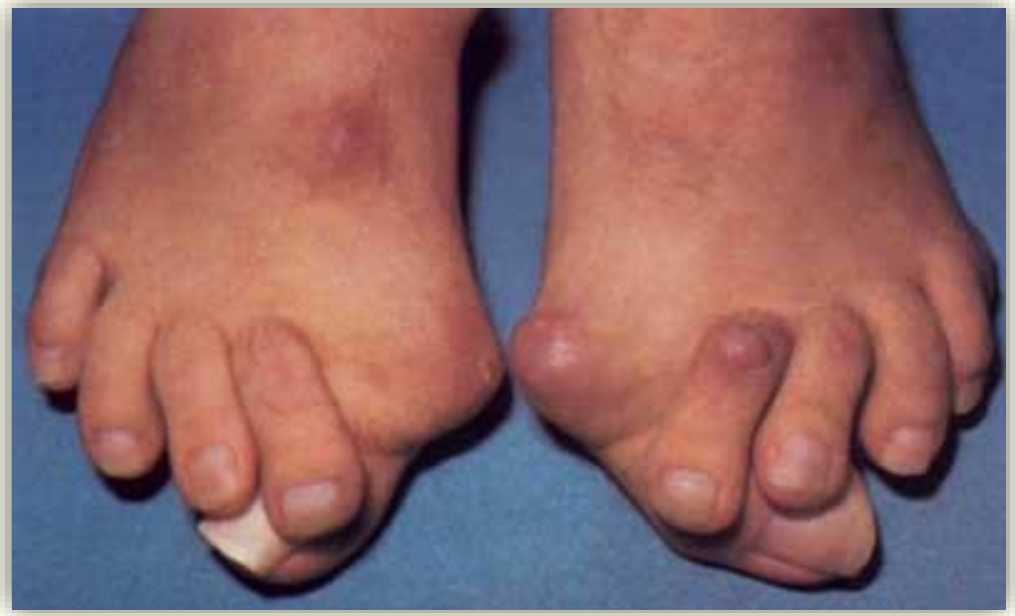
Initial

4 years

7 years

First MTP (Bunion)

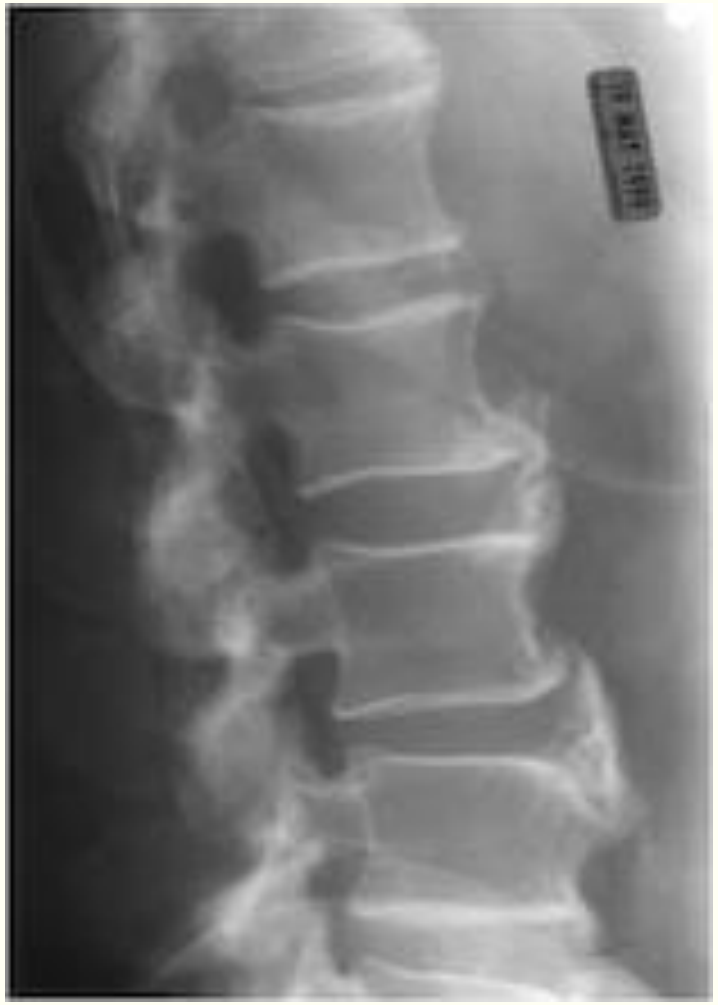




DISH Syndrome

Diffuse idiopathic skeletal hyperostosis

- Non-inflammatory
- Spiny ankylosis
- Enthesopathy

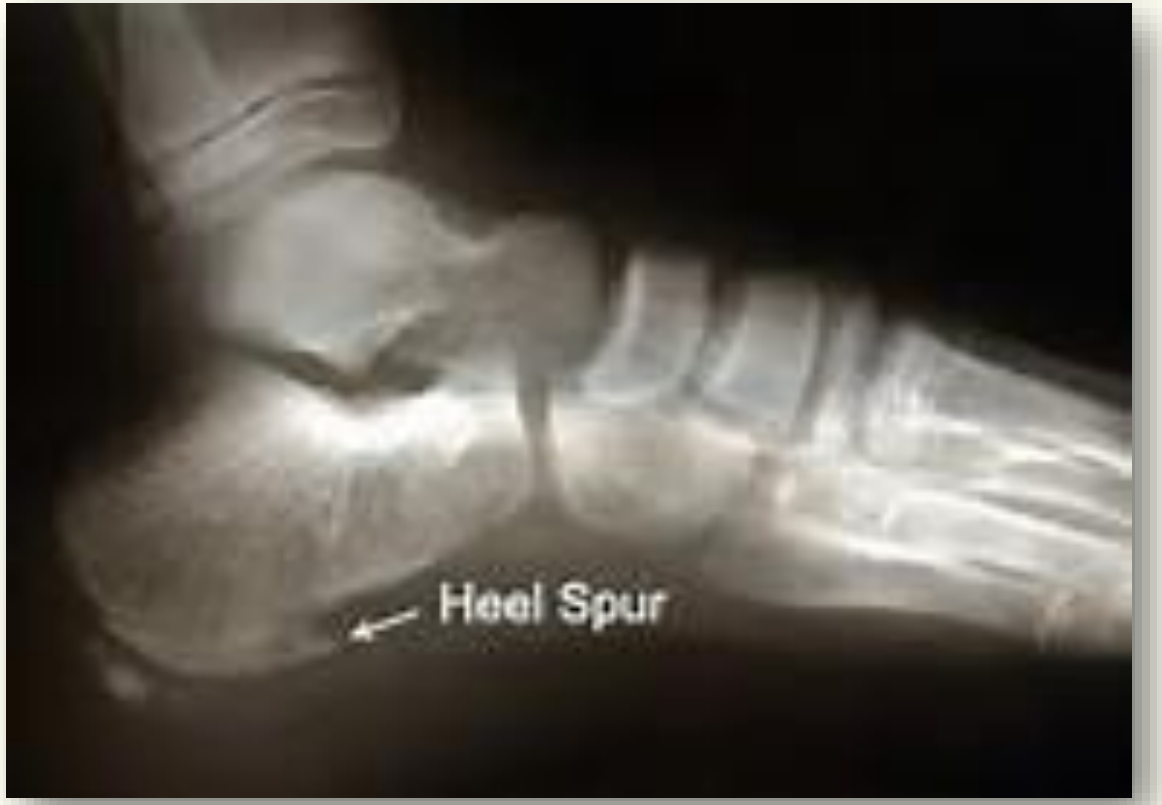


OA - Characteristics

- Insidious onset of joint pain, tenderness & limitation of movement
- Aggravated with joint movement and weight bearing
- Joints stiffen with rest and improve quickly after starting to move (gelling phenomenon)
- Not symmetrical

OA – X-ray Findings

- Narrowing of joint spaces
- Sharpened articular margins
- Osteophyte formation



OA – Management Plan

- Exercise – both aerobic and strengthening
- Weight loss (if indicated)
- Walking aids and knee braces
- Local warm/cold packs
- Regularly scheduled rest
- Relaxation techniques

(Deveza, 2017; Goroll & Mulley, 2009)

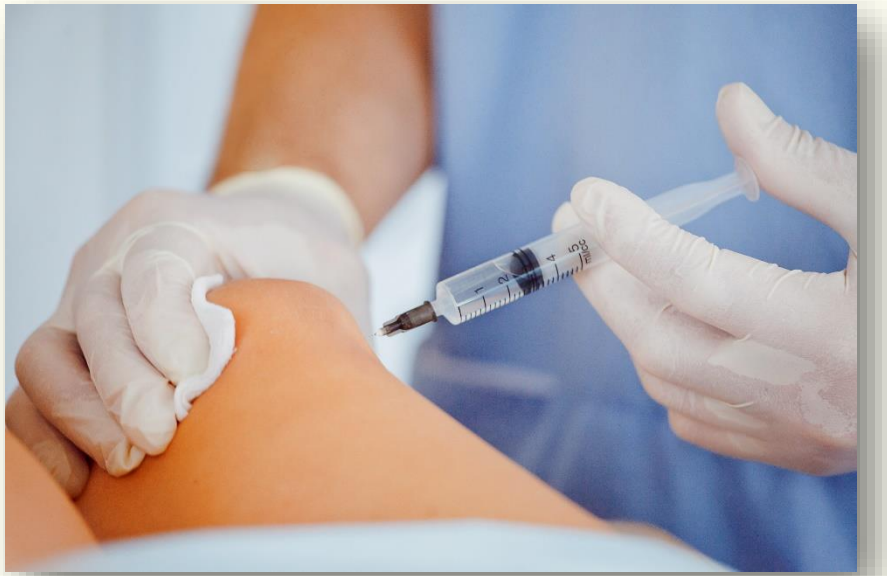
OA – Pharmacologic Therapy

- First line
  - Acetaminophen
  - Topical NSAIDs
- Second line
  - NSAIDs
  - Duloxetine
- Third line
  - Narcotic analgesics

(Deveza, 2017; Goroll & Mulley, 2009)

OA – Other Treatment Considerations

- Intra-articular joint injections
  - Steroids
  - Hyaluronic acid (given every 6 months)
- Surgery
  - Usually last resort



OA – Uncertain Benefit

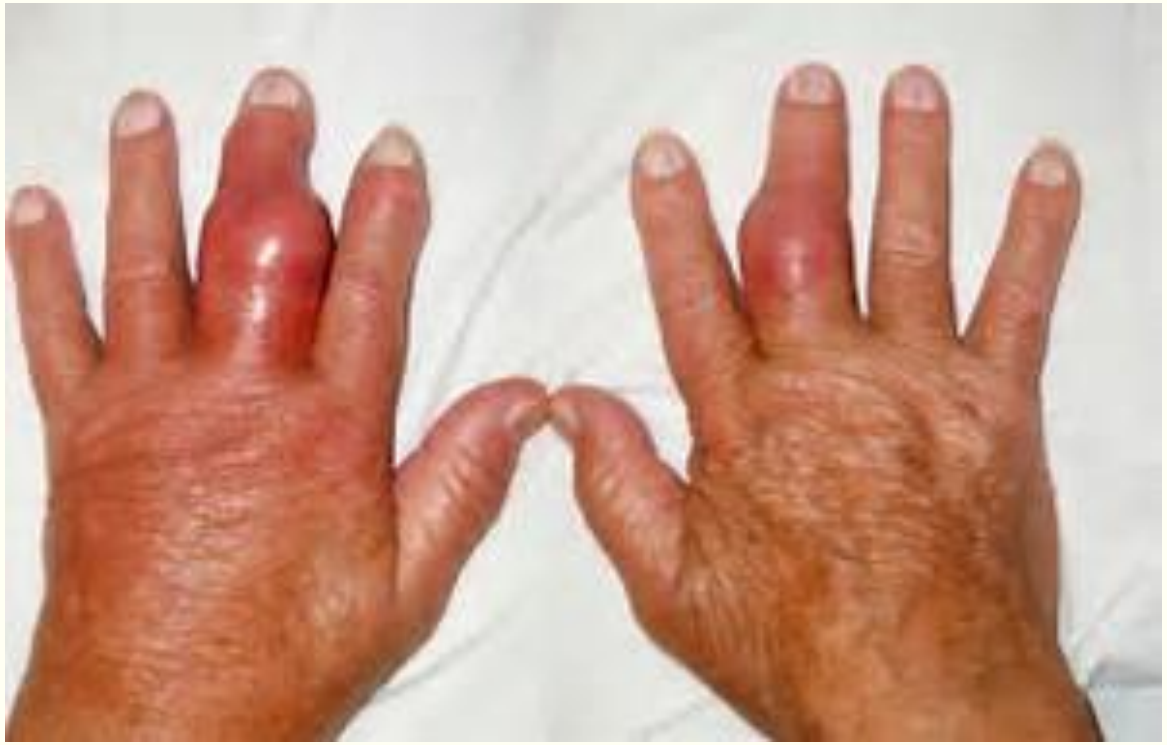
- Nutritional supplements
  - Glucosamine/chondroitin (mixed data)
  - Fish oil (low-dose may help)
- Insoles – lateral wedge has modest benefit
- Platelet-rich plasma knee injections
- Transcutaneous electrical nerve stimulation
- Acupuncture (minimal benefit in trials)

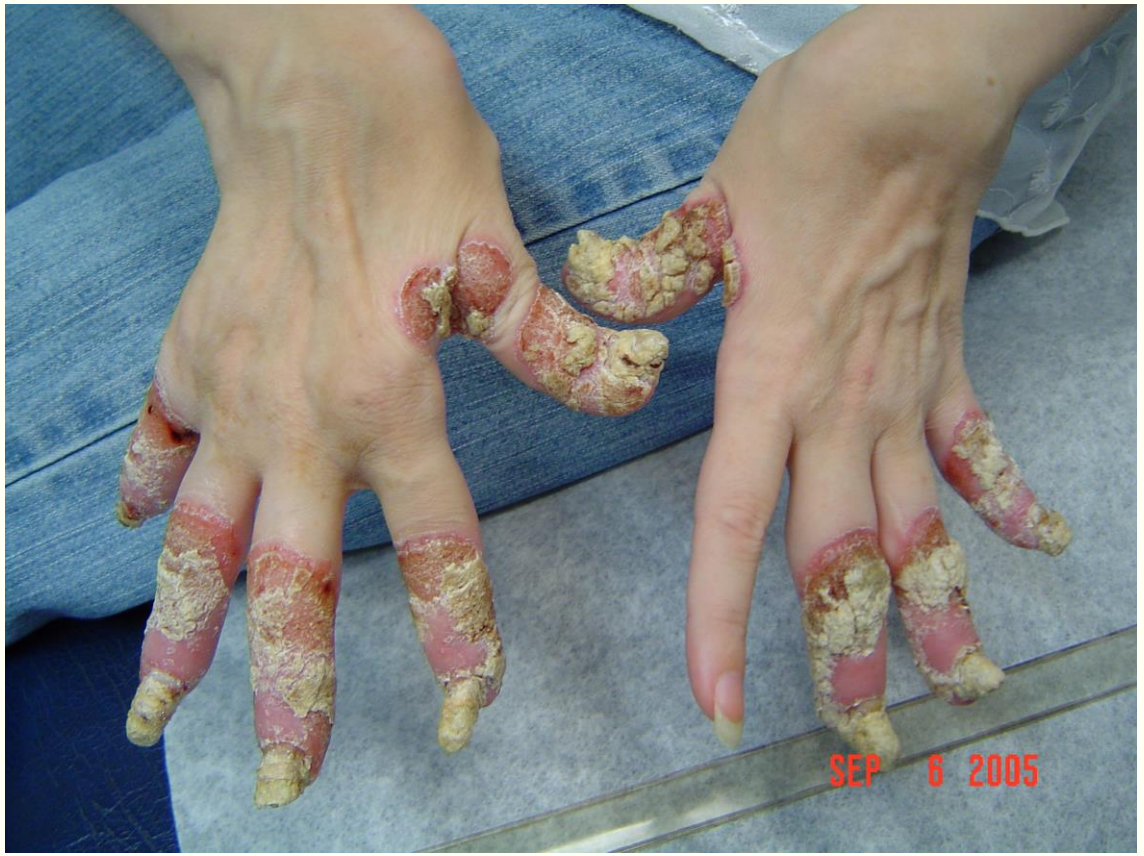
(Deveza, 2017)

INFLAMMATORY ARTHRITIS

Inflammatory Arthritis

- Rheumatoid arthritis
- Lupus
- Scleroderma
- Psoriatic arthritis
- Gout and pseudogout
- Sarcoidosis
- Vasculitis-related
- Infectious-related
  - Streptococcal
  - Gonococcal
  - Lyme disease
  - Post-viral




SEP 6 2005

Inflammatory Arthritis

- Influx of inflammatory cells into the synovial membrane/fluid
- Often presents with associated extra-articular symptoms
- Onset is acute

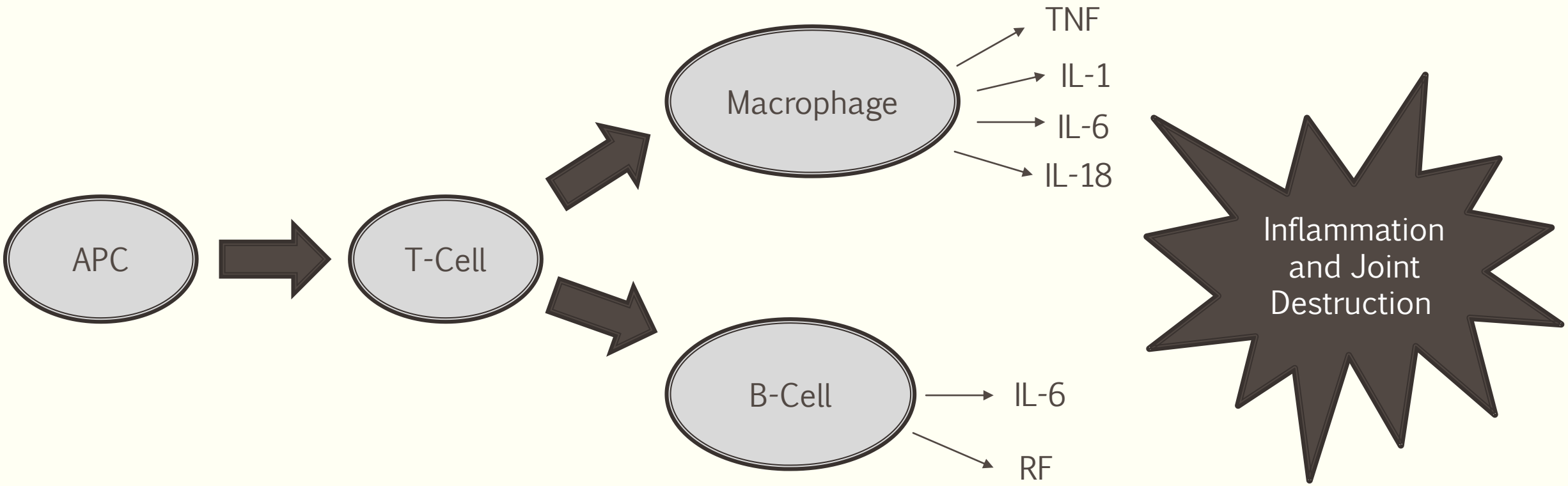
(Pujalte & Albano-Aluquin, 2015; Smolen, 2016)

Rheumatoid Arthritis

- Unknown etiology
- Genetic factors
- Autoimmune condition
- Affects about 1% of the population
- Injury to synovial microvasculature with inflammation & damage
- Overproduction of pro-inflammatory cytokines

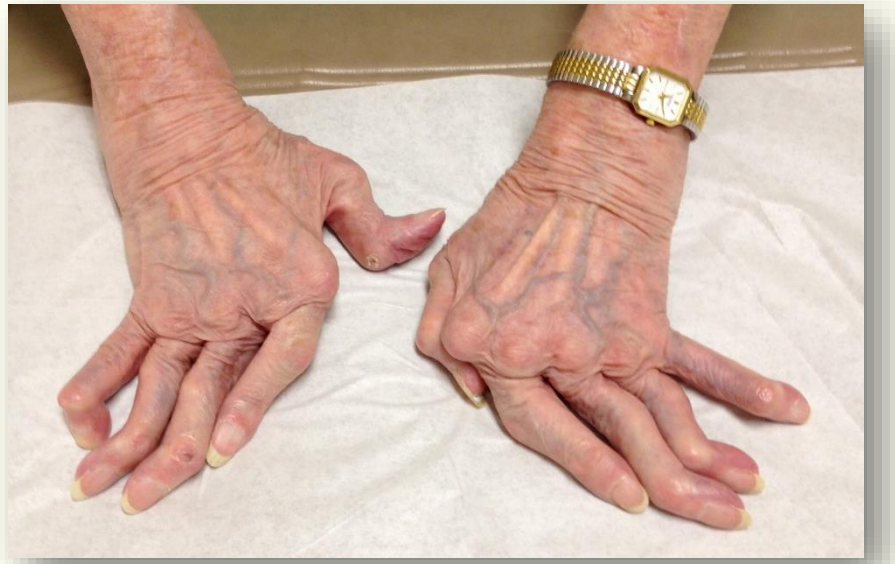
(Firestein, 2017; Matteson, 2016)

Inflammatory Cascade



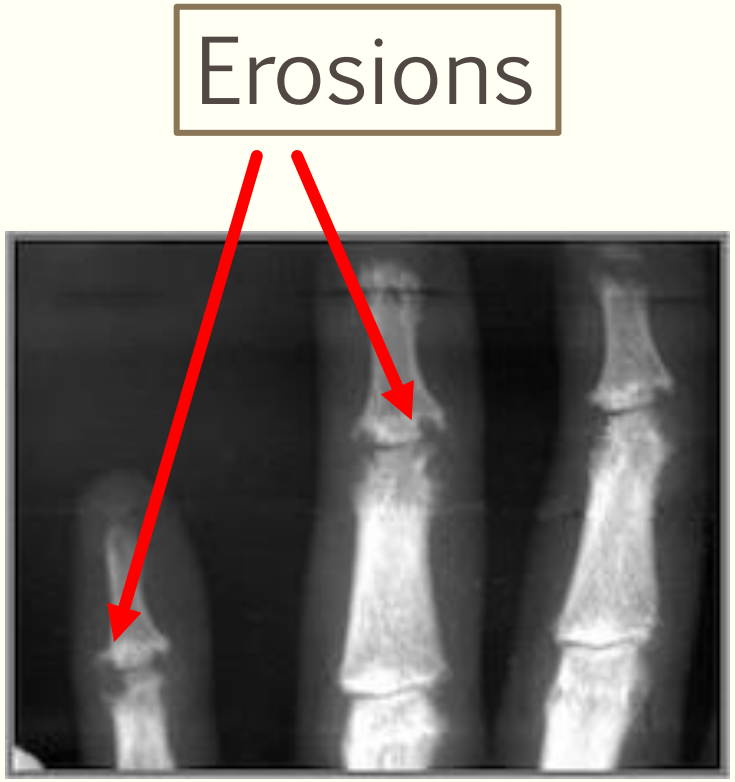
RA - Presentation

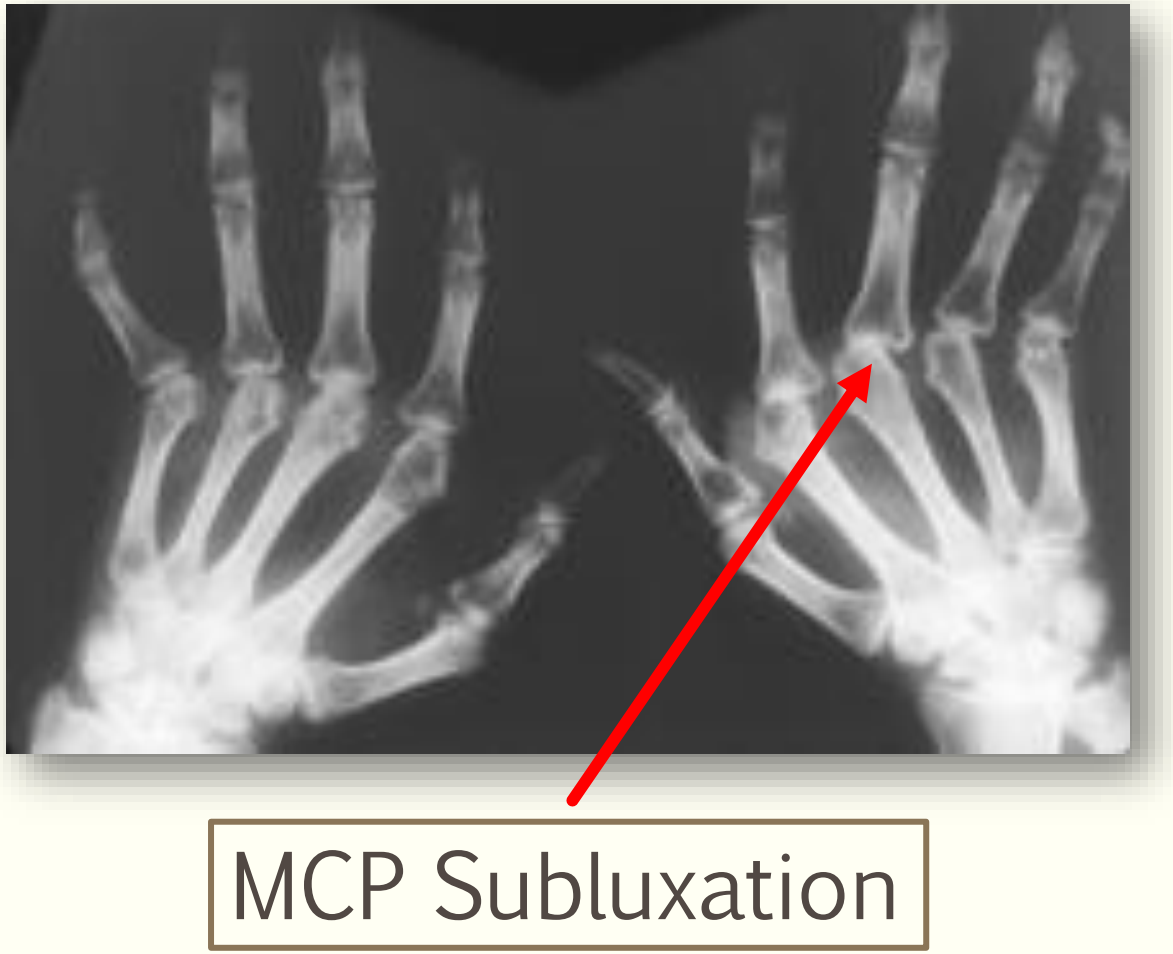
- Symmetric, inflammatory peripheral polyarthritis
- Acute or gradual onset
- Morning stiffness > 1 hour
- Typically MCP, PIP, MTP involvement
- Extra-articular features



(Venables & Maini, 2016)

RA – X-ray Findings





RA Diagnostic Criteria

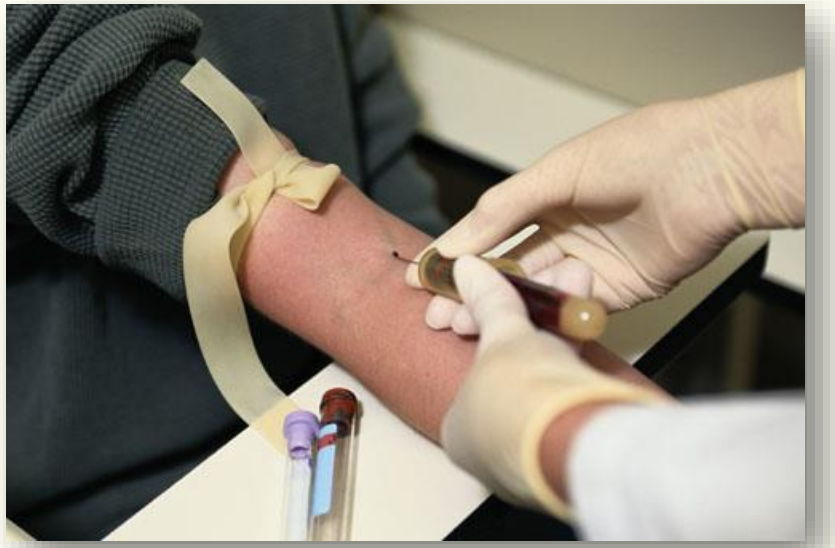
- At least 1 joint with definite clinical synovitis
- Synovitis not better explained by another disease
- Score of 6 out of 10 needed

(Aletaha et al., 2010)

Criteria	Points
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 *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive APCA	3
C. Acute-phase reactants	
Normal CRP *and* normal ESR	0
Abnormal CRP *or* abnormal ESR	1
D. Duration of symptoms	
< 6 weeks	0
≥ 6 weeks	1

RA - Evaluation

- Laboratory studies:
  - CBC
  - CMP
  - ESR, CRP
  - Rheumatoid factor
  - ACPA (anti-CCP antibody)



(Cohen & Mikuls, 2016)

RA – Management

- Rheumatology referral
- May need to prescribe NSAID and/or glucocorticoid for symptomatic relief
  - Celebrex 200mg bid or Ibuprofen 800mg tid
  - Prednisone 5-20 mg/day depending on severity

(Cohen & Mikuls, 2016)

RA – Specialized Treatments

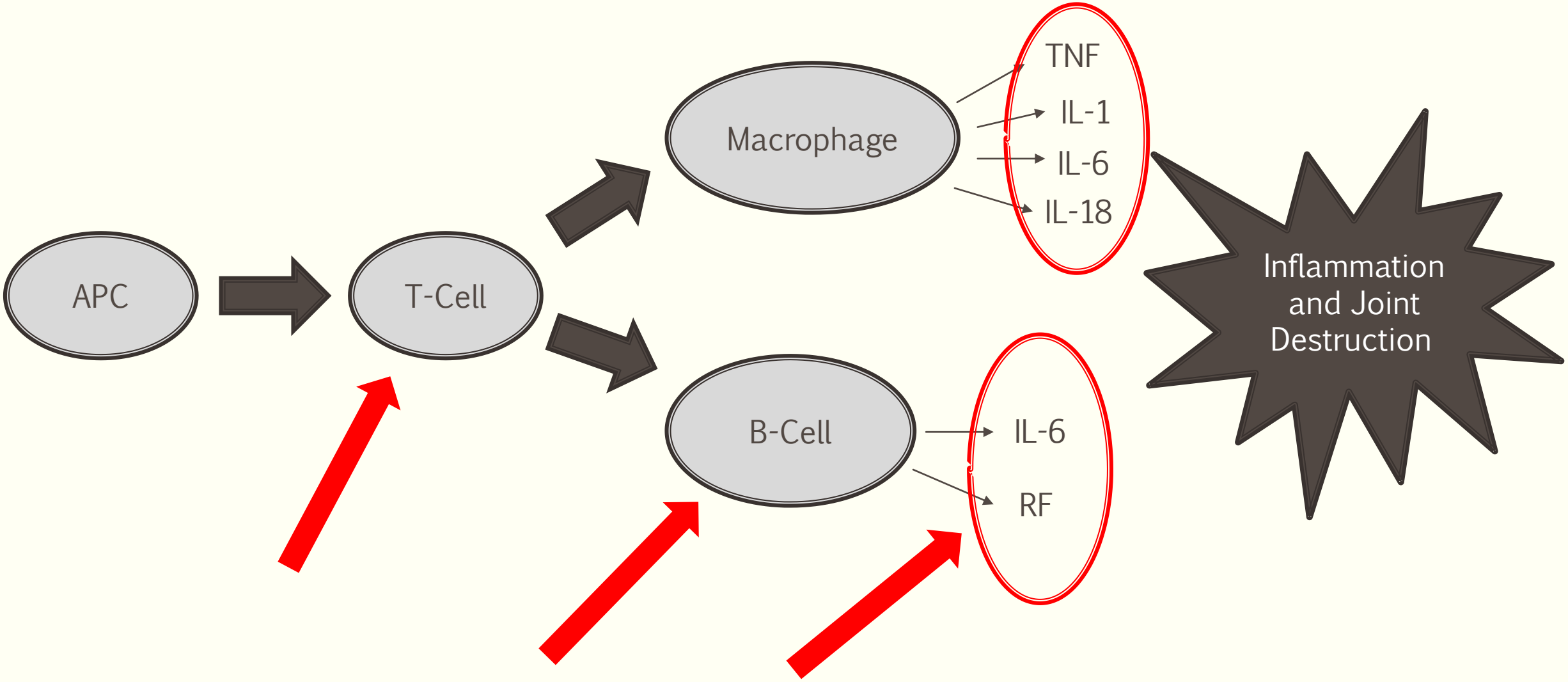
- **Traditional disease-modifying anti-rheumatic drugs (DMARDs)**
  - Methotrexate 10-25mg *once weekly*
  - Leflunomide 20mg daily
  - Sulfasalazine 500mg 2-3 tabs bid
  - Hydroxychloroquine 200-400mg daily

(Cohen & Mikuls, 2016)

RA – Specialized Treatments

TARGET	MEDICATION
Tumor Necrosis Factor alpha (TNF-alpha) inhibitors	Infliximab (Remicade) Adalimumab (Humira) Etanercept (Enbrel) Golimumab (Simponi and Simponi Aria) Certolizumab pegol (Cimzia)
Interleukin-6 (IL-6) receptor antagonist	Tocilizumab (Actemra) Sarilumab (Kevzara)
T-cell Modulator	Abatacept (Orencia)
CD20-directed cytolytic antibody	Rituximab (Rituxan)
Janus kinase (JAK) inhibitor	Tofacitinib (Xeljanz) Baricitinib (Olumiant)

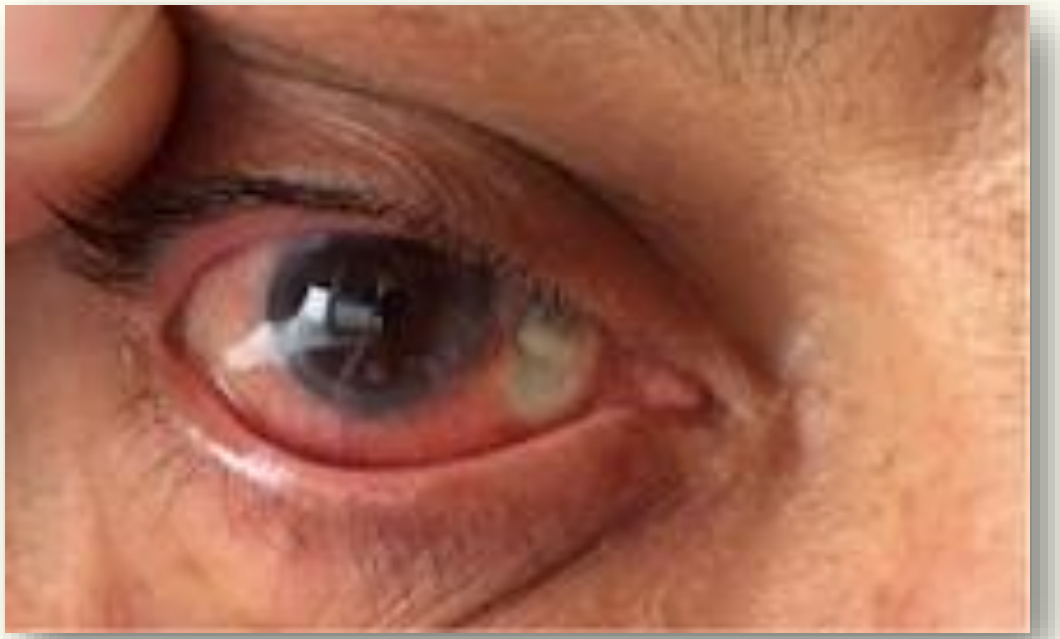
Inflammatory Cascade



Treatment Monitoring

- The biologic DMARD agents are often given in combination with a traditional DMARD
- Hepatitis panel obtained prior to start of therapy
- Tuberculosis screening initially and yearly for biologic agents
- CBC, CMP every 2-3 months
- Other special considerations for certain drugs

Reactive Arthritis

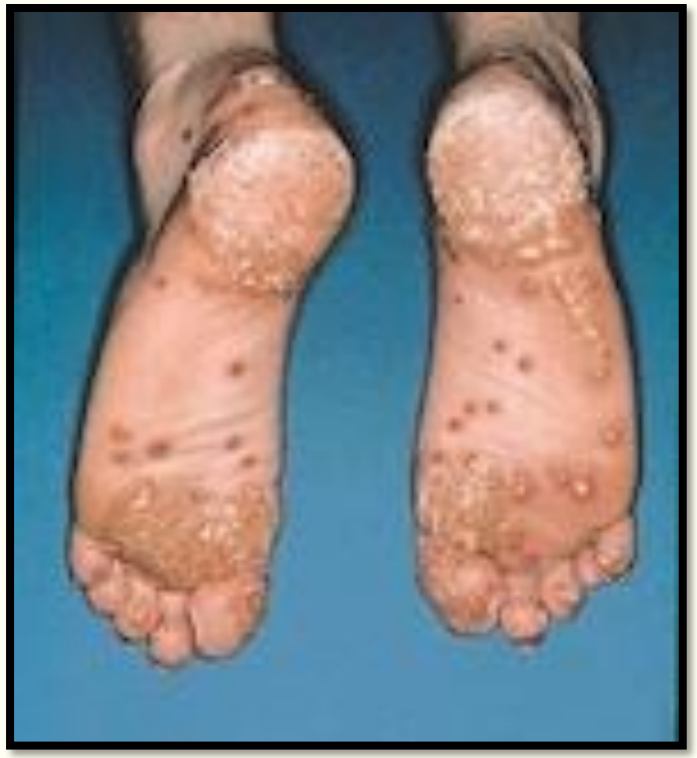


Scleritis/Uveitis

- Develops after an infection
  - Chlamydia
  - Salmonella
  - Shigella
  - Campylobacter
  - Escherichia coli
  - C. difficile

(Yu, 2016)

Reactive Arthritis



Keratoderma Blennorrhagicum

- **Extra-articular features:**
  - Conjunctivitis, uveitis
  - Urethritis, balanitis
  - Oral lesions, mucosal ulcers
  - Keratoderma blennorrhagica
  - Enthesitis

(Yu, 2016)

Reactive Arthritis

- 30-50% of patients have a positive HLA-B27
- Check CBC, CMP, ESR, CRP, UA
- If joint effusion, synovial fluid analysis is helpful to rule out septic arthritis
- Most cases resolve within one year

Reactive Arthritis

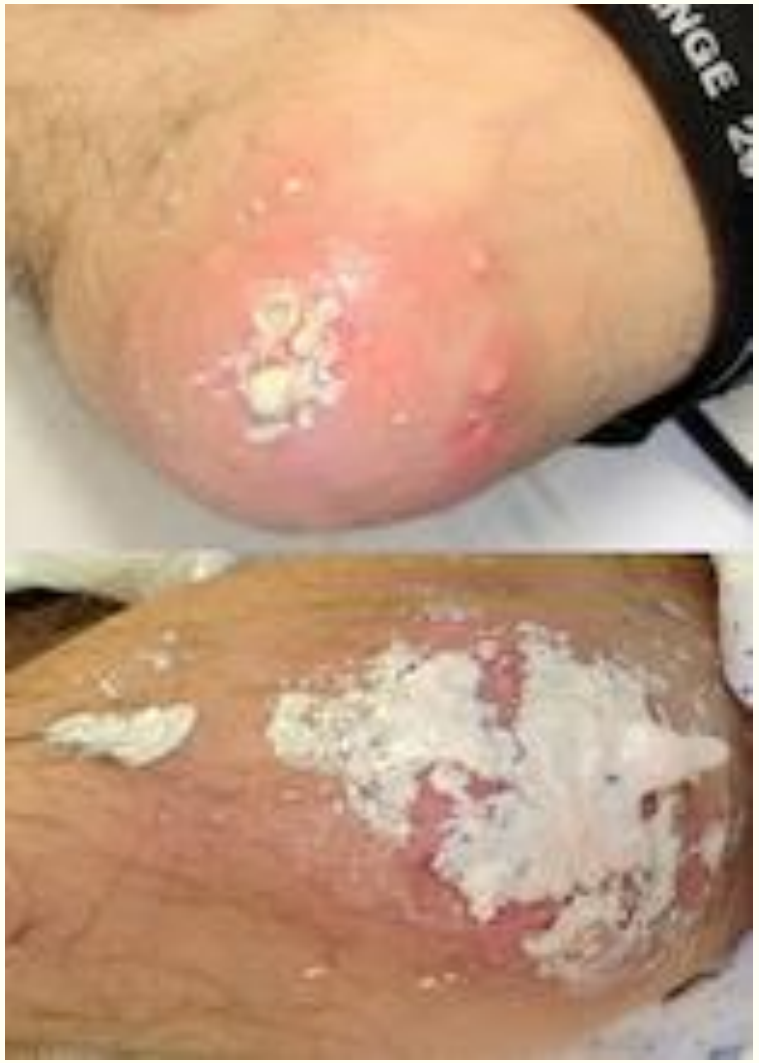
- **Treatment**
  - NSAIDs – Naproxen 500mg 2-3 times daily
  - Intra-articular and/or systemic glucocorticoids may be required
  - For chronic disease DMARDs such as sulfasalazine or methotrexate may be needed

(Gladman & Ritchlin, 2017)

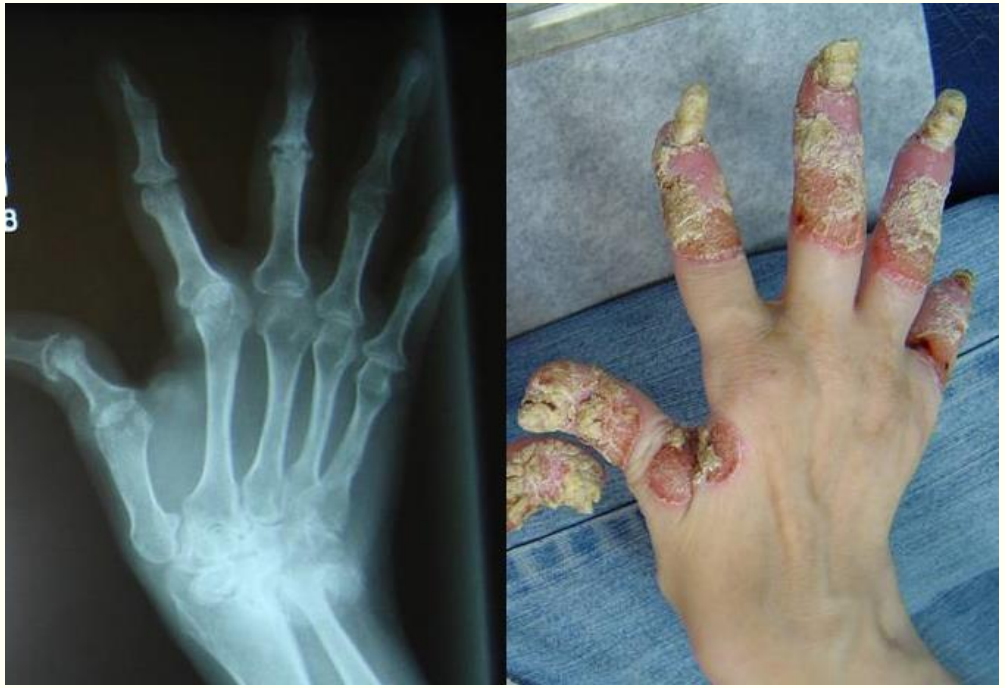
Psoriatic Arthritis

- Inflammatory arthritis associated with skin psoriasis
- Up to 30% of people with skin psoriasis go on to develop arthritis

(Gladman & Ritchlin, 2017)

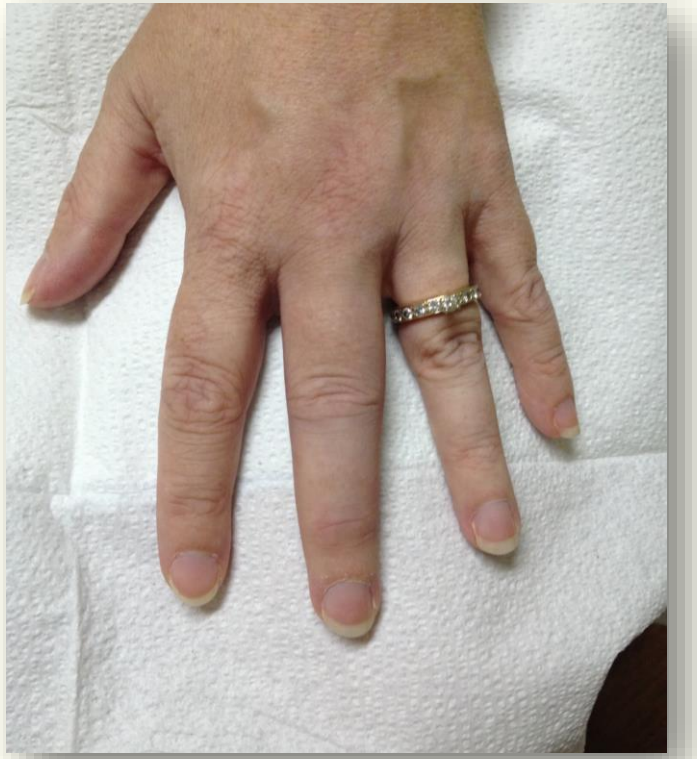


Psoriatic Arthritis (PsA)

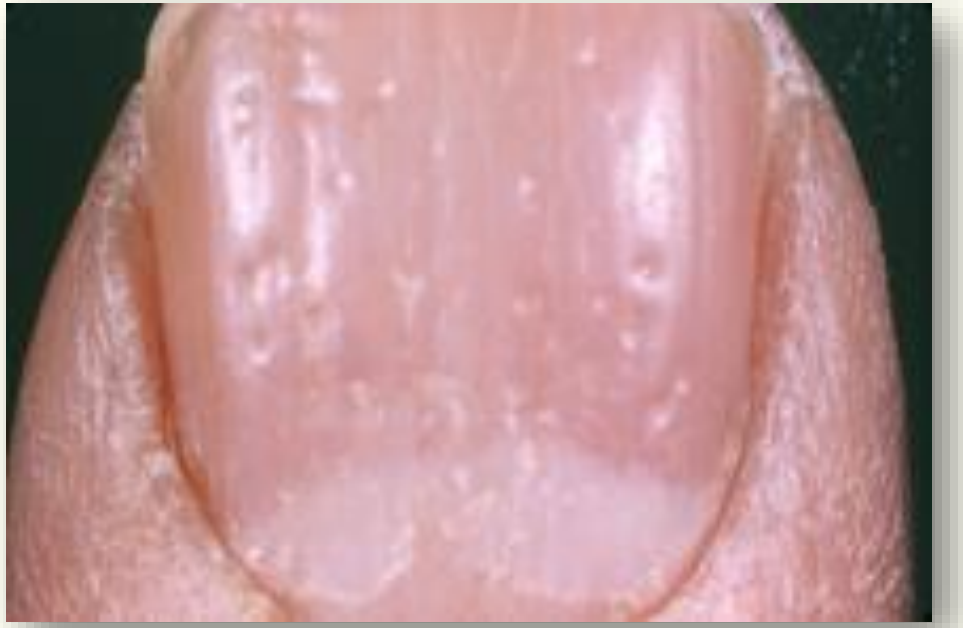


- May be symmetric or asymmetric
- May involve axial or peripheral joints
- Enthesitis, tenosynovitis and dactylitis may occur

PsA - Presentation



Dactylitis



Nail pitting

PsA – Laboratory Findings

- No specific tests available for diagnosis
- RF, ACPA, or ANA can be positive in ~10%
- HLA-B27 present in ~25% with axial inflammation
- ESR and CRP elevated in ~40%

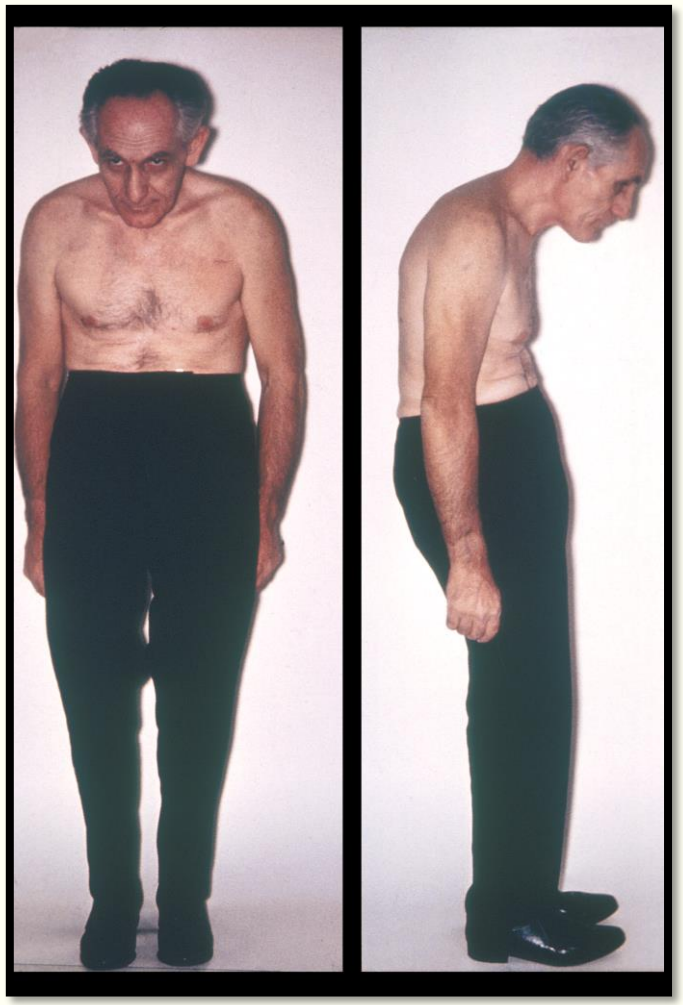
PsA – Specialized Treatments

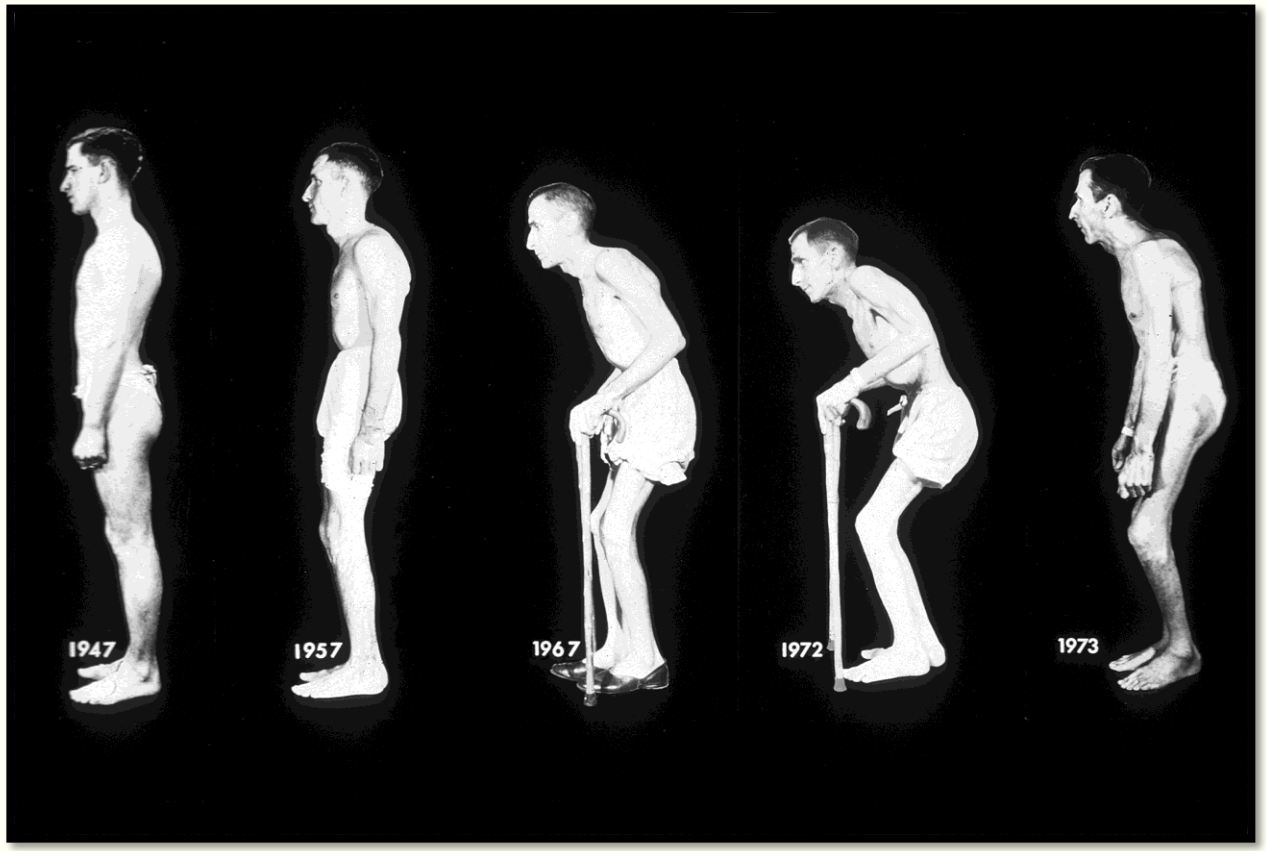
TARGET	MEDICATION
Tumor Necrosis Factor –alpha (TNF-alpha) inhibitors	Infliximab (Remicade) Adalimumab (Humira) Etanercept (Enbrel) Golimumab (Simponi and Simponi Aria) Certolizumab pegol (Cimzia)
Interleukin-17 (IL-17) inhibitors	Secukinumab (Cosentyx) Ixekizumab (Taltz)
T-cell Modulator	Abatacept (Orencia)
Interleukin-12 and -23 (IL-12, IL-23) inhibitor	Ustekinumab (Stelara)

Ankylosing Spondylitis (AS)

- Inflammatory condition associated with axial and peripheral arthritis
- Insidious onset of back pain and stiffness that improves with exercise
- Enthesitis and/or sacroiliitis often present
- Typically in men <40 years

AS





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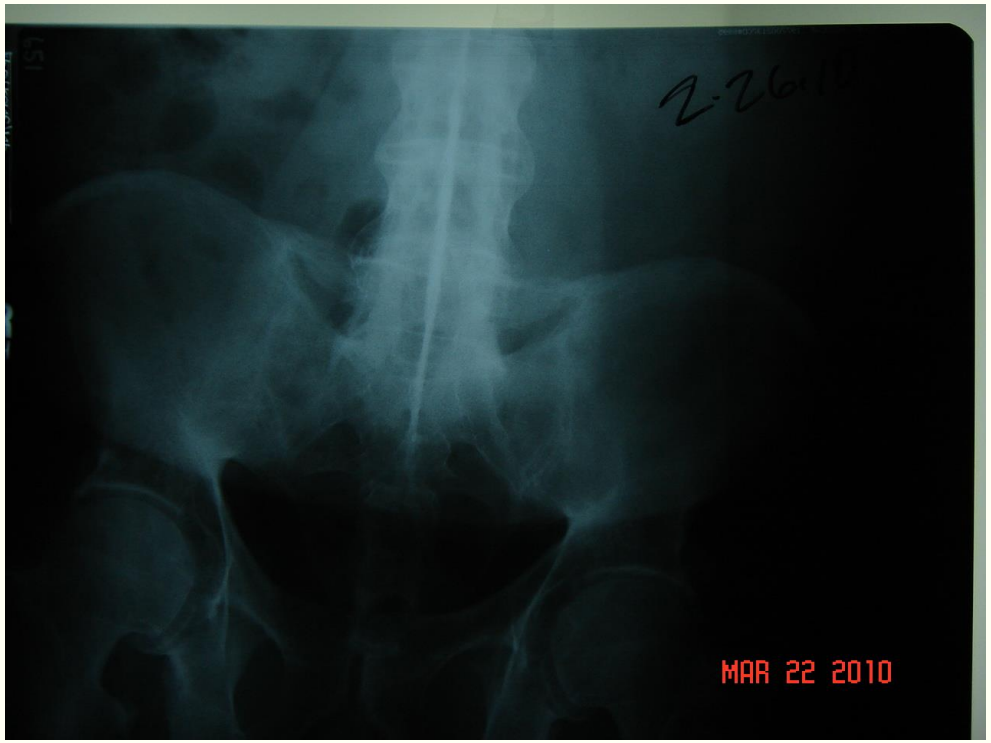
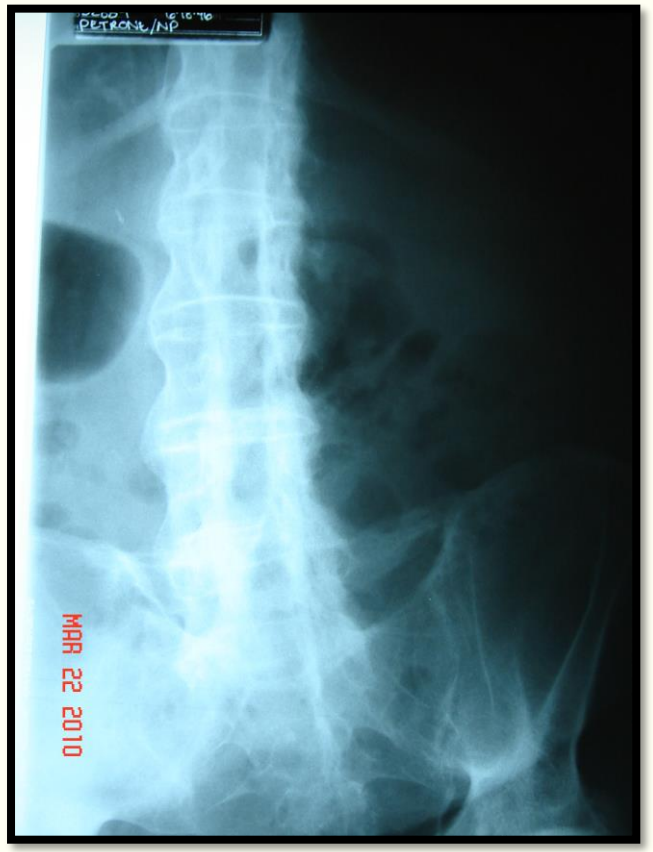
AS – X-ray Findings



Fused SI Joints

"Bamboo" Spine



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AS – Extra-Articular Manifestations

- Iritis occurs in up to 40% of cases
- Upper lobe, bilateral pulmonary fibrosis
- Cardiac – aortic incompetence, cardiomegaly, and conduction defects
- Constitutional – fatigue, weight loss, low-grade fever, anemia

AS - Presentation

- LBP and stiffness > 6 months improving with exercise but not relieved with rest
- Limitation of lumbar spine movements in sagital and frontal planes
- Limitation of chest expansion relative to normal values for age and sex

AS – Laboratory Findings

- HLA-B27 genetic marker (not diagnostic, but strong association with symptoms)
- Up to 5% of Caucasian patients with AS are negative for HLA-B27
- HLA-B27 prevalent in Native Americans

AS - Management

- NSAIDs – Naproxen, Diclofenac, Celebrex
- TNF alpha inhibitors – etanercept (Enbrel), adulimumab (Humira), infliximab (Remicade), certolizumab pegol (Cimzia), golimumab (Simponi)
- Sulfasalazine may be used for peripheral joint involvement

Back Pain

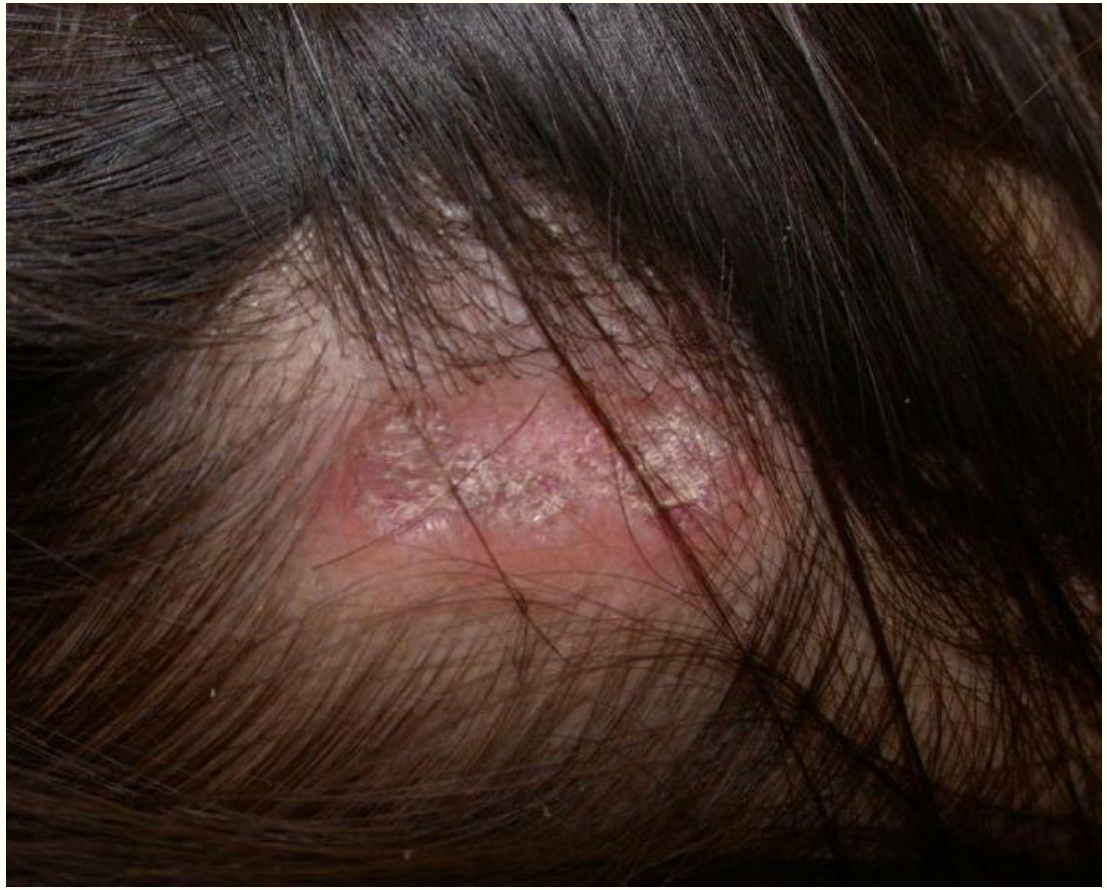
Non-Inflammatory

- Onset usually in people >50
- Mechanical condition
- Improves with rest

Inflammatory

- Onset usually in people <40
- Autoimmune condition
- Worse with rest, improves with exercise
- Extra-articular manifestations (i.e. enthesitis, bowel disease, eye inflammation)

SYSTEMIC LUPUS ERYTHEMATOSUS & RELATED DISORDERS



Systemic Lupus Erythematosus (SLE)

- Chronic inflammatory disease
- Immunologic abnormalities
  - Presence of autoantibodies
- Can affect any organ system
- Women > men prevalence

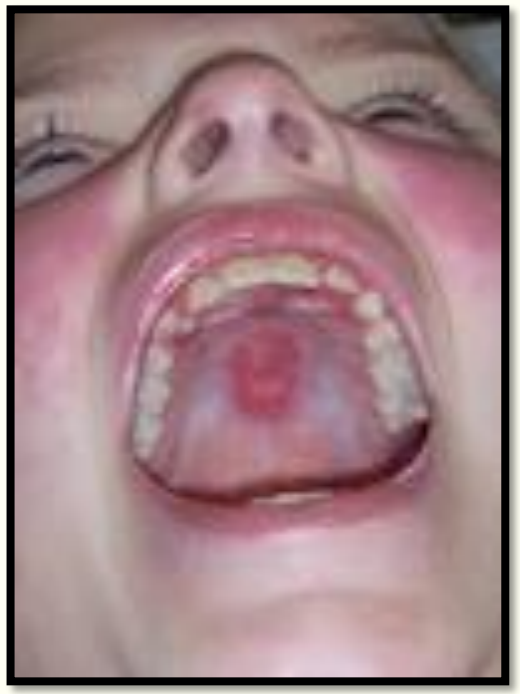
SLE – Classification Criteria

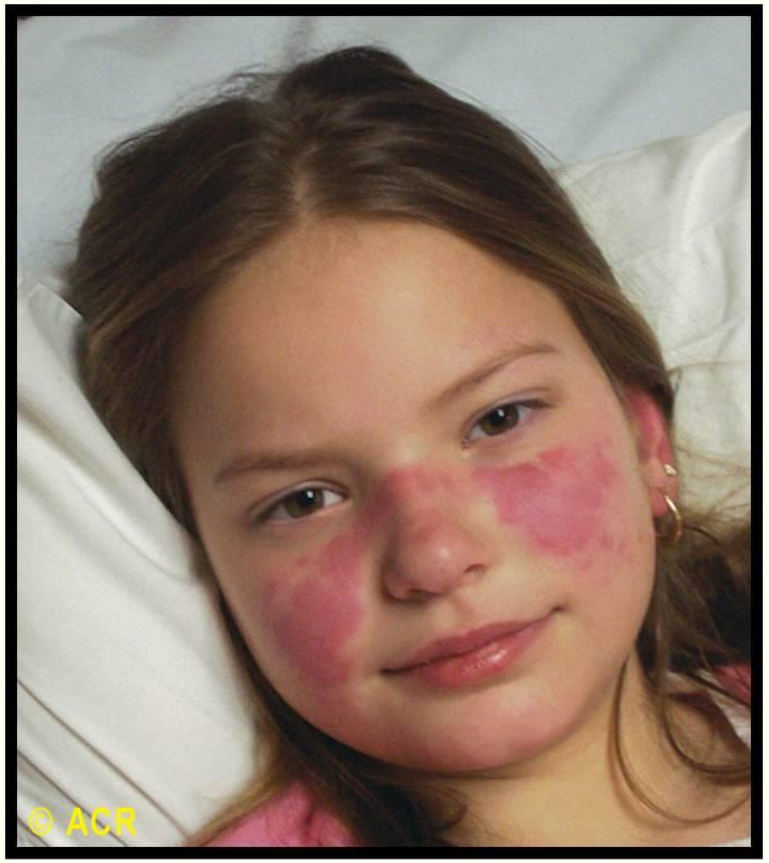
1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcers
5. Arthritis
6. Serositis
7. Renal disorder
8. Neurological disorder (i.e. seizures)
9. Hematological disorders
10. Immunological disorders
11. Antinuclear antibody in raised titer

4 criteria need to be present

SLE – Mucocutaneous Findings

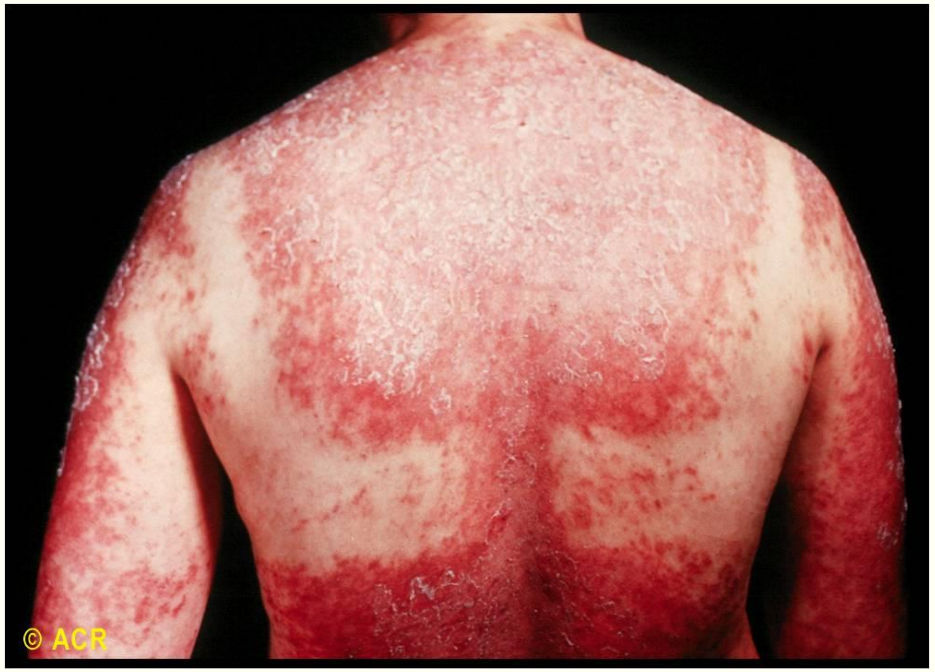
Oral Ulcer





Malar Rash

Photosensitivity Rash



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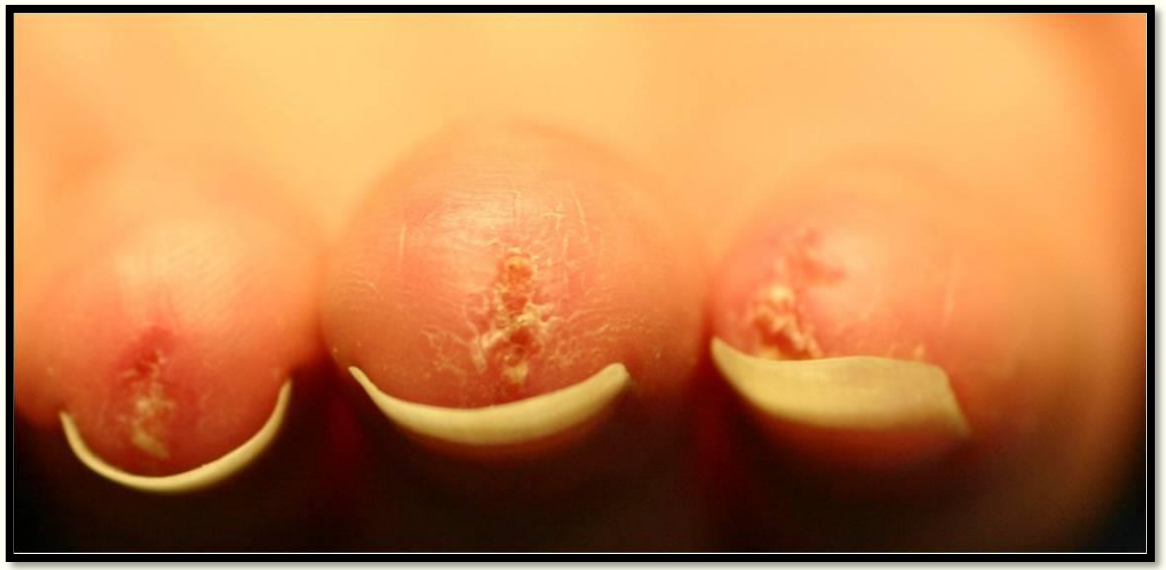
SLE – Vasculitic Findings

Raynaud's Phenomenon



Digital Ulcers

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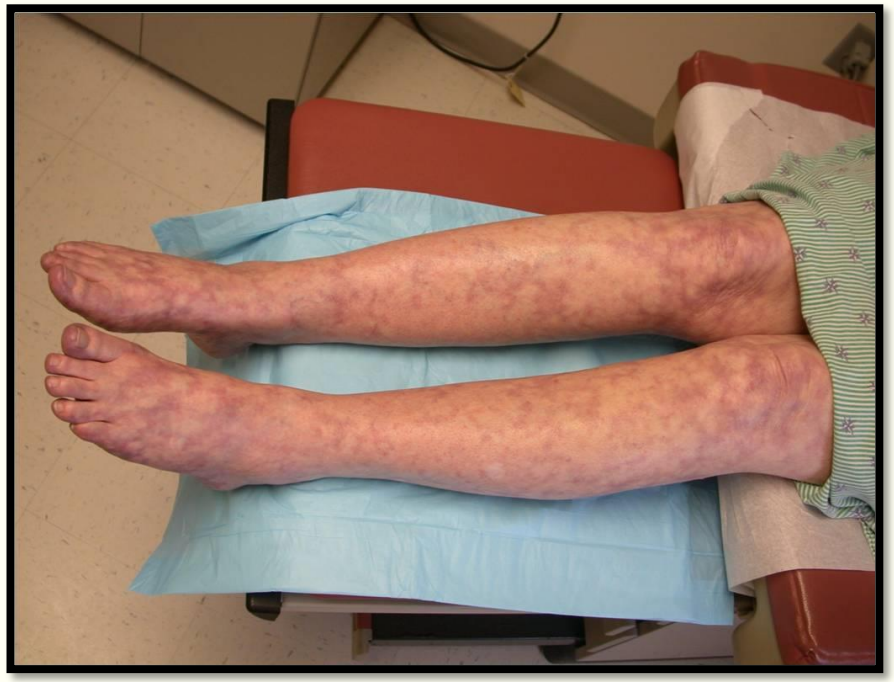
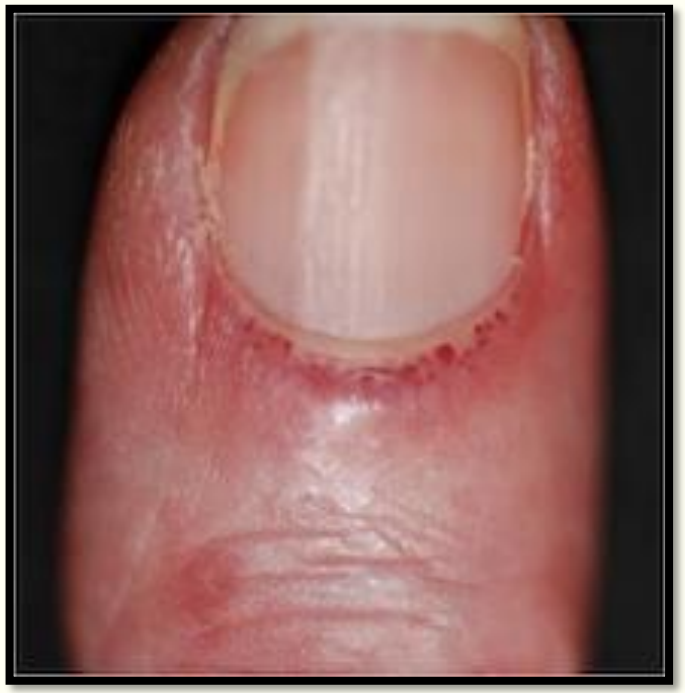
SLE – Vasculitic Findings

Levido Reticularis





Nailfold Capillaries

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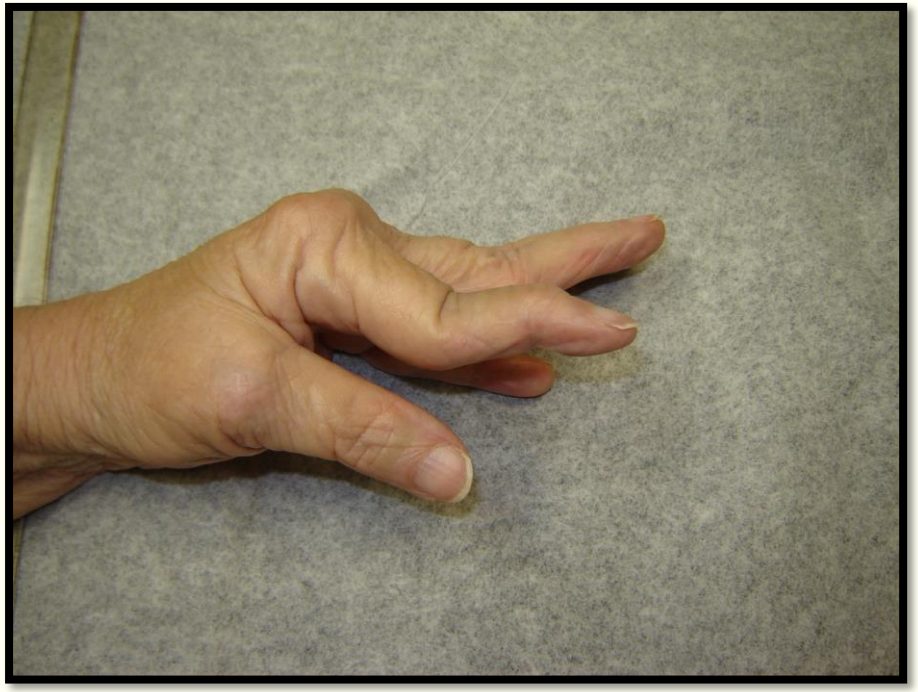
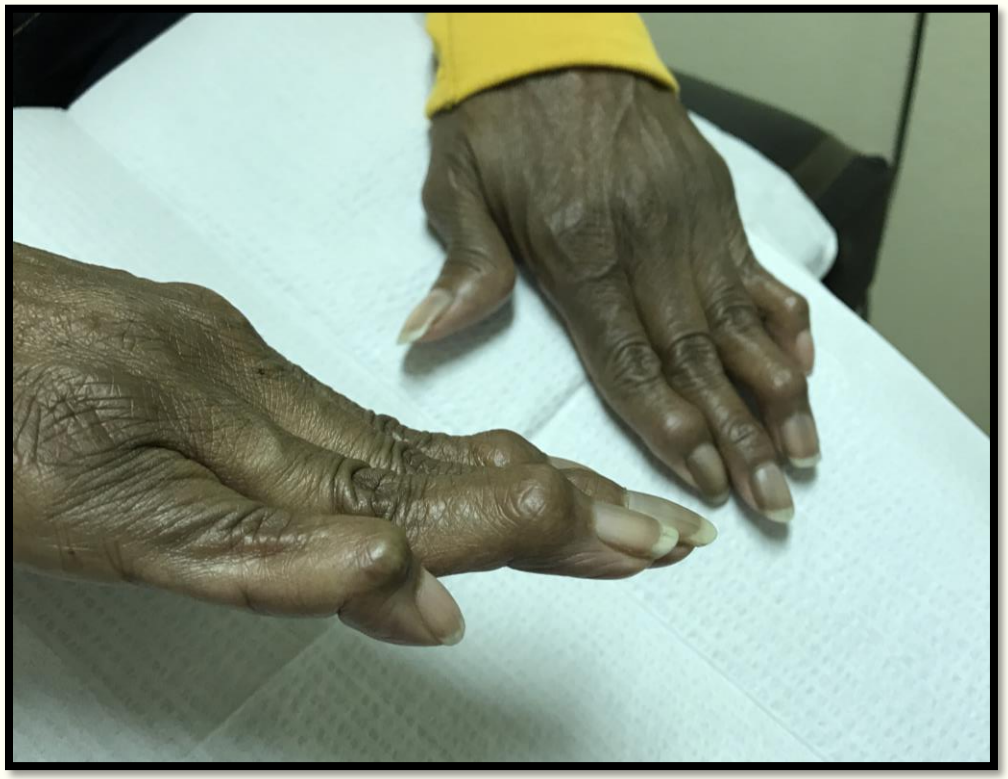
SLE – Joint Findings

Swan Neck Deformity – Jaccoud Arthropathy





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SLE – Associated Findings

- Fatigue
- Alopecia – patchy or diffuse
- Proteinuria and/or hematuria
- Anemia (leukopenia, neutropenia, lymphopenia, thrombocytopenia)

SLE - Evaluation

- CBC
- CMP
- Urinalysis
- ESR, CRP
- Lupus antibody panel (ANA, ENA, dsDNA)
- C3, C4

SLE - Management

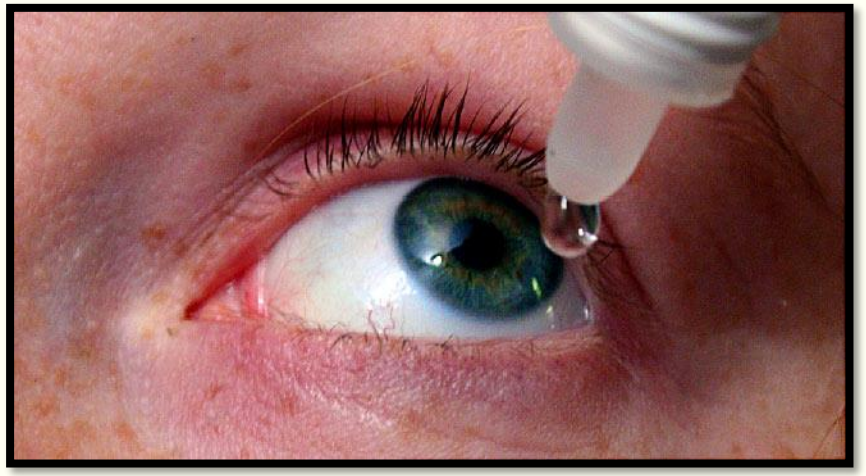
- **Drug therapy:**
  - Prednisone
  - Hydroxychloroquine (Plaquenil)
  - Azathioprine (Imuran)
  - Mycophenolate mofetil (Cell-Cept) - nephritis
  - Belimumab (Benlysta) – B-lymphocyte stimulator-specific inhibitor
  - Cyclophosphamide IV (severe flares)

SLE - Management

- Rest
- Wear sunscreen
- Wear gloves (Raynaud's)
- Calcium & vitamin D for bone health
- Pregnancy planning, contraception use (lupus may flare with pregnancy)

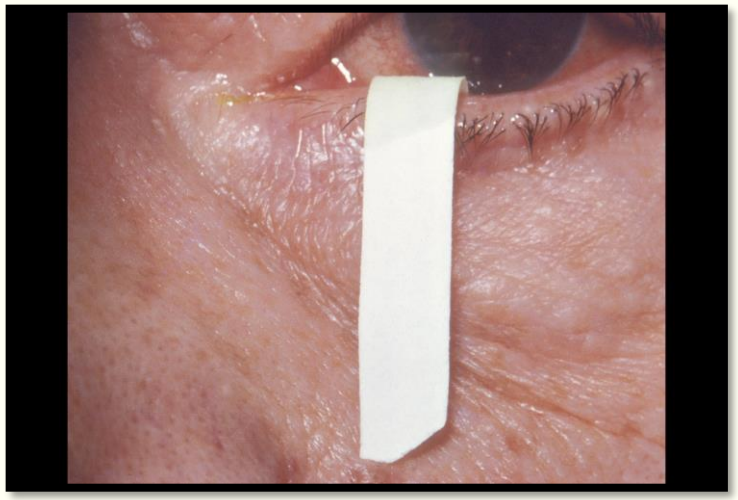
Sjogren's Syndrome

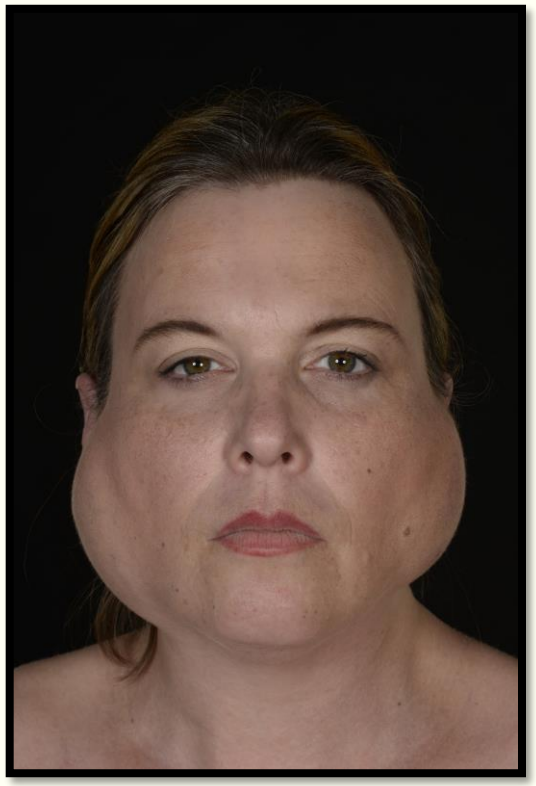
- Lymphocytic infiltration of exocrine glands resulting in xerostomia and keratoconjunctivitis sicca
- Women > men ratio 9:1
- Generally 40-50 years of age
- Prevalence ~ 1%



SS - Findings

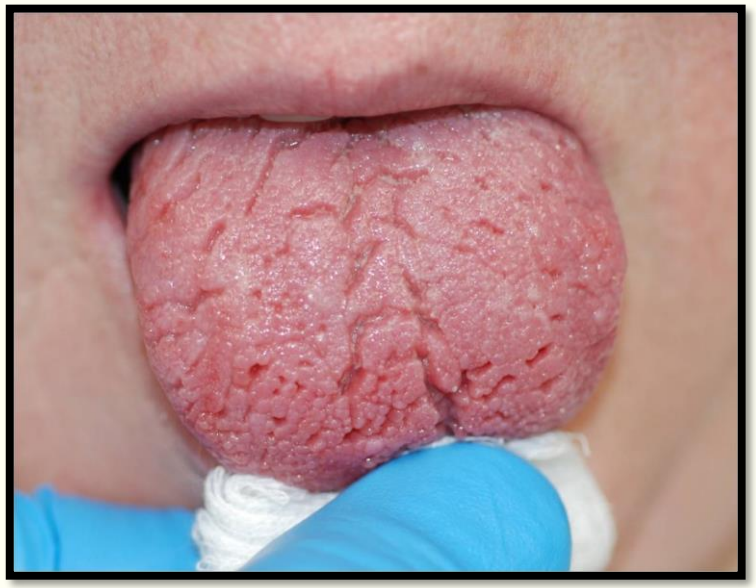
Schirmer's Test





Parotid Gland Enlargement

Xerostomia



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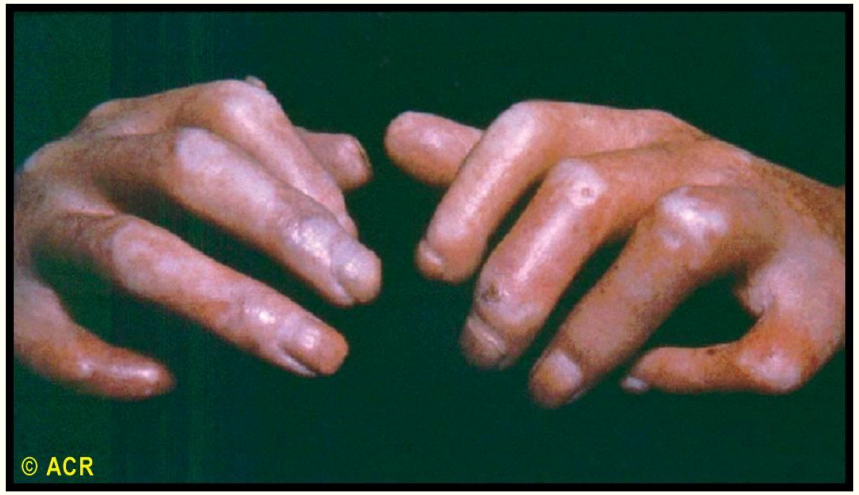
SS - Management

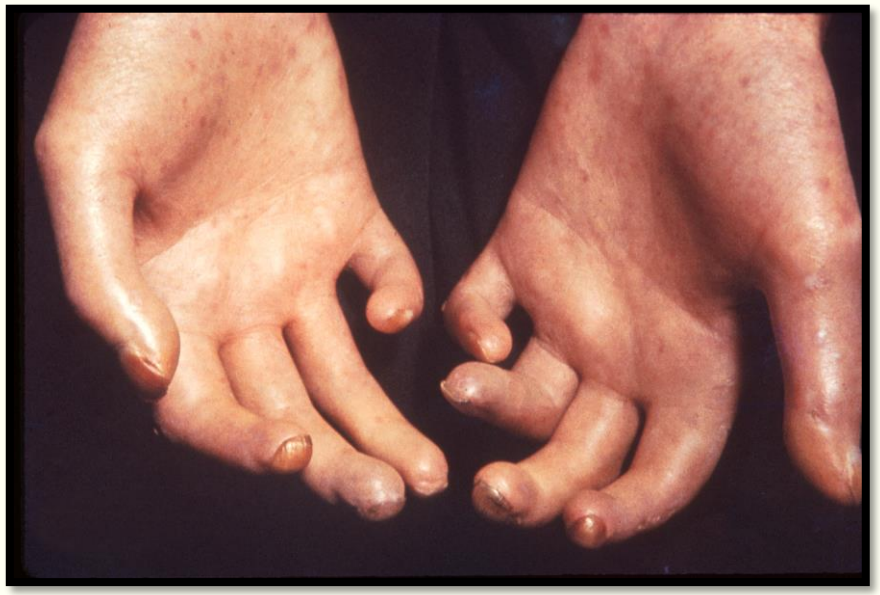
- Treatment is usually symptomatic
  - Artificial Tears; Restasis; punctal plugs
  - Biotene products; artificial saliva
  - Pilocarpine or Evoxac for dry mouth
- If they have extraglandular disease, may consider hydroxychloroquine for arthralgias

Systemic Sclerosis (Scleroderma)

- Disorder of the connective tissue affecting the skin, internal organs, and vasculature.



Sclerodactyly



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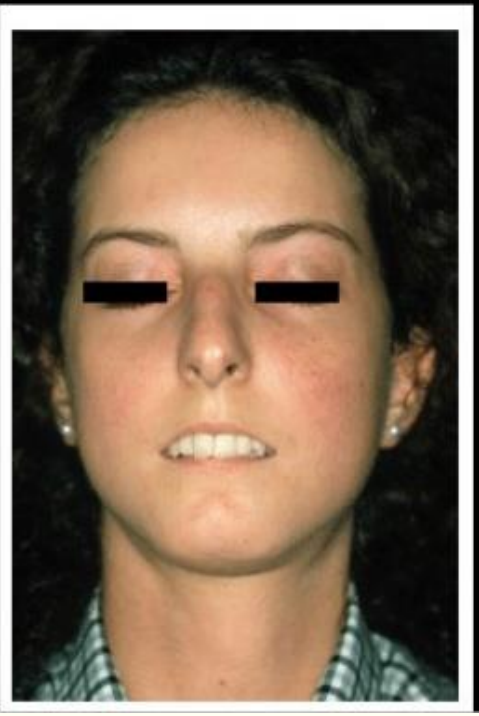
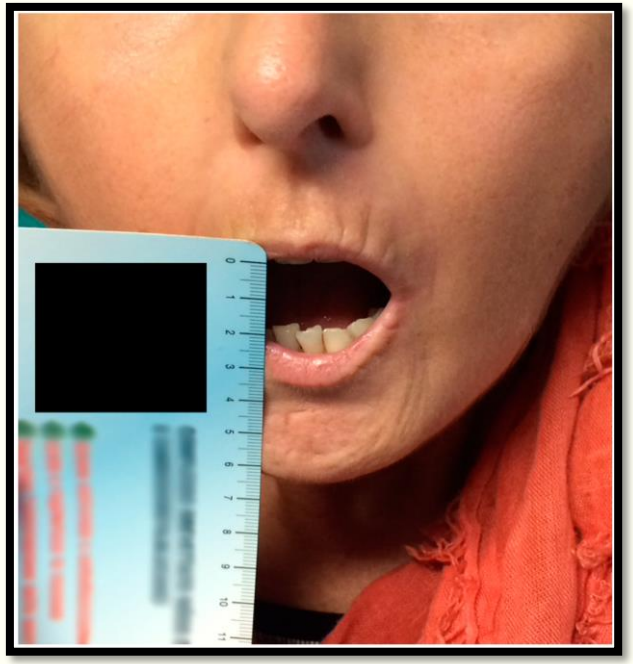
SSc – Findings

Facial changes

- Pinched nose ("mauskopf")
- Pursed lips
- Cannot evert eyelids
- Lip thinning and retraction
- Immobile facies





Reduced Oral Aperture

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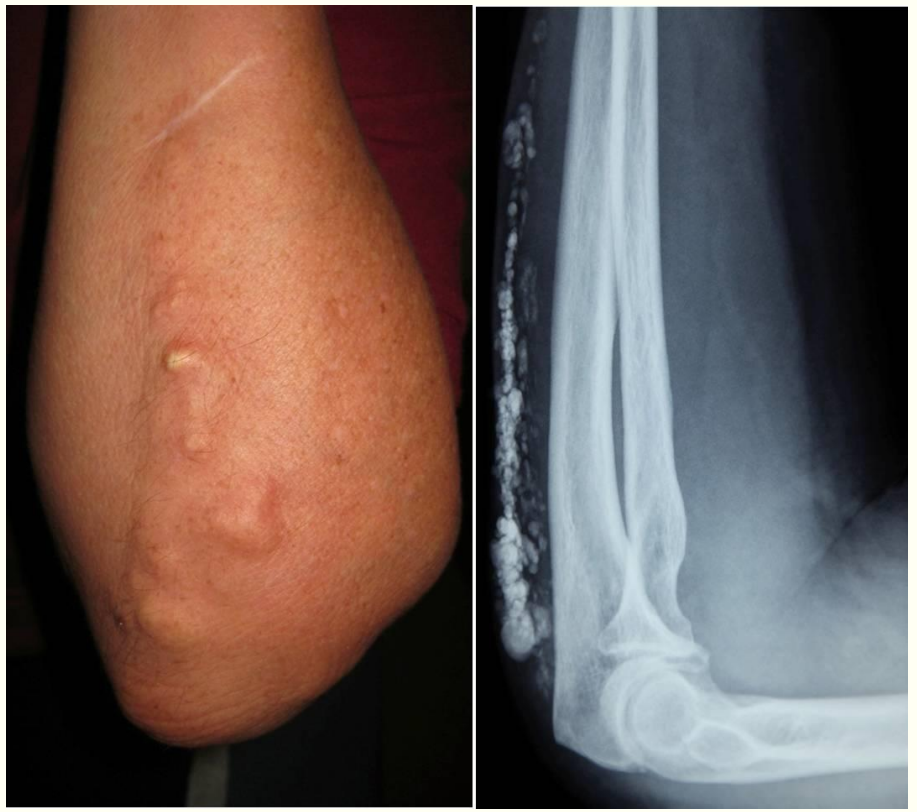
SSc - Findings

- Raynaud's; nail fold capillary changes
- Autoantibodies – Scl-70, ANA nucleolar pattern
- Skin changes within 1 year of Raynaud's
- Tendon friction rubs
- Organ disease – lung, renal, cardiac, GI

Limited Cutaneous Sclerosis (CREST Syndrome)

- Calcinosis
- Raynaud's
- Esophageal dysmotility
- Sclerodactyly
- Telangectasias



Cutaneous Calcinosis

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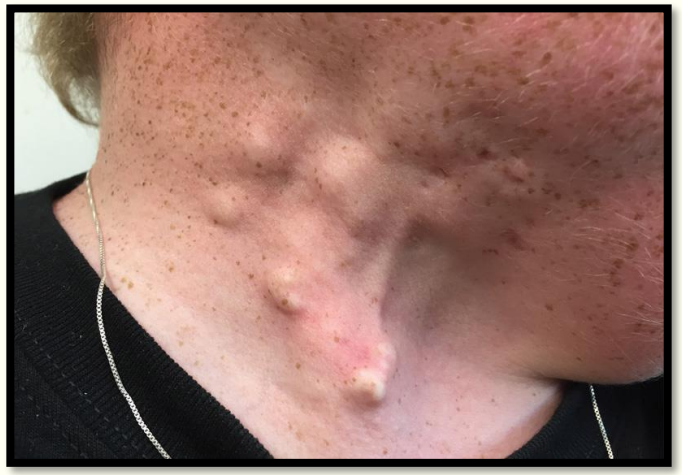
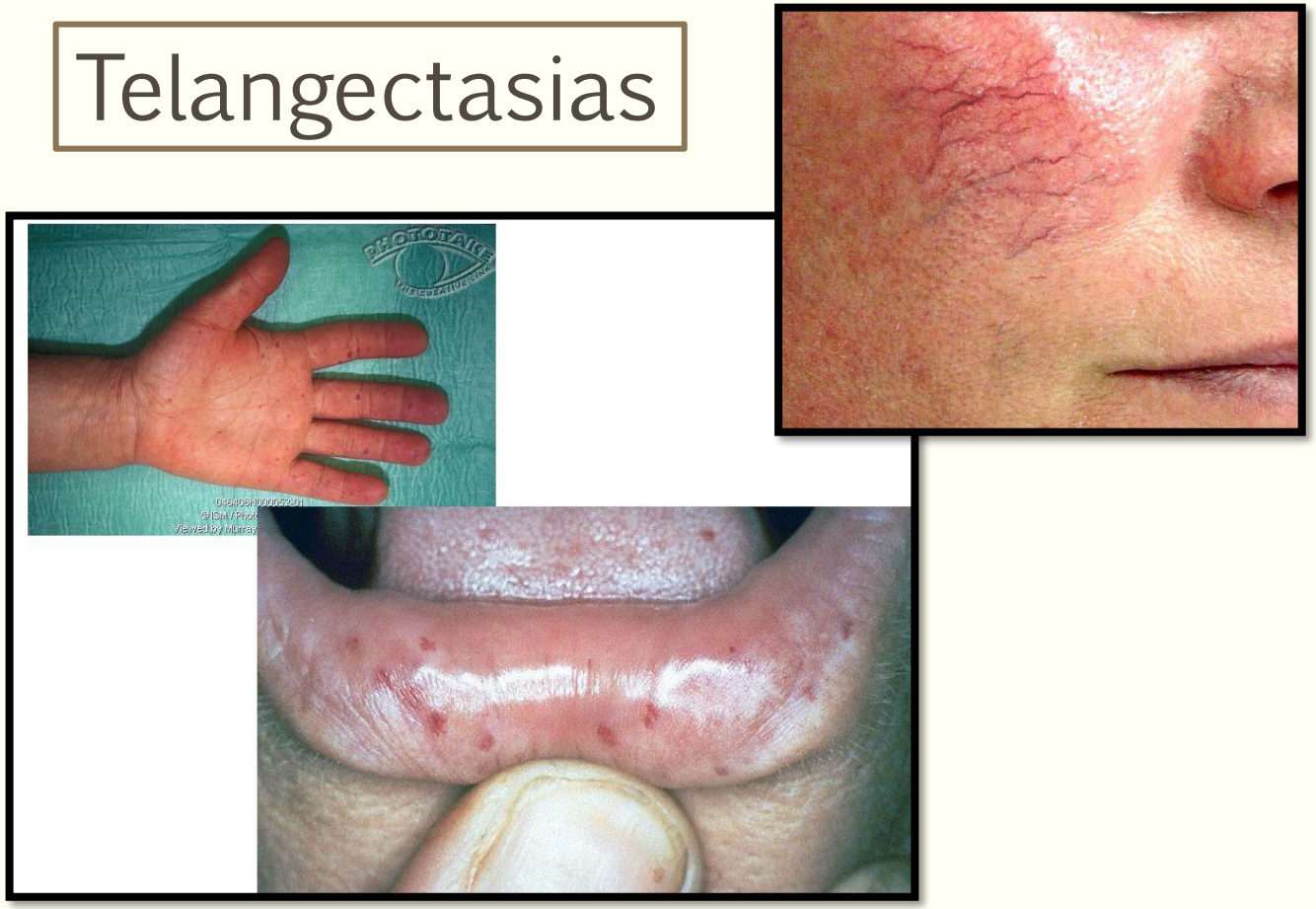
SSc/CREST - Findings



Cutaneous Calcinosis

Telangectasias



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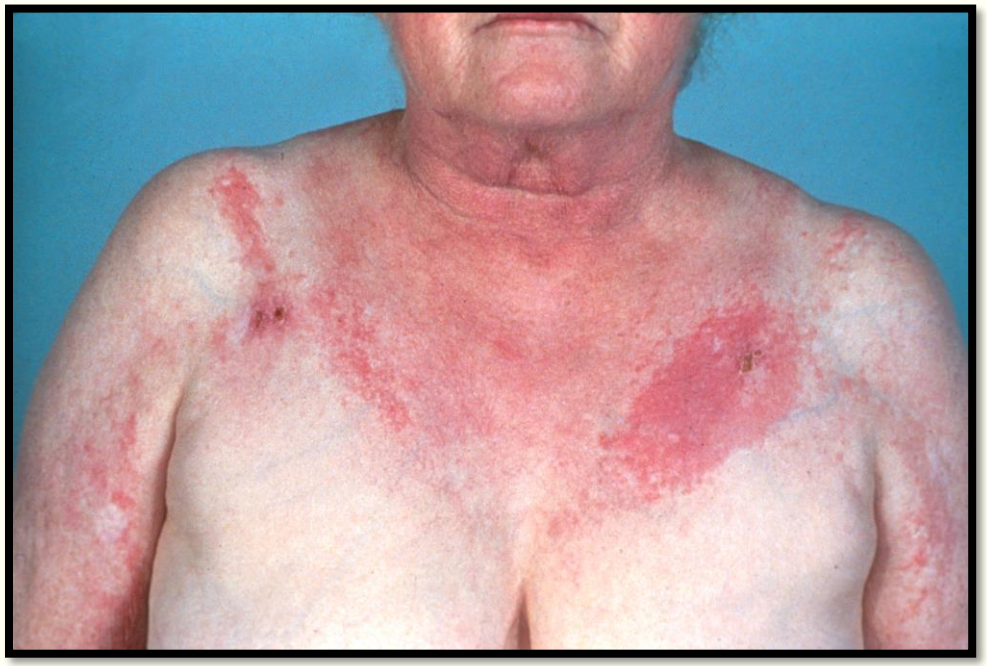
SSc - Management

- No treatment currently available to slow or stop disease.
- Management is directed at symptoms such as gastric reflux, lung disease, etc.

Polymyositis/Dermatomyositis

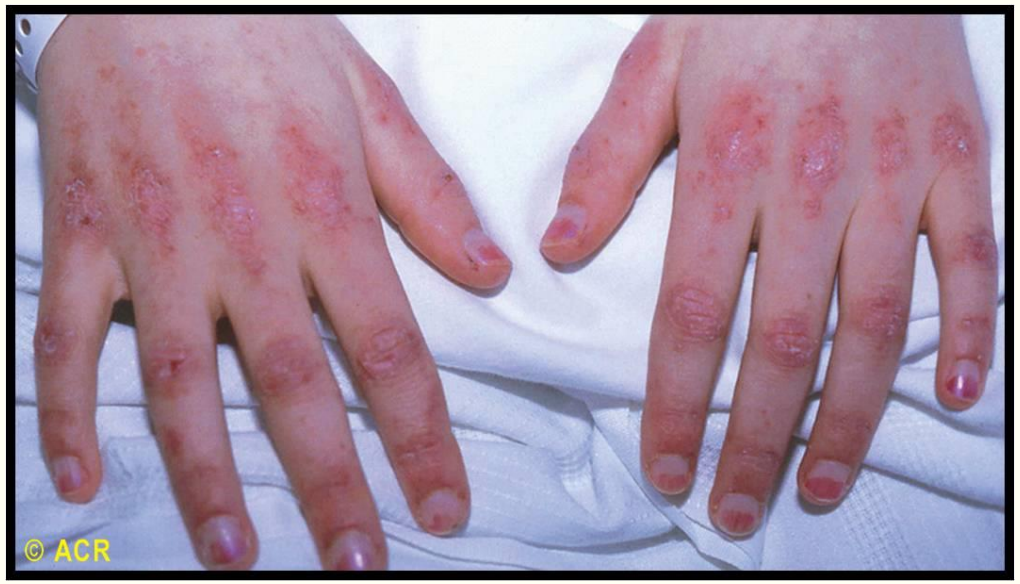
- Idiopathic inflammatory myopathies
- Proximal muscle weakness
- Incidence highest 40-65 years of age
- Male to female ratio 2:1
- African-American to Caucasian 3-4:1
- Increased incidence of malignancies

DM - Presentation



"Shawl sign" of Dermatomyositis

Gottron's Sign



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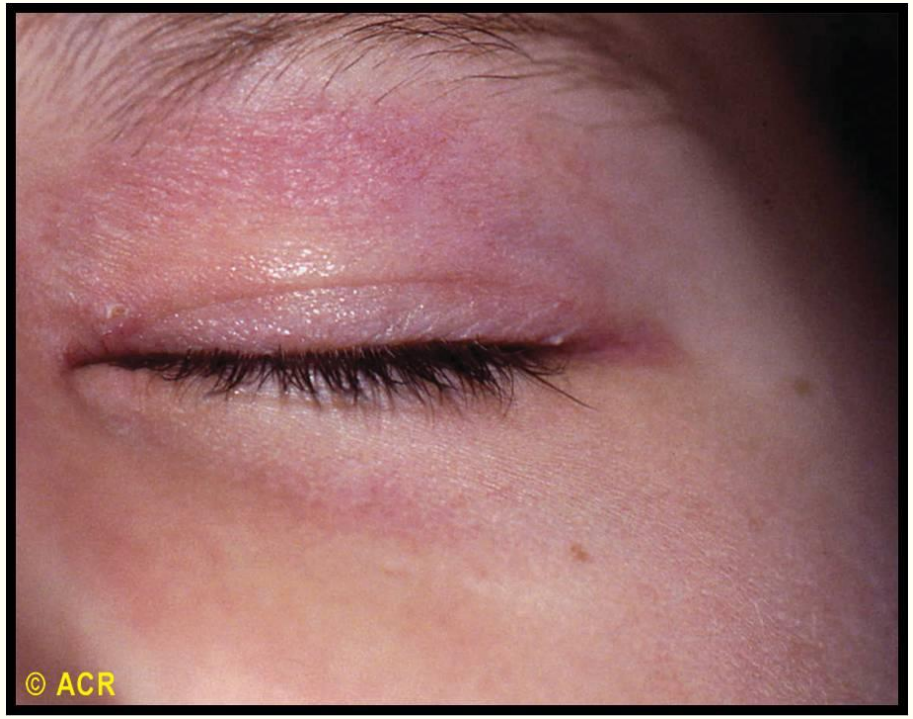
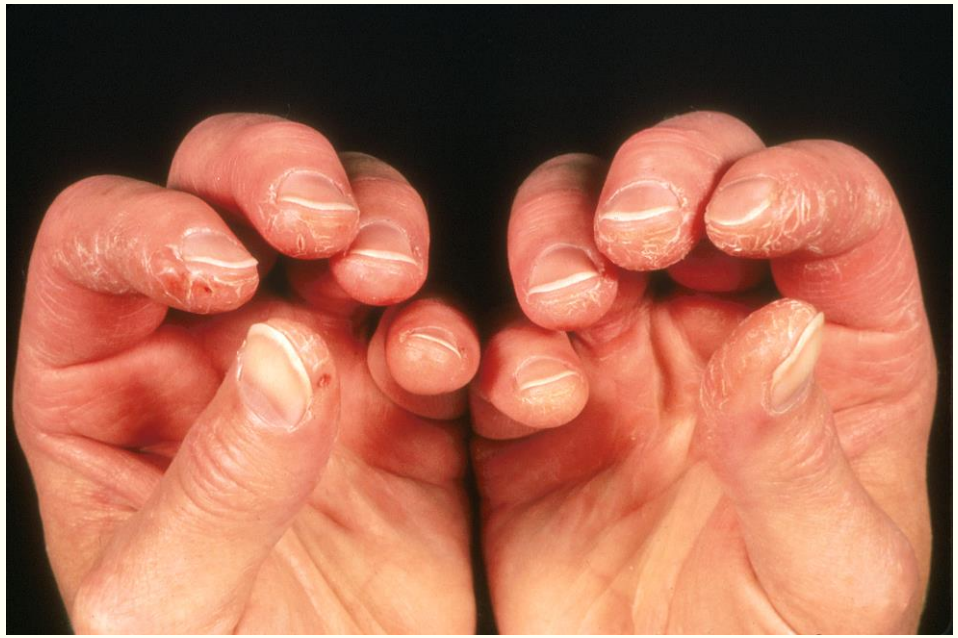
DM - Presentation

Heliotrope Rash





"Mechanic's Hands"

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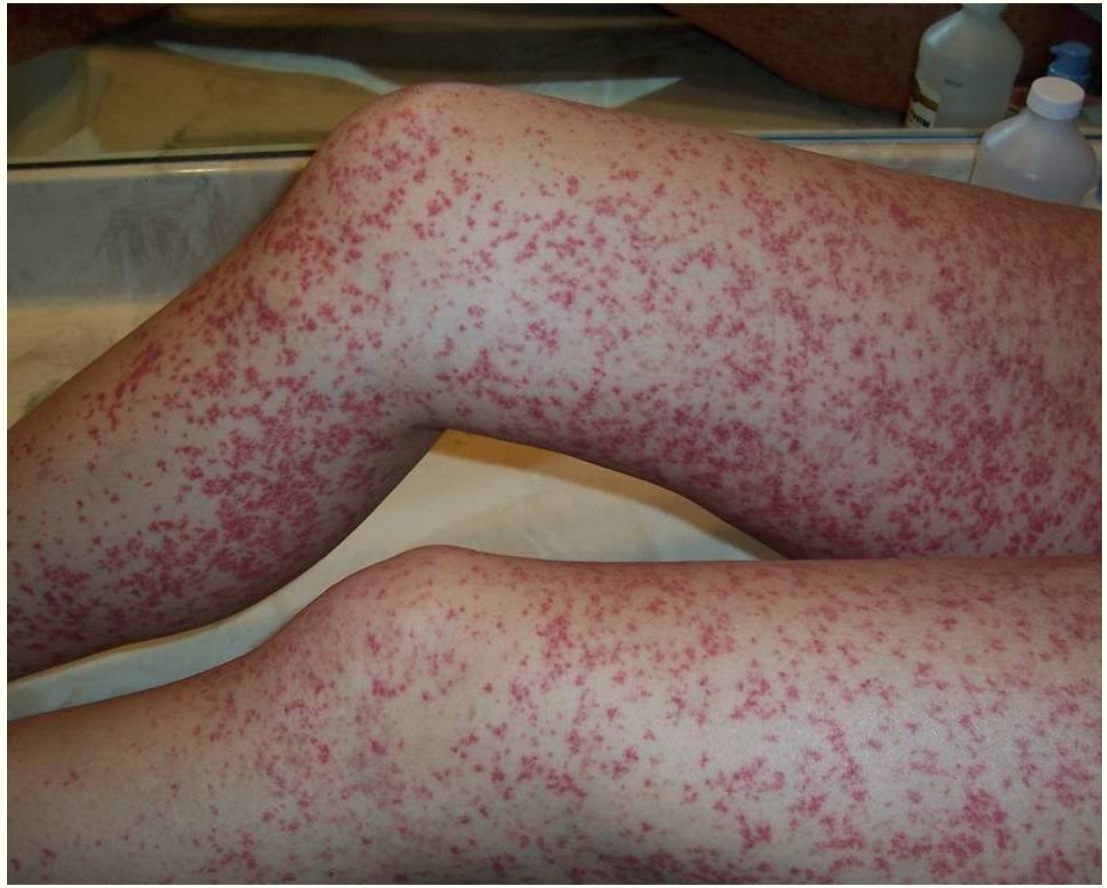
PM/DM - Evaluation

- Muscle enzyme levels – CK, aldolase
- Muscle biopsy
  - DM = perivascular inflammatory infiltrate (B lymphocytes, CD4 T lymphocytes) with capillariits
  - PM = Intramuscular inflammatory infiltrate (CD8+ T lymphocytes) with muscle fiber degeneration and replacement with fat

PM/DM - Management

- Prednisone 1mg/kg/day until decline in CK
- Methotrexate and/or Azathioprine may be considered
- Other, more potent therapies have been tried in resistant cases (i.e. rituximab, Cytoxan)

VASCULITIS



Vasculitis - Overview

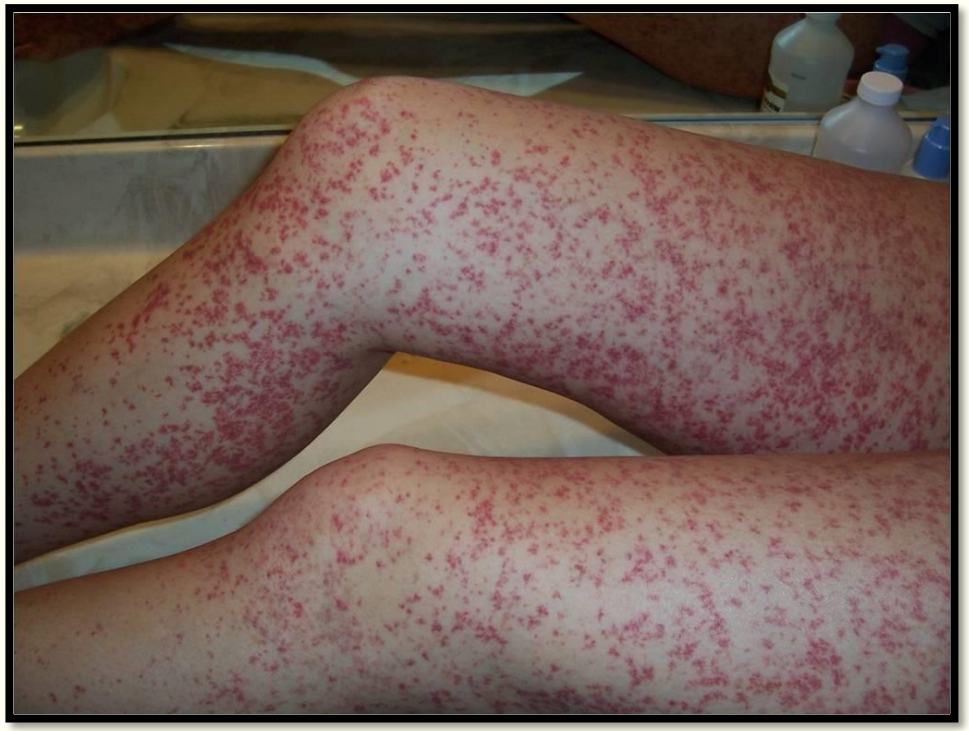
- Vascular inflammation
  - Vessel wall destruction
  - Stenosis (tissue ischemia and necrosis)
- Affects small, medium and large blood vessels
- Not common, but very serious!

Vasculitis – Classification Criteria

Dominant Vessel	Primary Disorders	Secondary Disorders
Large Arteries	Giant Cell Arteritis Takayasu's Isolated angiitis	Aortitis in RA; Infection
Medium Arteries	Polyarteritis nodosa Kawasaki Disease	Infection
Medium Arteries/Small Vessels	Wegener's granulomatosis Churg-Strauss syndrome Microscopic polyangiitis	Autoimmune Disease; Malignancy; Drugs; Infection
Small Vessels (leukocytoclastic)	Henoch-Schonlein purpura Cryoglobulinemia Cutaneous leukocytoclastic angiitis	Drugs; Malignancy; Infection

Vasculitis

Leukocytoclastic Vasculitic Rash



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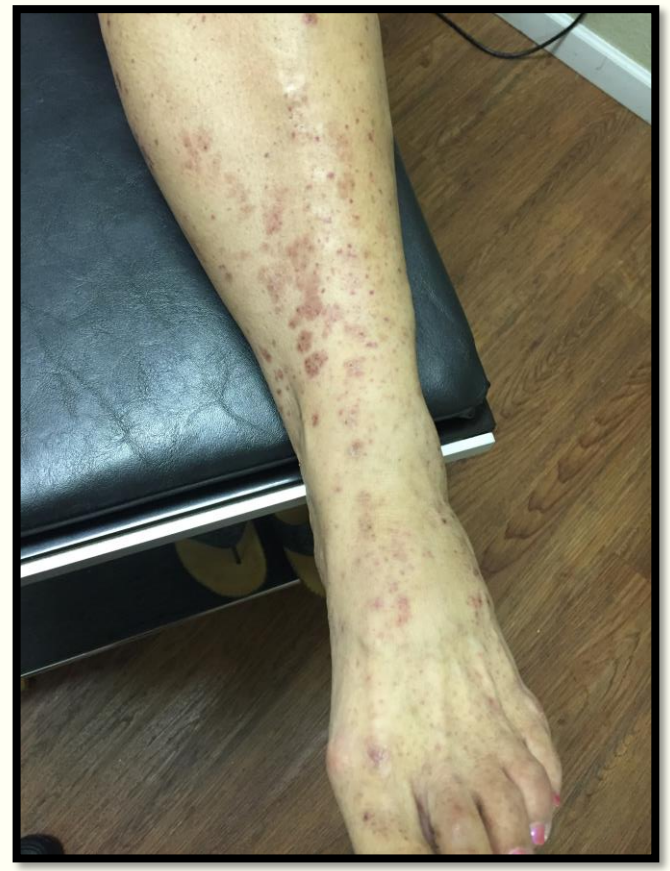

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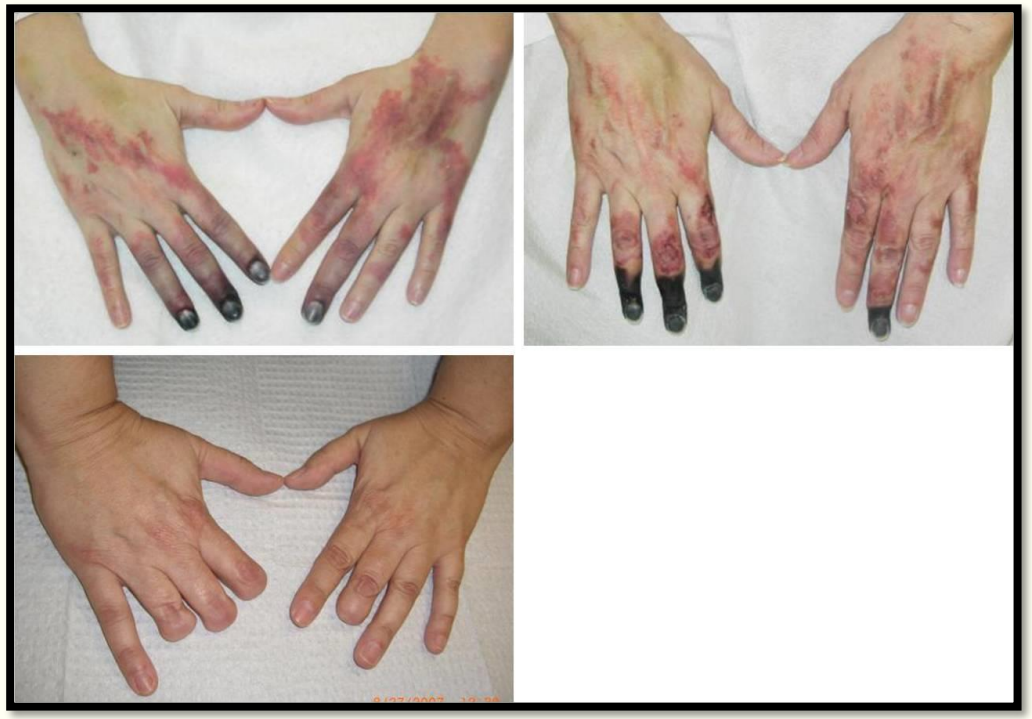
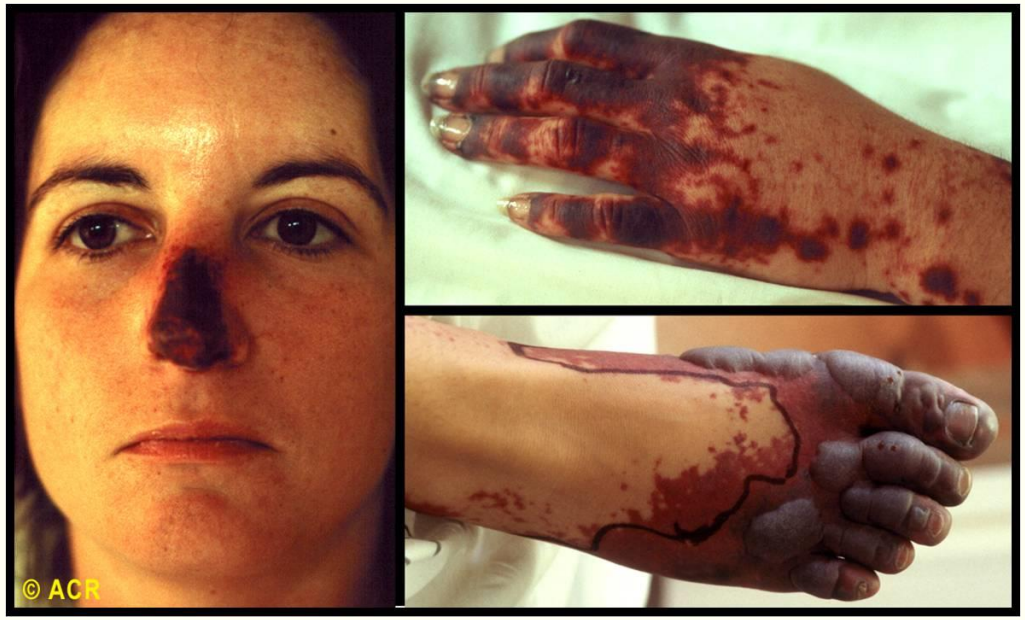
Vasculitis

Cryoglobulinemia





Cold Agglutinin Disease

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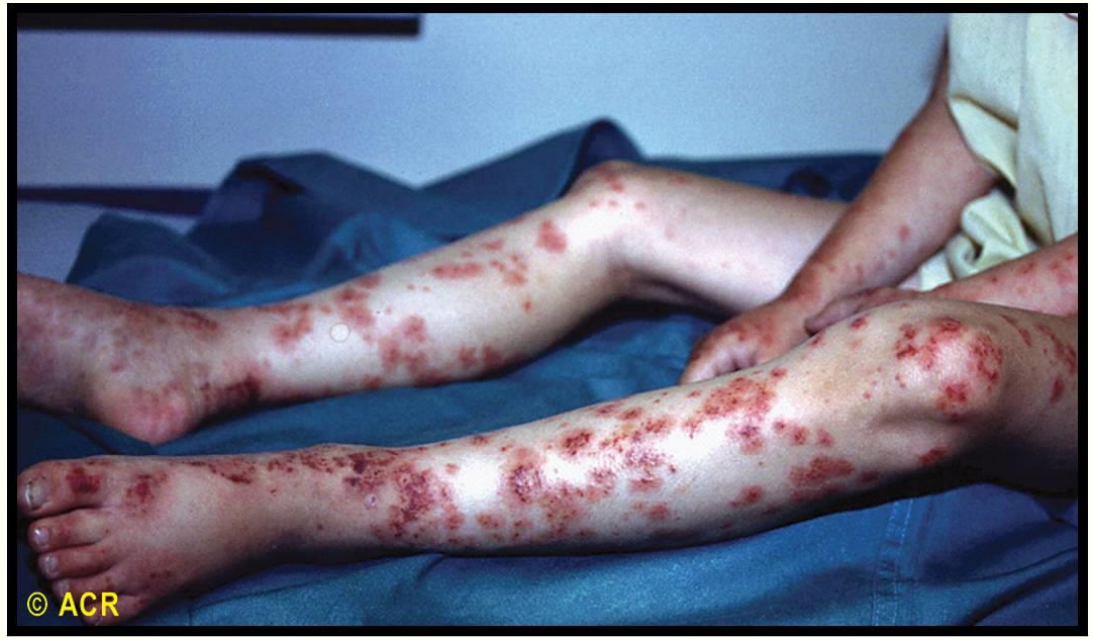
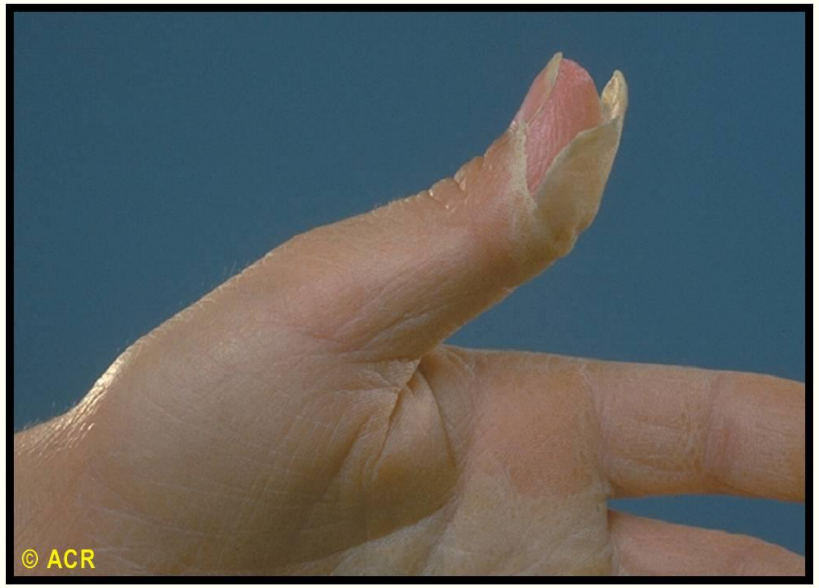
Vasculitis

Henoch-Schonlein Purpura





Kawasaki Disease (desquamation)

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Vasculitis – Laboratory Findings

- Antineutrophil cytoplasmic antibody (ANCA)
  - c-ANCA (Wegener's granulomatosus)
  - P-ANCA (Churg-Strauss; microscopic polyangiitis)
  - Elevated sedimentation rate

Vasculitis - Management

- Prednisone 1mg/kg/day
- Methotrexate 20-25mg weekly
- TNF alpha inhibitors
- Cyclophosphamide 2mg/kg/day

LABORATORY EVALUATIONS

Acute Phase Reactants

- Acute Phase Reactants (APR) are a group of proteins that normally produced in the liver driven by pro-inflammatory cytokines (IL-1, IL-6 and TNF-alpha)
  - Erythrocyte sedimentation rate (ESR)
  - C-reactive protein (CRP)

(Cush, Kavanaugh, & Stein, 2015)

Acute Phase Reactants

ESR

- Ranges from 0 to 13 mm/hr in young men
- Ranges from 13 to 20 mm/hr in young women
- ESR increases with age
- ESR rises and falls slowly and is preferred to monitor chronic conditions

CRP

- Normally <0.8 mg/dL
- Less affected by age or gender
- Increases rapidly
- Half life of 19 hours

(Cush, Kavanaugh, & Stein, 2015)

Acute Phase Reactants

- Not all patients with inflammatory conditions will have an increased ESR or CRP
- Extreme elevations are seen in vasculitis, polymyalgia rheumatica, infections, Still's disease, and neoplasias

(Cush, Kavanaugh, & Stein, 2015)

Rheumatoid Factor (RF)

- Antibodies that react against the Fc portion of IgG
- 80% of RA patients are RF positive
- Other conditions can cause a positive result
  - (i.e. hepatitis, syphilis, lymphoma, endocarditis)
- RF titers don't correlate with disease activity
- RF positivity is seen in 5% of healthy, young individuals and as many as 15% of elderly individuals

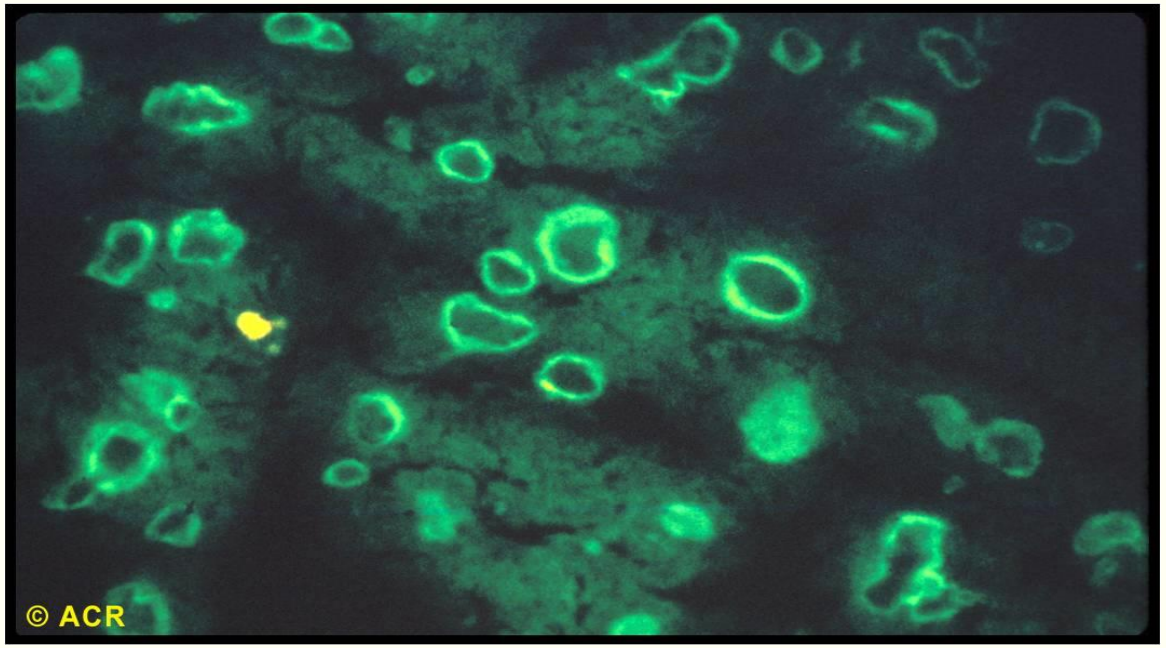
Anti-cyclic Citrullinated Protein Antibodies (ACPA or Anti-CCP)

- Bind to proteins containing the amino acid citrulline
- Normal or negative value <20 U
- Higher specificity for RA than rheumatoid factor
  - (88-95%)
- CCP titers are not expected to significantly change with treatment
- There is little value in serial assessment in individuals with a positive titer

(Cush, Kavanaugh, & Stein, 2015)

Anti-Nuclear Antibody (ANA)

- Antibodies that react with components of the cell nucleus
- Sensitive, but not specific for SLE



(Cush, Kavanaugh, & Stein, 2015; Photo Copyright 2019 ACR)

ANA

- Results reported as titer and pattern
- Positive titer >1:160
- Equivocal or non-specific titers <1:80
- High prevalence of low-titer ANA in healthy individuals
- Other conditions can cause ANA positivity
  - (i.e. thyroid disease, chronic renal, liver or lung disease)

(Cush, Kavanaugh, & Stein, 2015)

ANA - Patterns

- Homogenous – non-specific
- Speckled – SLE, or non-specific
- Centromere – CREST syndrome
- Nucleolar – Systemic sclerosis, SLE, myositis
- SSA/Ro & SSB/La – Sjogren's syndrome

(Cush, Kavanaugh, & Stein, 2015)

Extractable Nuclear Antigens (ENA)

Antigen	Frequency in SLE	Frequency in Other Diseases	Clinical Associations
Sm	30-40%	Very uncommon	Interstitial lung disease
snRNP	30-40%	100% in patients with MCTD	Symptoms are an overlap of SLE, DM/PM, SSc
Ro (SSA)	25-30%	70% Sjogren's	Subacute cutaneous lupus, neonatal lupus, elderly onset
La (SSB)	10-15%	60% Sjogren's	Also seen in RA, SLE, cutaneous LE, SSc
Histone	50-70%	>95% drug-induced lupus	Also common in idiopathic SLE
Scl-70	<5%	40%-70% Systemic sclerosis	Specific for scleroderma
Jo-1	<5%	20% PM/DM	Myositis, interstitial lung disease, arthritis

(Cush, Kavanaugh, & Stein, 2015)

Double-stranded DNA Antibody

- dsDNA only found in SLE patients
- 30-50% SLE patients are negative
- Higher incidence of renal involvement with positive result
- Titer can vary with disease activity

Complement System

- Complex sequential cascade in which inactive proteins become active
- Important body defense mechanism against infection
- Activation of complements result in cell lysis

Complement Component C3 & C4

- Can be “used up” in reactions that occur in some antigen-antibody reactions
- C3 normal range: 75-175 mg/dL
- C4 normal range: 14-40 mg/dL
- ***Decreased levels*** associated with active immune complex disease

(Fischbach & Fischbach, 2018)

Summary

- Determine if the arthritis is inflammatory or non-inflammatory
- Treatment is contingent on type of disease
- Many extra-articular manifestations such as skin, eye, and hematologic disorders can occur
- Laboratory findings can be instrumental in determining diagnosis and disease activity

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