Investigations In Medicine

Rheumatology

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Overview

- General principles
- Inflammatory arthritis (IA)
  - Crystal, RA, SpA, infectious
- Connective tissue diseases (CTD)
  - SLE, Sjogren's, Scleroderma, IgG4RD
- Myositis
- Vasculitis

Overview

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General Principles

- Tests in rheumatology
  - Consider each condition
    - Serology
    - Biopsy
    - Imaging

- Divided into
  - ***Diagnosis*** vs. ***disease activity monitoring*** (overlap)
  - ***Prognostic*** indicator

- No test is 100% sensitive (Sn**N**out) and specific (Sp**P**in)
  - Differential diagnoses
  - Each test must be interpreted in context of **clinical** presentation/features

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Inflammatory Arthritis (IA)

1. Crystal arthritis
2. Rheumatoid arthritis (RA)
3. Spondyloarthritis/spondyloarthropathy (SpA)
4. Infectious

Inflammatory Arthritis (IA)

1. **Crystal arthritis**
2. Rheumatoid arthritis (RA)
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4. Infectious

1. Crystal Arthritis – Diagnosis

i. **Fluid aspiration** (**gold standard**)
   - Sites: joints, bursa, tophus
   - Intracellular monosodium urate crystals
   - Sensitivity: 85%
   - Specificity: 100%

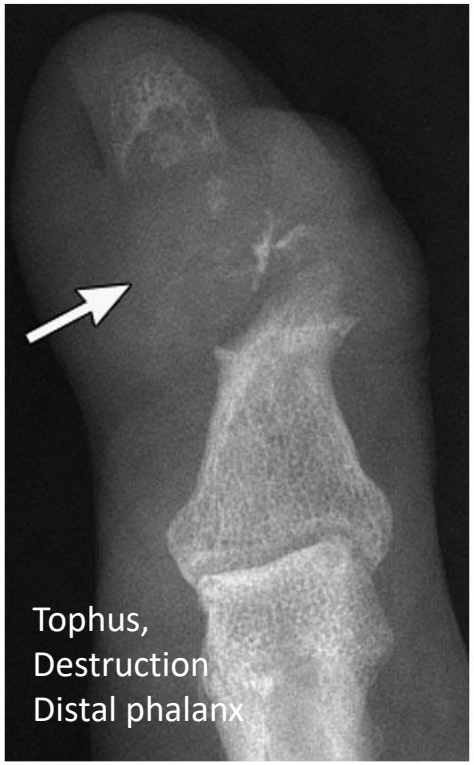
ii. X-ray

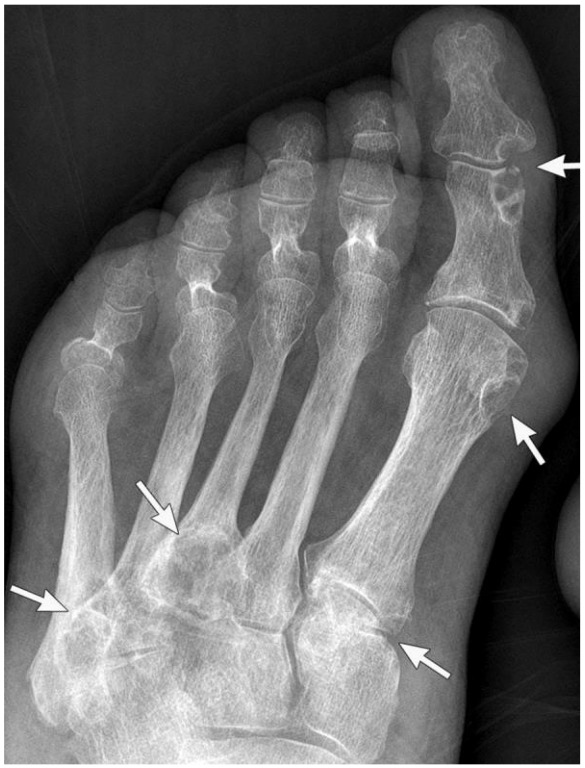
iii. Ultrasound

iv. Dual-energy computerised tomography (DECT)

v. Magnetic resonance imaging (MRI)

X-Ray Findings in Gout



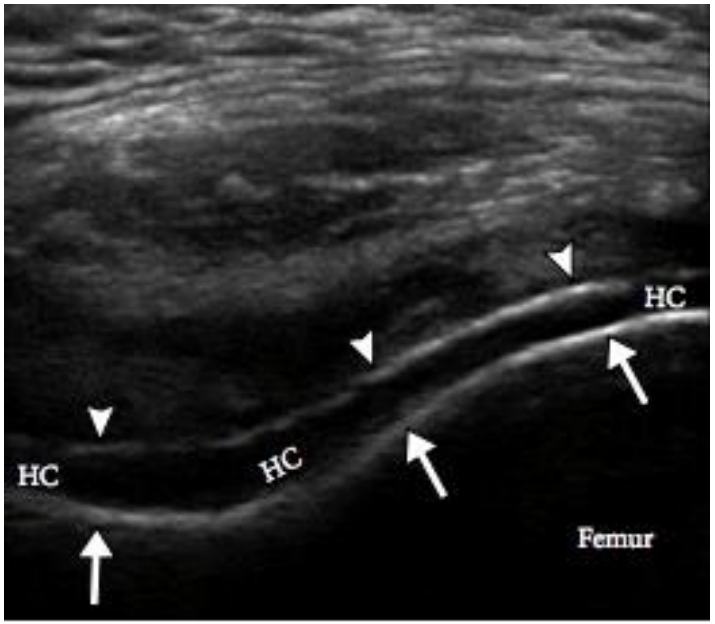


Multiple punched-out sclerotic erosions (arrows), with soft-tissue swelling.

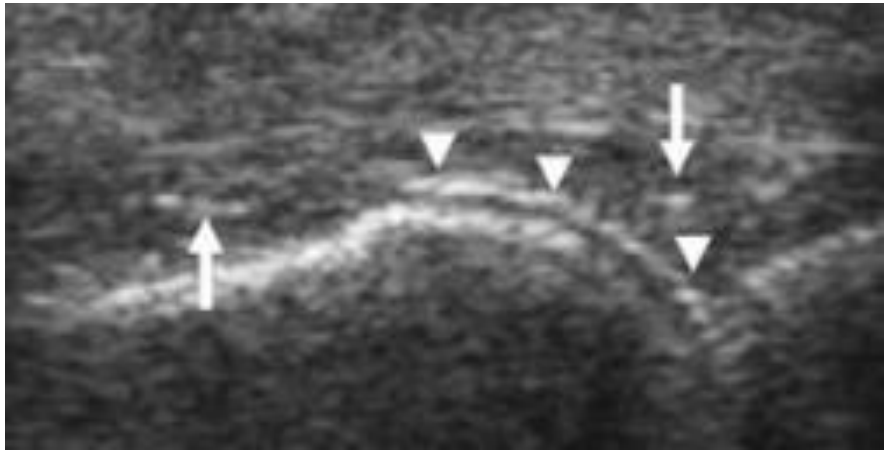
- Limited role in (early) diagnosis
- Δs occur late in disease

Radiology. 2008;248(3):737-747

Ultrasound Findings in Gout



A



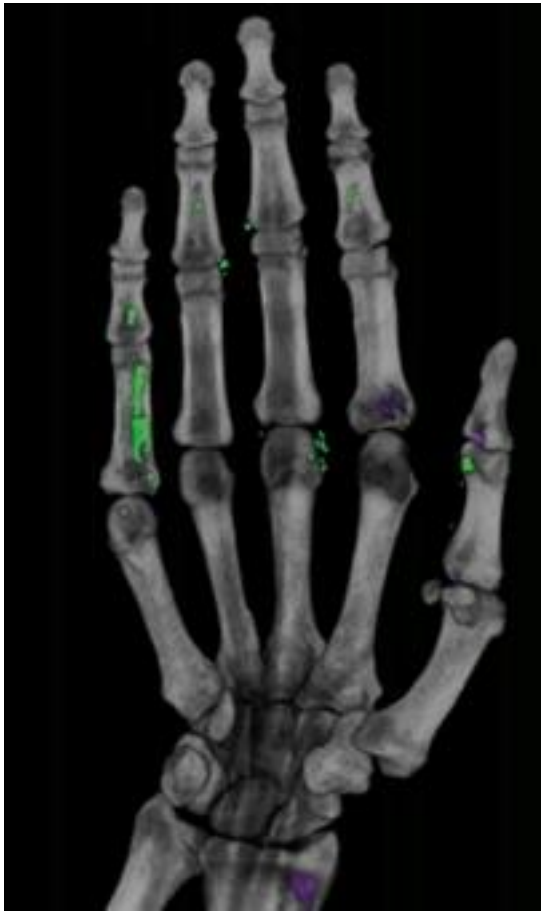
B

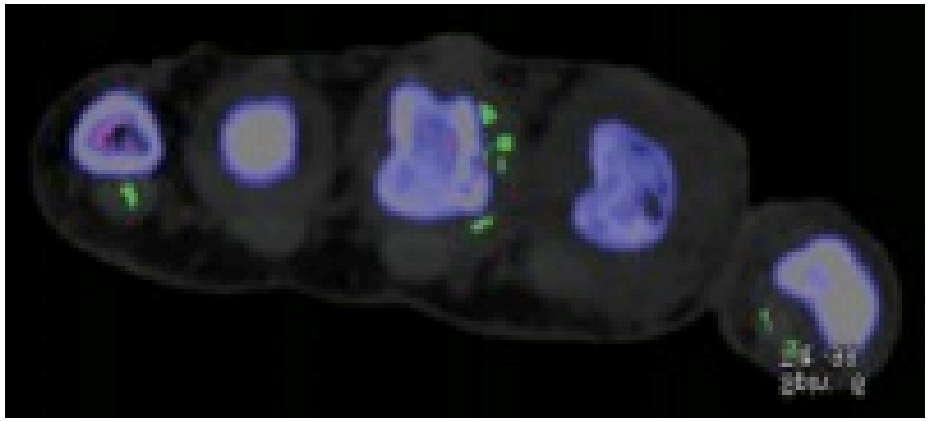
A. "**Double contour sign**" (DCS) – echogenic line of urate deposition over hyaline cartilage (HC)
   - Sensitivity: 44%
   - Specificity: 99%

B. "**Hyperechoic cloudy area**" (HCA) – tophaceous deposits in thickened synovial membrane or tendons
   - Sensitivity: 79%
   - Specificity: 95%

Girish G et al.. Hindawi Publishing Corporation Arthritis. Vol 2013, Article ID 673401, 10 pages. http://dx.doi.org/10.1155/2013/673401

Dual Energy Computerised Tomography (DECT) in Gout

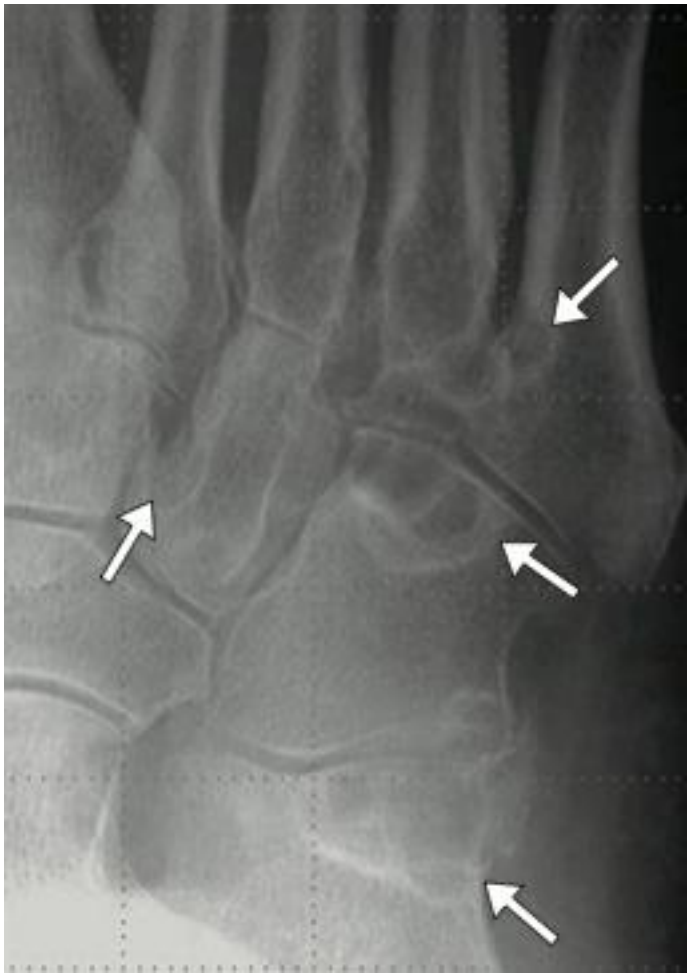




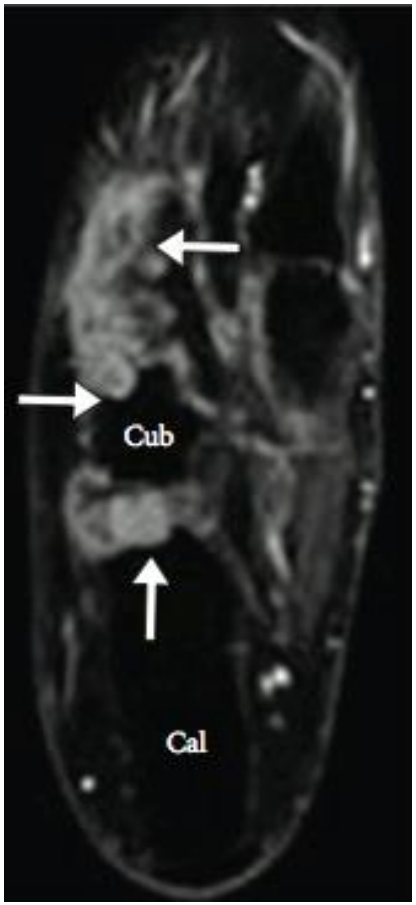
- Helps in:
  - Identifying urate deposits in articular & periarticular locations
  - Distinguishing between crystal deposition diseases
  - Quantifying the volume of urate crystals

Girish G et al.. Hindawi Publishing Corporation Arthritis. Vol 2013, Article ID 673401, 10 pages. http://dx.doi.org/10.1155/2013/673401

MRI in Gout



Axial x-ray: intraosseous midfoot gout – multifocal gout crystal deposits in the tarsal bones (arrows)



STIR MRI: corresponding intermediate-to-high signal (arrows) on STIR images.
Cal: calcaneum. Cub: Cuboid

Helpful in:

i. localization of gout deposits
ii. imaging deeper tissues not amenable to clinical examination

Girish G et al.. Hindawi Publishing Corporation Arthritis. Vol 2013, Article ID 673401, 10 pages. http://dx.doi.org/10.1155/2013/673401

Crystal Arthritis – Monitoring

i. Uric acid level
   - Goal of treatment: <0.36 mmol/L

ii. Ultrasound
   - Diminishing tophus size
   - Disappearance of DCS
   - Resolution of synovial hypertrophy, joint effusion
   - **Unable** to visualise bone marrow oedema (BMO)

iii. DECT: follow-up resolution of tophus

iv. MRI: best for resolution of synovial proliferation & BMO

Inflammatory Arthritis (IA)

1. Crystal arthritis
2. **Rheumatoid arthritis (RA)**
3. Spondyloarthritis/spondyloarthropathy (SpA)
4. Infectious

2. Rheumatoid Arthritis – Diagnosis

i. **Serology**
   - Rheumatoid factor (RhF)
   - Anti-citrullinated protein antibodies (ACPA) detected via anti-cyclic citrullinated peptide (CCP) assay

ii. Acute phase reactants
   - Erythrocyte sedimentation rate (ESR)
   - C-reactive protein (CRP)

iii. X-ray

iv. Ultrasound

v. MRI

2. Rheumatoid Arthritis – Diagnosis

	IgM Rheumatoid Factor	Anti-Citrullinated Protein Antibodies
Sensitivity, % (95% CI)	**70** (66–73)	67 (64–70)
Specificity, % (95% CI)	79 (74–83)	**95** (94–96)

2. Rheumatoid Arthritis – Diagnosis

	IgM Rheumatoid Factor	Anti-Citrullinated Protein Antibodies
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Specificity, % (95% CI)	79 (74–83)	**95** (94–96)
Positive Likelihood Ratio (95% CI)	3.3 (2.7–3.9)	**14.4** (11.6–18.0)
Negative Likelihood Ratio (95% CI)	0.39 (0.35–0.42)	0.35 (0.32–0.38)

Causes of RhF +ve:

- **Autoimmune**: Sjogren's syndrome, MCTD, PM/DM, Scleroderma, AAV, Polyarteritis nodosa, Primary Biliary Cirrhosis, sarcoidosis
- **Chronic infections**: SBE, mTB, leprosy, syphilis, Hep C & B (cryoglobulins), viral & parasitic infections
- **Other**: idiopathic pulmonary fibrosis, silicosis, asbestosis, malignancy, age≥65

2010 ACR/EULAR Classification Criteria for RA (Cutoff for RA: ≥6/10)

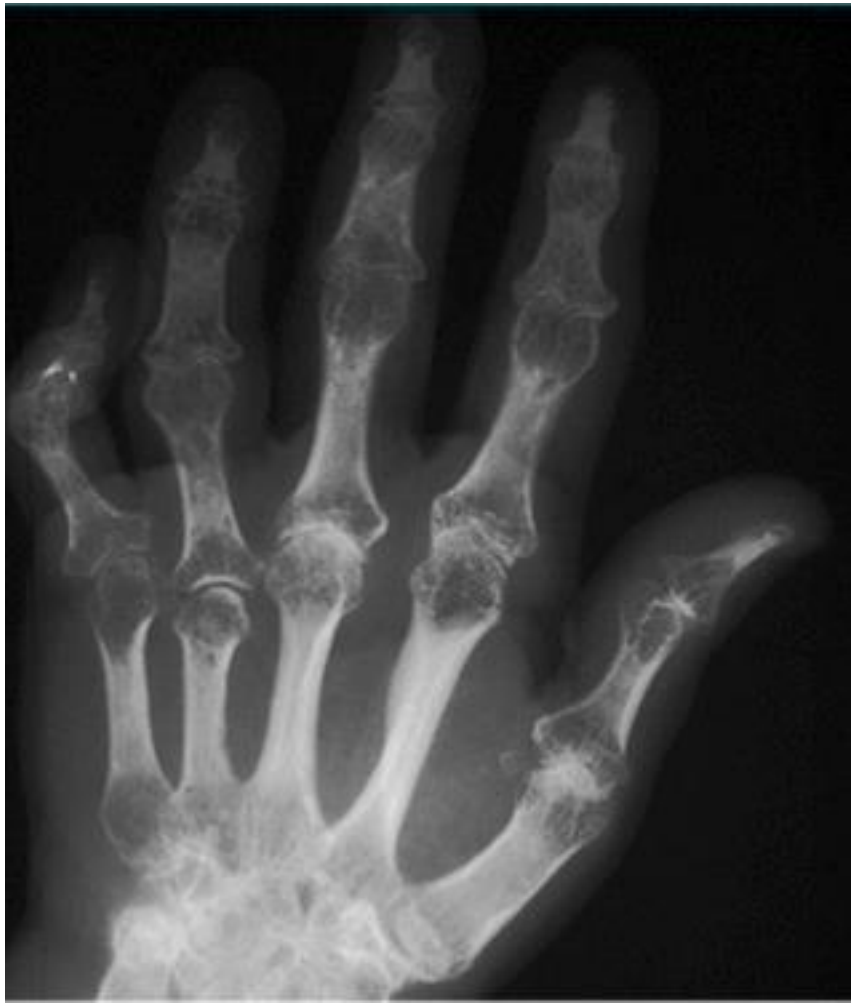
	Score
Target population (Who should be tested?): Patients who	
1) have at least 1 joint with definite clinical synovitis (swelling)*	
2) with the synovitis not better explained by another disease†	
Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of ≥6/10 is needed for classification of a patient as having definite RA)‡	
A. Joint involvement§	
1 large joint¶	0
2–10 large joints	1
1–3 small joints (with or without involvement of large joints)#	2
4–10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)**	5
B. Serology (at least 1 test result is needed for classification)††	
Negative RF *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡	
Normal CRP *and* normal ESR	0
Abnormal CRP *or* abnormal ESR	1
D. Duration of symptoms§§	
<6 weeks	0
≥6 weeks	1

Arthritis Rheum 2010;62(9):2569-2581

X-Ray Findings in RA

- Screen bilateral hands & feet
  - soft tissue swelling
  - periarticular osteopaenia
  - joint
    - subluxation
    - malalignment
    - ankylosis
  - juxta-articular cortical **erosions***
  - **joint space narrowing** (JSN)*
    - surrogate measure of cartilage loss

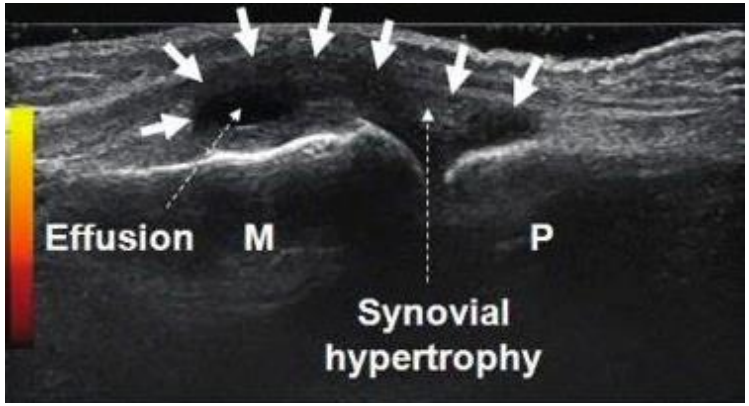
*the latter two signs are more specific for RA

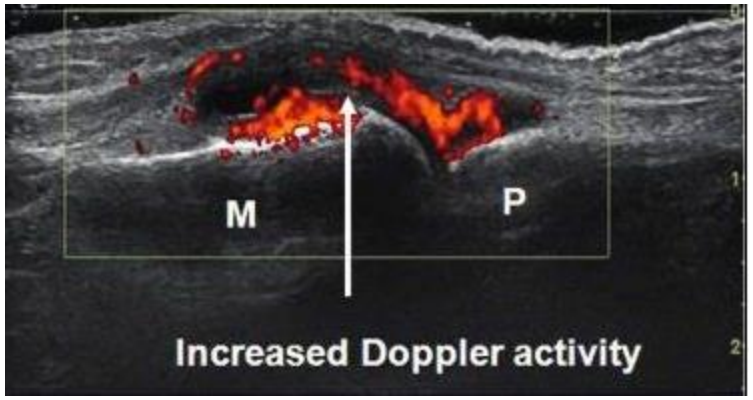


Radiology. 2008;248(3):737-747.

Ultrasound Findings in RA

- Modes – grey-scale (GS) & **power Doppler** (PD)
  - **synovitis**
    - synovial hypertrophy & joint effusion on GS
    - increased vascularity on PD
  - tenosynovitis
  - tendon rupture
  - enthesitis
  - bone erosions
  - reduced cartilage thickness





M: metacarpal, P: phalanx

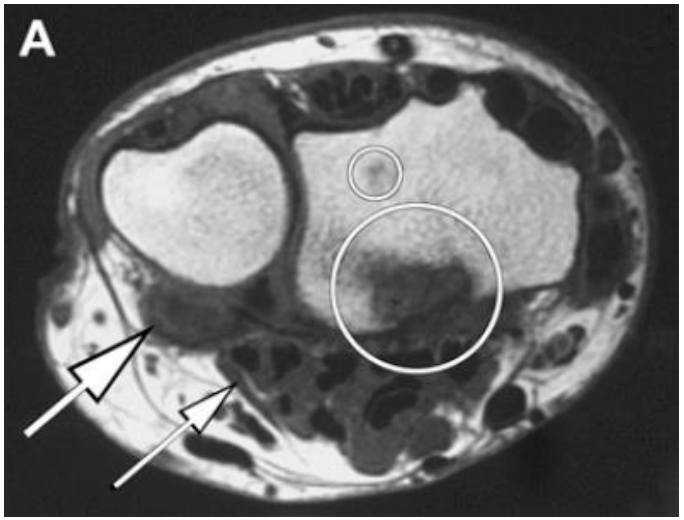
MRI Findings in RA

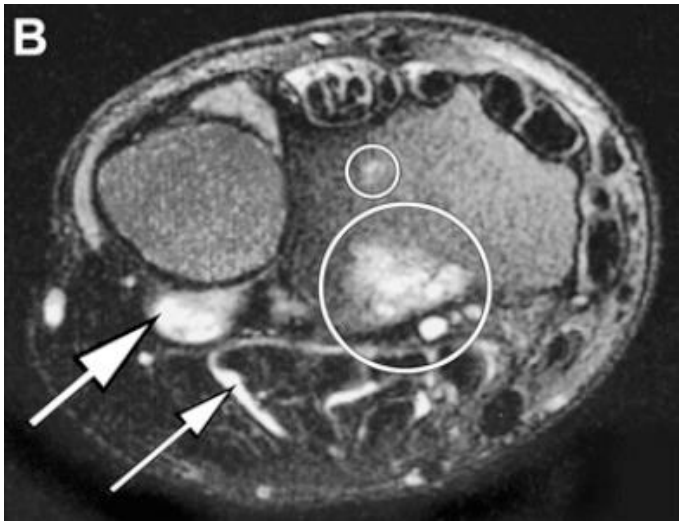
- ***Earlier*** detection of

  i. damage
     - joint dislocation
     - tendon rupture

  ii. inflammation
     - synovitis*
     - effusions
     - tenosynovitis

  iii. BMO





*Gold standard for imaging synovitis

Best Practice & Research Clinical Rheumatology. 2007;21(5):841-856

2. Rheumatoid Arthritis – Monitoring

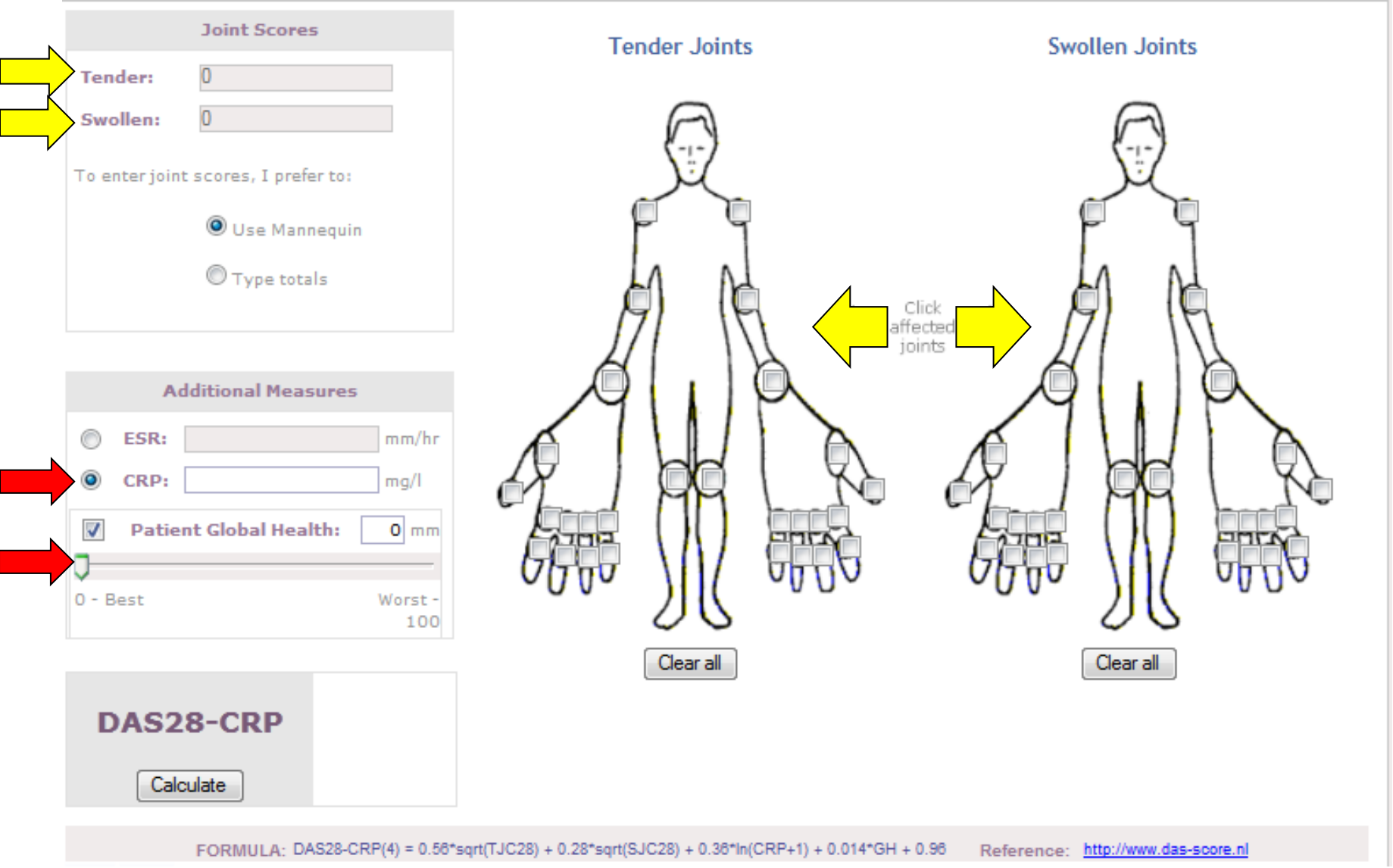
1. **Acute phase reactant (ESR, CRP)**
   - Incorporated into **D**isease **A**ctivity **S**core (DAS)

2. X-ray
   - No progression of erosions, deformity, JSN

3. Ultrasound
   - Resolution of synovitis on PD

4. MRI
   - Resolution of synovitis, BMO

DAS-28-CRP: Monitoring in RA



http://www.4s-dawn.com/DAS28/

Inflammatory Arthritis (IA)

1. Crystal arthritis
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3. **Spondyloarthritis/spondyloarthropathy (SpA)**
4. Infectious

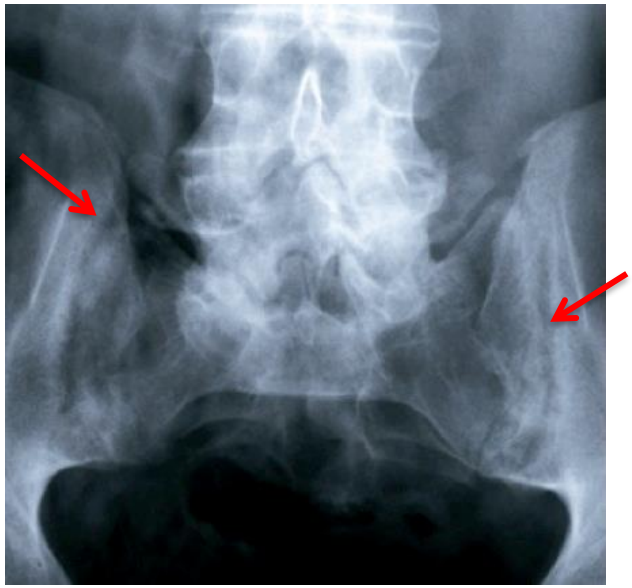
3. Ankylosing Spondylitis – Diagnosis

1. Inflammatory markers (ESR, CRP)
   - **elevated** in **50-70%** with **active** disease
   - correlates better with peripheral > axial disease activity

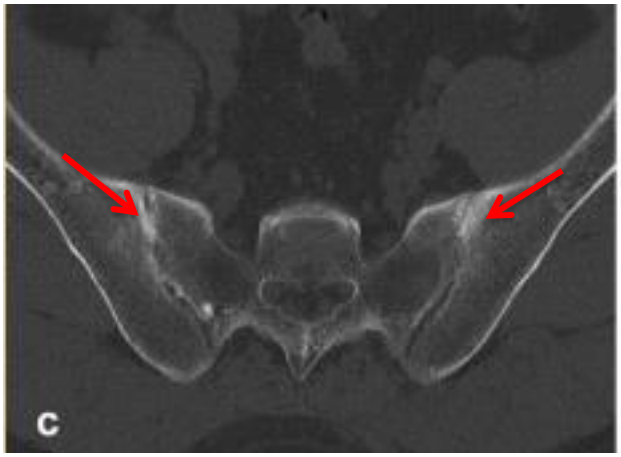
2. HLA–B27 (90–95%)

3. **Imaging**
   - **X-ray – pelvis (AP view)**, lumbar spine
   - MRI (early, inflammation)
   - CT (late, structural)

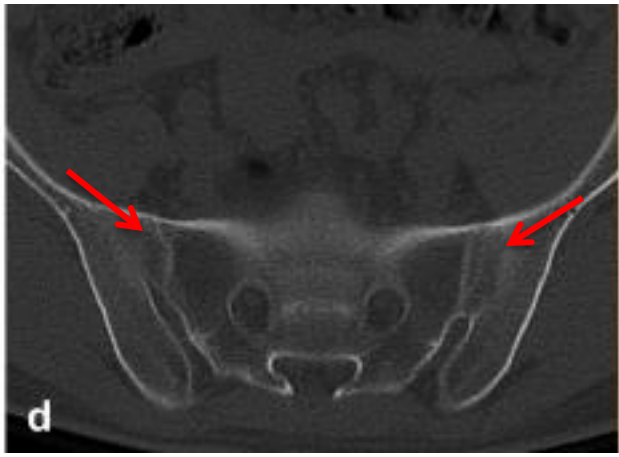
Imaging in Ankylosing Spondylitis



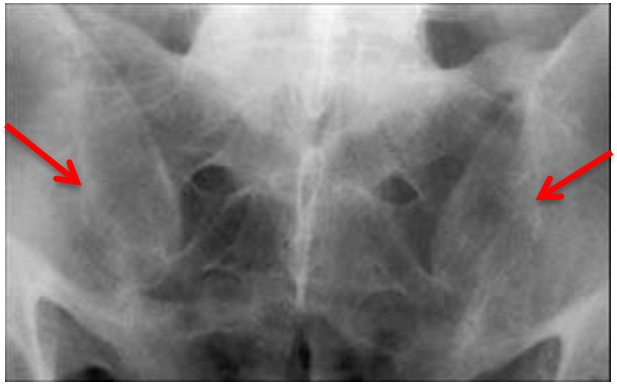
XRAY GRADE 3



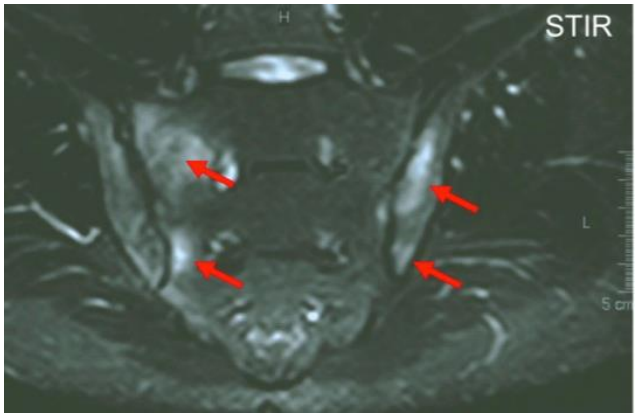
CT GRADE 3



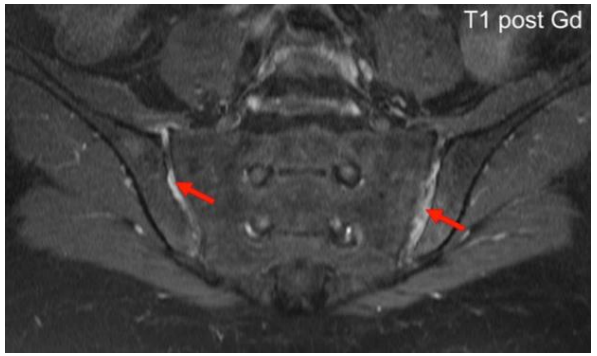
CT GRADE 4



XRAY GRADE 4



MRI Sacroiliitis (Bilateral)



MRI Synovitis

Ann Rheum Dis 2009;68:1520–1527

Diagnosis of Ankylosing Spondylitis

- No formal diagnostic criteria

- **Chronic low back pain (≥3 months)**
  - **Symptom onset <45 years**
  - **X-ray pelvis: sacroiliitis**
    - **≥ grade 2 bilateral or grade 3 unilateral**

- Symptoms but no radiographic sacroiliitis
  - 2013 **A**ssessment of **S**pondylo**A**rthritis International **S**ociety **(ASAS) criteria for axial SpA**

ASAS (2010) Criteria for Axial SpA

- In patients with chronic back pain (**> 3 months**):
  - Inflammatory back pain (IBP)
  - Heel pain (Enthesitis)
  - Dactylitis
  - Uveitis
  - Positive family history for SpA
  - Inflammatory bowel disease
  - Alternating buttock pain
  - Psoriasis
  - Asymmetric arthritis
  - Positive response to nonsteroidal antiinflammatory drugs (NSAIDs)
  - Elevated acute phase reactants (ESR or CRP)

- Criteria are fulfilled if score **≥ 4 out of 11** parameters are present
  - **Non radiographic axial spondyloarthritis**

Ann Rheum Dis 2009;68(Suppl II):ii1–ii44

ASAS (2010) Criteria for IBP

- In patients with chronic back pain (> 3 months):

  i. Age at onset < 40 years
  ii. Insidious onset
  iii. Improvement with exercise
  iv. No improvement with rest
  v. Pain at night (with improvement upon getting up)

- Criteria are fulfilled if score **≥ 4 out of 5** parameters are present

Ann Rheum Dis 2009;68(Suppl II):ii1–ii44

Diagnosing Ankylosing Spondylitis

- If <4 of 11 ASAS criteria
  - 2 to 3 SpA features
    - No radiographic sacroiliitis ➔ test HLA-B27
    - HLA-B27 –ve but clinical suspicion remains high ➔ MRI

- If HLA-B27 +ve
  - no radiographic sacroiliitis
  - ≤1 out of 11 ASAS criteria
    - ➔perform MRI

3. Ankylosing Spondylitis – Monitoring

i. **Acute phase reactants**

ii. X-ray
   - (research)
     - Lateral views of cervical & lumbar spine vertebral bodies

iii. MRI – resolution of sacroiliitis (uncommon)

iv. Clinical Assessment
   - **i.** **B**ath **A**nkylosing **S**pondylitis **D**isease **A**ctivity **I**ndex (**BASDAI**)
   - **ii.** **A**nkylosing **S**pondylitis **D**isease **A**ctivity **S**core (**ASDAS**)

3. Psoriatic Arthritis (PsA) – Diagnosis

1. Inflammatory markers (ESR, CRP)

2. HLA–B27 (50–60%)

3. Imaging
   - X-ray
   - US
   - MRI

CASPAR (ClASsification criteria for Psoriatic ARthritis)

Table 6 – Classification criteria for psoriatic arthritis[a]

Criterion	Points
1. Evidence of current psoriasis, a personal history of psoriasis, or a family history of psoriasis	
Evidence of current psoriasis on examination	2
Personal history	1
Family history	1
2. Typical psoriatic nail dystrophy (onycholysis, pitting, hyperkeratosis) on examination	1
3. Negative test for rheumatoid factor	1
4. Dactylitis (inflammatory swelling of an entire finger or toe)	
Current dactylitis on examination	1
Personal history	1
5. Radiographic evidence of juxta-articular new bone formation on plain radiographs of hands or feet	1

[a] To meet **CASPAR** (**ClAS**sification criteria for **P**soriatic **AR**thritis) criteria, a patient must have inflammatory articular disease (joint, spine, or entheseal) with ≥ 3 total points from any of the 5 categories.

Adapted from Taylor W et al; CASPAR Study Group. *Arthritis Rheum.* 2006.[47]

- ≥3 points
- **Sensitivity**: 91.4%
- **Specificity**: 98.7%

Ann Rheum 2006; 54:2665-2673

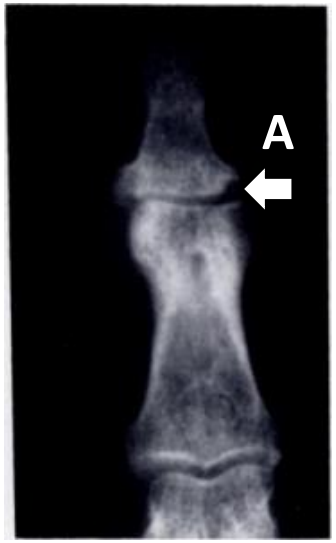
X-Ray Findings in PsA

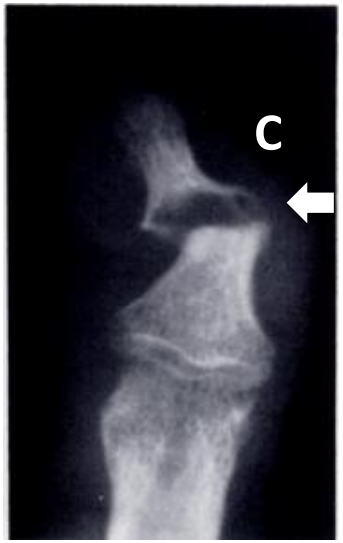
A. Joint
- erosions
- space narrowing

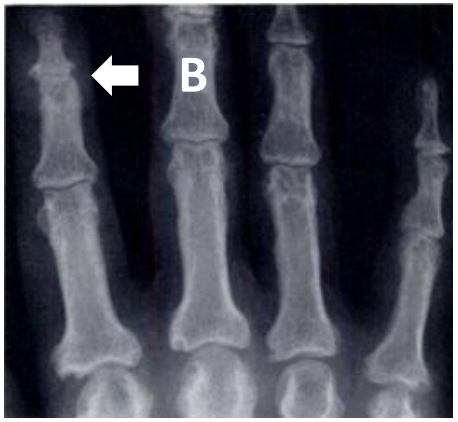
B. Bony proliferation incl.
- periarticular
- shaft periostitis

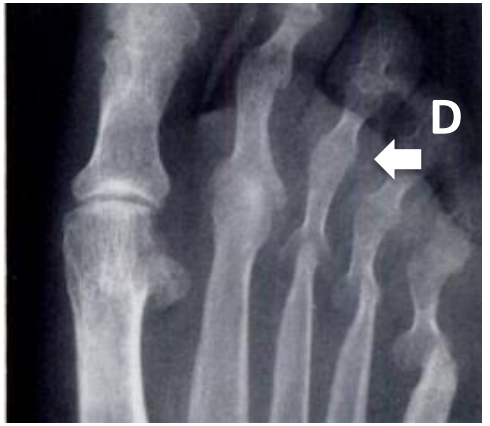
C. Osteolysis incl.
- ‘‘pencil in cup’’ deformity
- acro-osteolysis

D. Ankylosis
- Spur formation
- Spondylitis





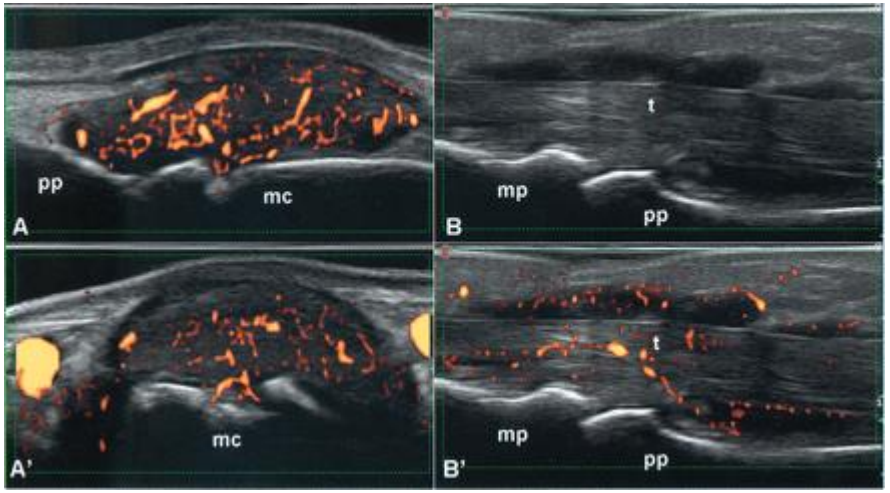




AJR 1980. 134:125-135

Ultrasound Findings in PsA

- On GS, joint
  - Effusion
  - Erosion
- On PD,
  - hyperaemia
  - Tenosynovitis
  - **Enthesitis**
    - **more specific feature of PsA**



A. Longitudinal view MC PD signal
A[1]. Transverse view MC PD signal
B. Longitudinal view volar PP - proliferative tenosynovitis.
B[1]. PD increased perfusion synovial tissue surround flexor tendon.
MP: middle phalanx, PP: prox phalanx, MC: metacarpal bone

J Rheumatol 2009;83;35-38

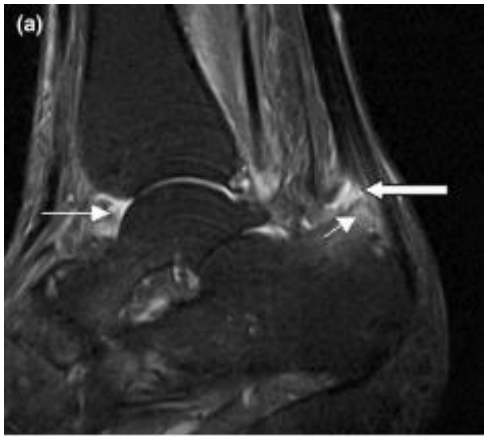
MRI* Findings in PsA

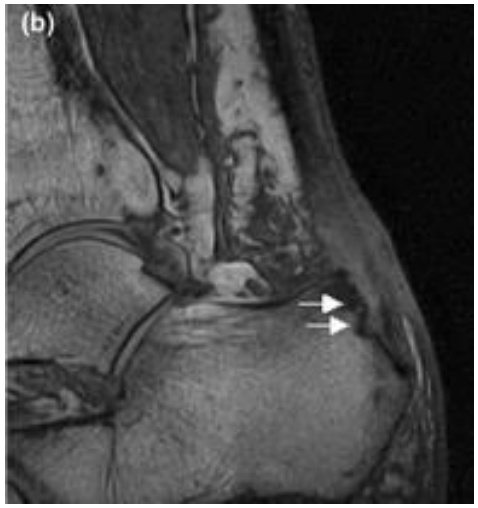
- Earlier detection of

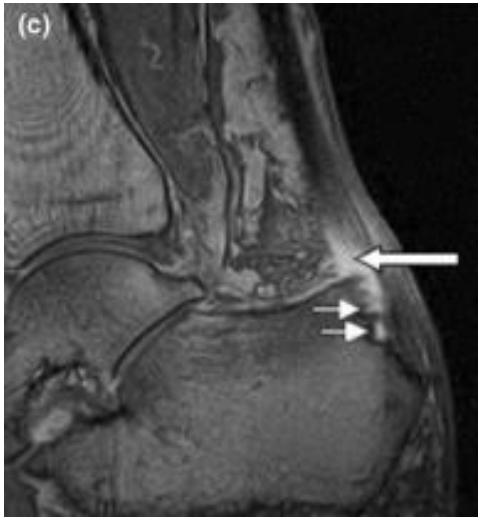
  i. Damage
     - Erosions

  ii. Inflammation
     - effusions
     - tenosynovitis
     - enthesitis

  iii. Bone oedema







*Gold standard for imaging synovitis

Arthritis Research & Therapy 2006, 8:207 (doi:10.1186/ar1934)

3. Psoriatic Arthritis – Monitoring

i. **Acute phase reactants**

ii. **X-ray**

iii. US

iv. MRI

v. **Clinical Assessment**

Inflammatory Arthritis (IA)

1. Crystal arthritis
2. Rheumatoid arthritis (RA)
3. Spondyloarthritis/spondyloarthropathy (SpA)
4. **Infectious**

4. Septic Arthritis – Diagnosis

i. **Synovial fluid aspiration (gold standard)**
   - gram stain (sensitivity 29-50%), **culture (sensitivity 70-90%)**, WCC & differential
   - US/CT/X-ray-guided or surgical arthrotomy: hip, SIJ

ii. Blood culture (ideally) prior to antibiotics
   - positive in 40-50% cases

iii. FBE

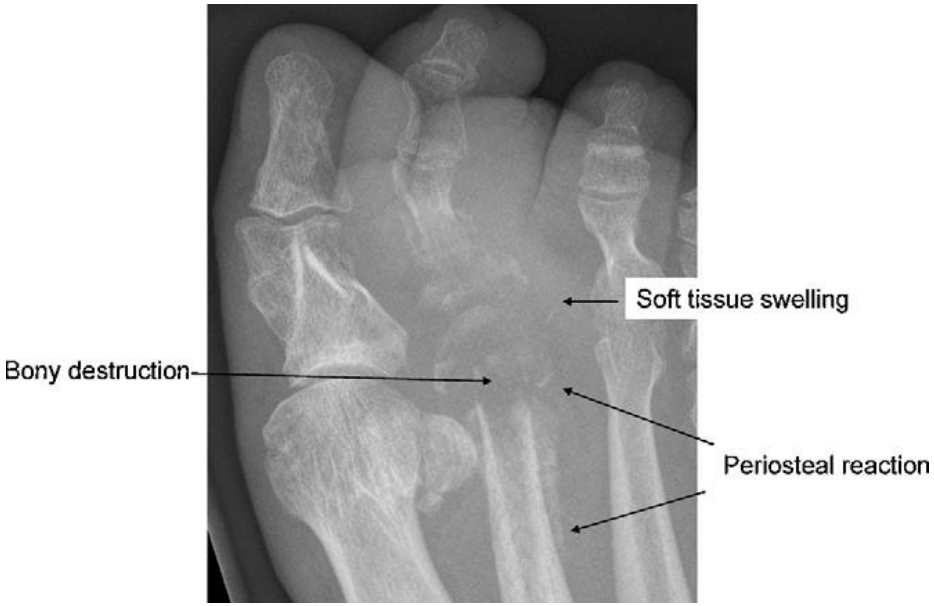
iv. Acute phase reactants (ESR, CRP)

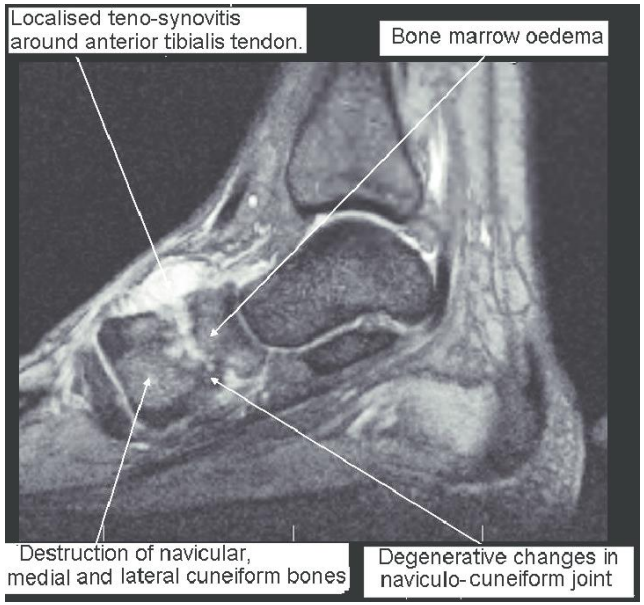
v. Imaging
   - X-ray – osteomyelitis, concurrent joint pathology, longitudinal followup
   - US, CT, MRI – difficult areas e.g. hip, spine & SIJ
   - bone scan – multiple joint involvement suspected

4. Septic Arthritis – Diagnosis

Diagnosis / Fluid Type	Findings		
	Macroscopic appearance	White cell count (10^6/L)	% Polymorphonuclear leucocyte/neutrophil
Normal	Clear, viscous, pale yellow	0 – 200	< 10%
Non-inflammatory	Clear to slightly turbid	200 – 2,000	< 20%
Inflammatory	Slightly turbid	2,000 – 50,000	20 to 70%
Septic	Turbid to purulent	>50,000	> 70%

4. Septic Arthritis – Diagnosis





X-ray:

- Subchondral bone destruction on both sides of a joint
- Juxta-articular osteoporosis
- Joint effusion / soft tissue swelling

MRI:

- (early) cartilaginous damage
- Synovial enhancement
- Peri-synovial oedema

The Foot 21 (2011) 149–153. Cases Journal 2009, 2:6859 doi: 10.4076/1757-1626-2-6859

4. Septic Arthritis – Monitoring

i. Acute phase reactants

ii. FBE

iii. (Repeat diagnostic arthrocentesis)

Overview

- General principles
- Inflammatory arthritis (IA)
  - Crystal, RA, SpA, infectious
- **Connective tissue diseases (CTD)**
  - **SLE, Sjogren's, Scleroderma, IgG4RD**
- Myositis
- Vasculitis

Connective Tissue Diseases (CTD)

1. Systemic lupus erythematosus (SLE)
2. Sjogren's Syndrome
3. Scleroderma
4. IgG4 Related Disease

Connective Tissue Diseases (CTD)

1. **Systemic lupus erythematosus (SLE)**
2. Sjogren's Syndrome
3. Scleroderma
4. IgG4 Related Disease

1. Systemic lupus erythematosus

- **Diagnosis**
  - **i. Serology**
    - ANA
    - dsDNA Ab
    - Anti-Sm Ab
    - Antiphospholipid Ab
      - Lupus anticoagulant
      - Anticardiolipin Ab
      - Anti-beta 2 glycoprotein Ab
      - Rapid plasma reagin (RPR): false +ve
    - Low complement
      - C3, C4 or CH50
    - Direct (Coombs') Antigen Test
    - (Acute phase reactants)
  - **ii. Biopsy** proven lupus nephritis

- **Monitoring**
  - FBE
    - Anaemia, leukopaenia, thrombocytopenia
  - Serum creatinine/eGFR
  - ESR, CRP
  - dsDNA titre
    - lupus nephritis
  - Complement levels
  - Spot urinary
    - protein_creatinine ratio
    - Phase contrast microscopy

2012 Systemic Lupus International Collaborating Clinics (SLICC) Criteria for SLE

- **Clinical**
  1. Acute cutaneous lupus
  2. Chronic cutaneous lupus
  3. Oral or nasal ulcers
  4. Non-scarring alopecia
  5. Arthritis
  6. Serositis
  7. Renal
  8. Neurologic
  9. Haemolytic anaemia
  10. Leukpaenia
  11. Thrombocytopenia ($<100,000/mm^3$)

- **Immunologic**
  1. ANA
  2. dsDNA
  3. Anti-Sm
  4. Antiphospholipid Ab
  5. Low complement
  6. Direct (Coombs') Antigen test
     - Not counted in presence of haemolytic anaemia

- SLICC criteria requirements:
  - ≥ 4 criteria (at least 1 clinical & 1 laboratory criteria OR
  - Biopsy-proven lupus nephritis + ANA or dsDNA positive

Connective Tissue Diseases (CTD)

1. Systemic lupus erythematosus (SLE)
2. **Sjogren's Syndrome**
3. Scleroderma
4. IgG4 Related Disease

2. Sjogren's Syndrome - Diagnosis

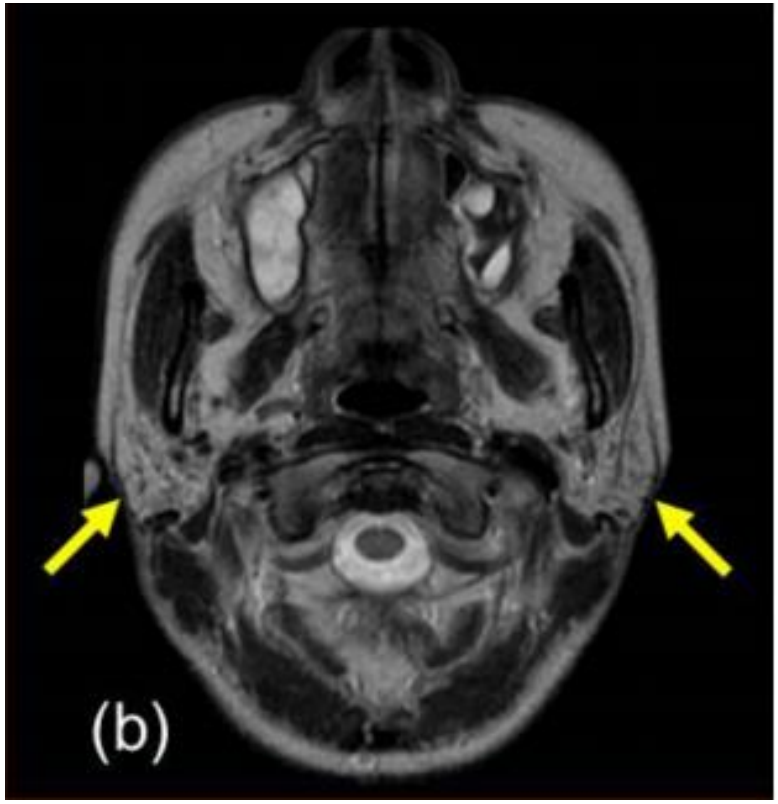
i. **Serology**
- ANA
- ENA (60%)
  - Ro/SSA
  - La/SSB
- Rheumatoid factor (90%)
- Hyperglobulinaemia
  - ESR
  - Total globulins
  - Immunoglobulin quantification
- Cryoglobulins
  - mixed, type II
- Centromere (5-6%)

ii. **Biopsy** – lower lip (labial)/minor salivary gland
- Confirm Sjogren's
- Exclude other conditions

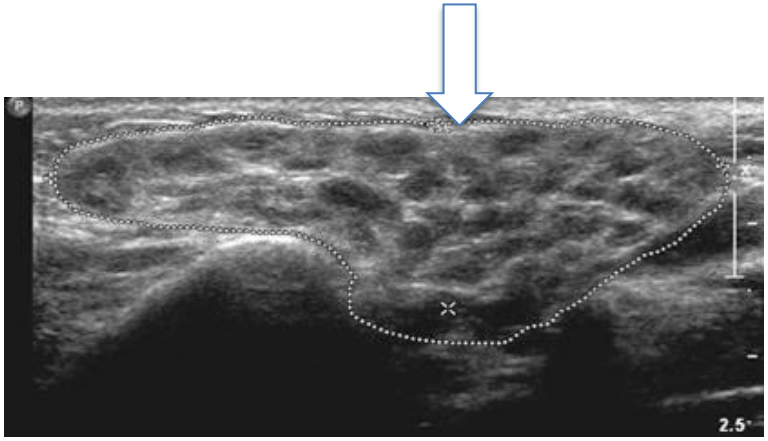
iii. **Imaging**
- MRI
  - Parenchymal heterogeneity
  - Nodular pattern
  - Sialography
- US
  - Hypoechoic areas bounded by hyperechoic bands
  - Cysts (advanced disease)
- CT: punctate parotid gland calcification (calculi)

Diagnosis requires one **immunologic** + one **ocular or oral** clinical feature

MRI & US Findings in Sjogren's Syndrome



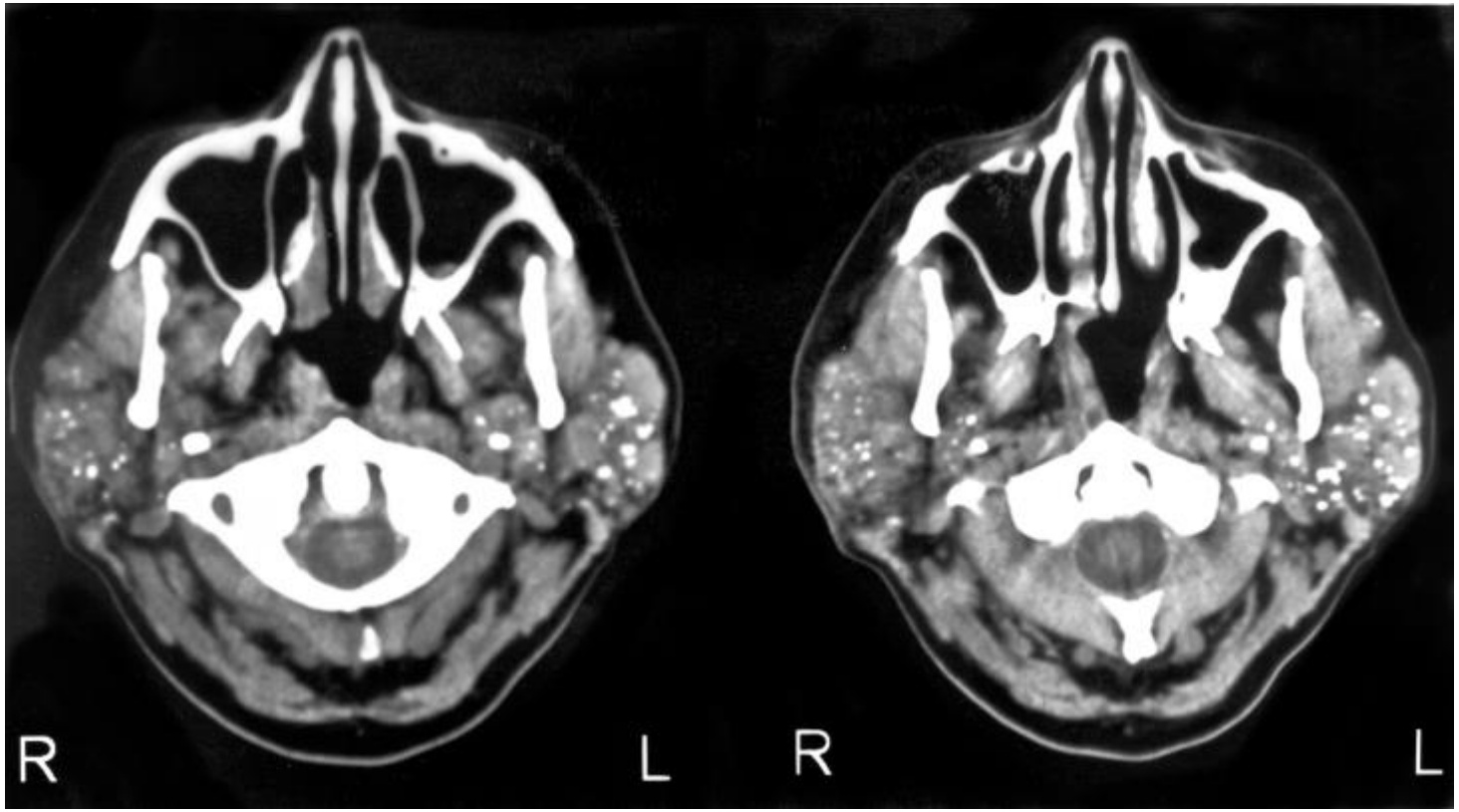
T2W – diffuse increased intensity with several low signal spots ('salt-and-pepper' appearance)



Transverse view of the parotid gland - parenchymal inhomogenecity with multiple oval shaped small hypoechoic changes

European Society of Radiology. 10.1594/ecr2011/C-1013. J Korean Med Sci 2013; 28: 497-507

CT Findings in Sjogren's Syndrome



CT scan of parotid regions (two axial sections) showing multiple calculi in parenchyma of both parotid glands (superficial and deep lobe of glands)

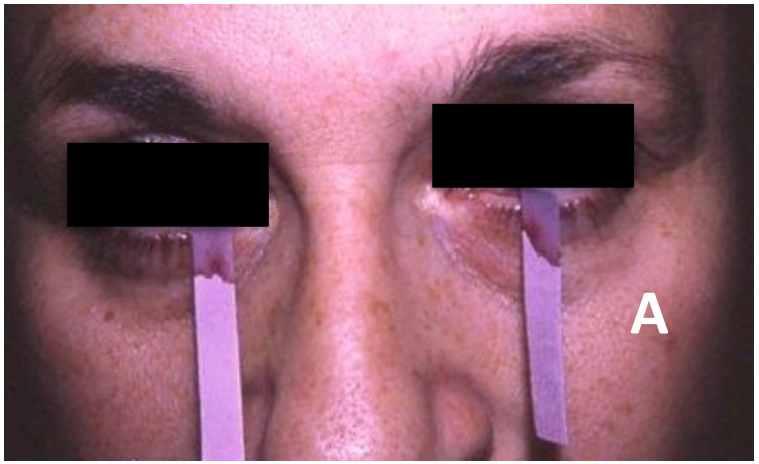
Acta Otorhinolaryngol Ital. 2007 Feb; 27(1): 41–44

2. Sjogren's Syndrome - Diagnosis

iv. Special tests

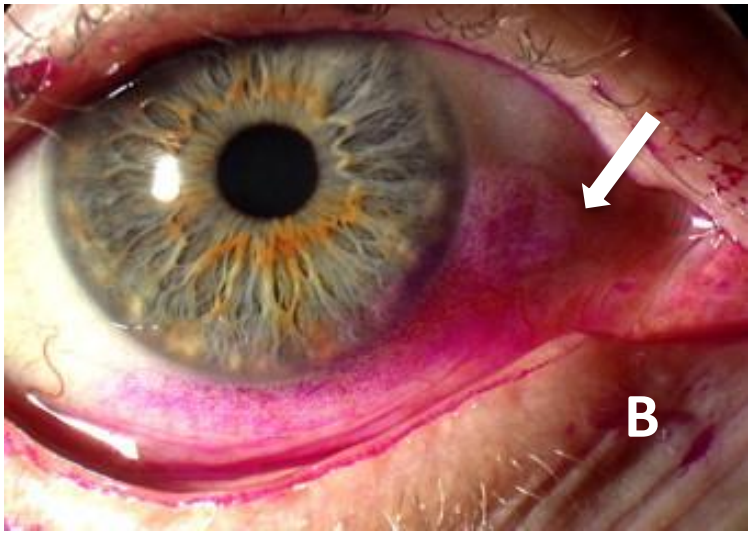
A. Schirmer's test*

- Reflex tear production
- Filter paper wetting over 5 minutes
- **AbN <5mm in 5min**



B. Ocular staining*

- Rose Bengal test
- Normal eye should not take up any stain



C. Tear Break-up Time

- Measures tear stability
- AbN ≤10 seconds

Contact Lens & Anterior Eye. 2013;36(6):272-280

2. Sjogren's Syndrome - Diagnosis

v. Quantifying salivary function
   - Mainly performed in **research** settings
     - Salivary gland scintigraphy
       - Decreased uptake & release of radionuclide
     - Sialometry
       - Measures salivary flow rate

Connective Tissue Diseases (CTD)

1. Systemic lupus erythematosus (SLE)
2. Sjogren's Syndrome
3. **Scleroderma**
4. IgG4 Related Disease

3. Scleroderma - Diagnosis

- ANA (95%)
- **Antitopoisomerase** I (anti-Scl-70) antibody (20-40%)
  - Diffuse skin disease, higher risk severe ILD
- **Anticentromere** antibody (20-40%)
  - CREST, severe digital ischaemia & loss
    - Also seen in Primary Biliary Cirrhosis, Sjogren's syndrome
- **Anti-RNA polymerase III** antibody
  - Rapidly progressive skin disease
  - Higher risk of renal crisis
- CXR/HRCT
  - Interstitial lung disease (ILD)
- Pulmonary function testing
  - Restrictive ventilatory defect
  - Pulmonary arterial hypertension (PAH)
  - Decreased DLCO
- Echocardiography
  - PAH
  - Defined: mean pulmonary artery pressure (mPAP) **≥25mmHg at rest**
  - NB: TTE provides right ventricular **systolic** pressure (RVSP = sPAP)

Connective Tissue Diseases (CTD)

1. Systemic lupus erythematosus (SLE)
2. Sjogren's Syndrome
3. Scleroderma
4. **IgG4 Related Disease**

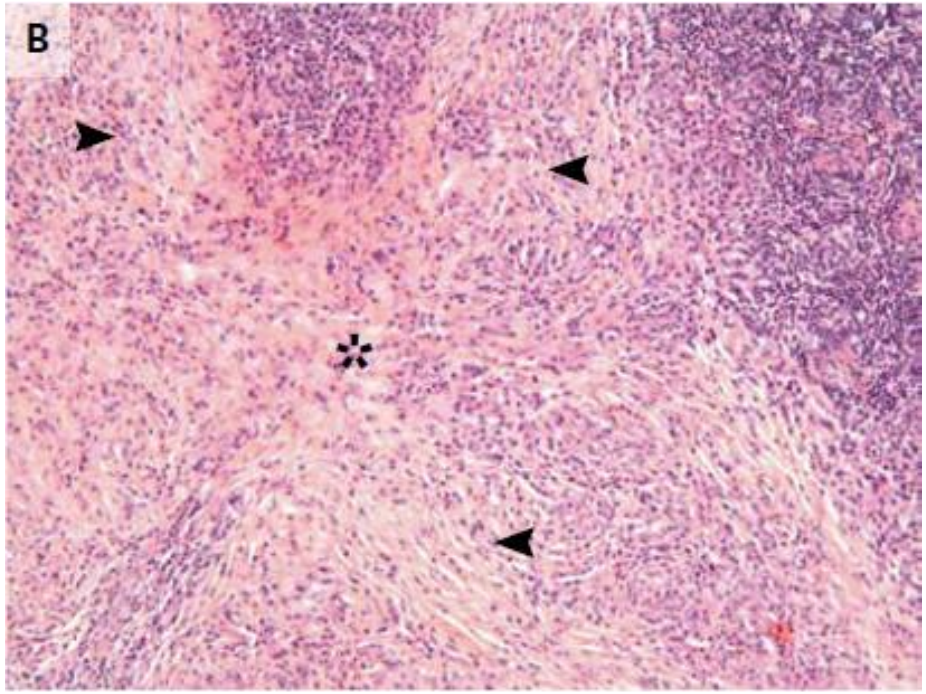
4. IgG4-related disease - Diagnosis

- Suspect in the presence of:
  - Pancreatitis of unknown origin, bilateral salivary &/or lacrimal gland enlargement, retroperitoneal fibrosis, orbital pseudotumour

1. **Tissue biopsy (Gold standard)**
   - lymphoplasmacytic tissue infiltration of mainly IgG4-positive plasma cells and lymphocytes
   - Storiform fibrosis
   - (often) obliterative phlebitis

2. Serum IgG4 elevation

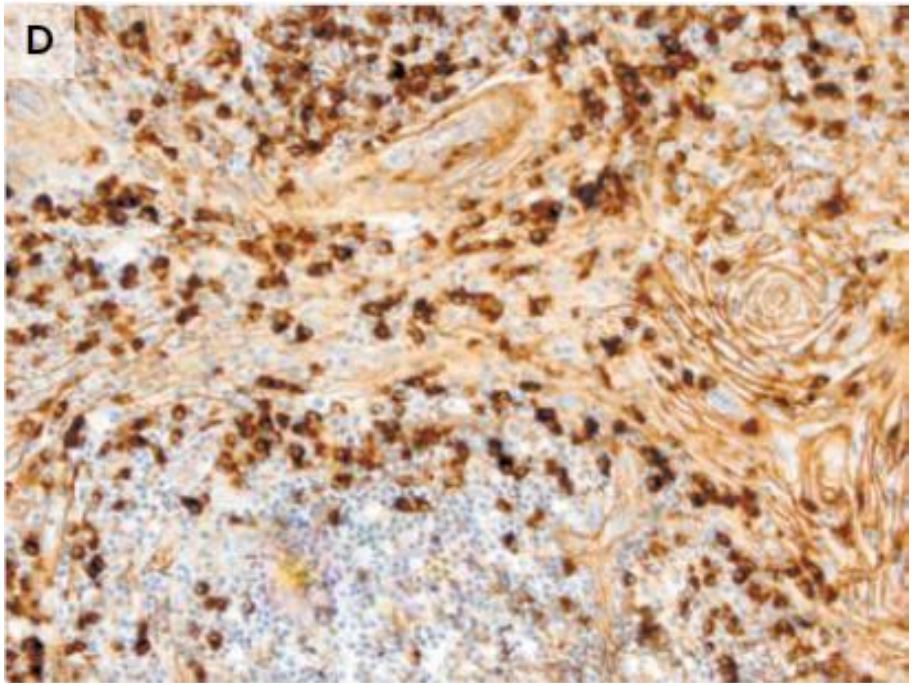
IgG4-RD - Histopathology



Panel B: Dacryoadenitis

Storiform fibrosis: cartwheel

Arrowheads: bands of fibrosis



Panel D: Dacryoadenitis

IgG4+ plasma cells on immunoperoxidase staining

Stone JH et al. IgG4-related disease. N Engl J Med 2012;366:539-51

Overview

- General principles
- Inflammatory arthritis (IA)
  - Crystal, RA, SpA, infectious
- Connective tissue diseases (CTD)
  - SLE, Sjogren's, Scleroderma, IgG4RD
- **Myositis**
- Vasculitis

Idiopathic Inflammatory Myositis - Diagnosis

1. Muscle enzymes
   - Creatinine kinase (CK)
   - Lactate dehydrogenase (LDH)
   - Aspartate aminotransferase (AST)
   - Alanine aminotransferase (ALT)

2. Acute phase reactants

3. ANA
   - 80% in dermatomyositis or polymyositis

Idiopathic Inflammatory Myositis - Diagnosis

4. Myositis-**Specific** Ab

A. Polymyositis

i. Anti-synthetase Syndrome

- Incl. anti-Jo-1 (most common)
- ILD, raynaud's, mechanic's hands, fever, non-erosive arthritis

ii. Necrotising Myopathy

– **Anti-SRP (Signal Recognition Particle)**
  - May be refractory to treatment

– **Anti-HMGCR**

B. Dermatomyositis

1. Clinically amyopathic DM

i. Anti-MDA-5/Anti-CADM-140
  - Rapidly progressive ILD

ii. Anti-SAE

– small ubiquitin-like modifier activating enzyme

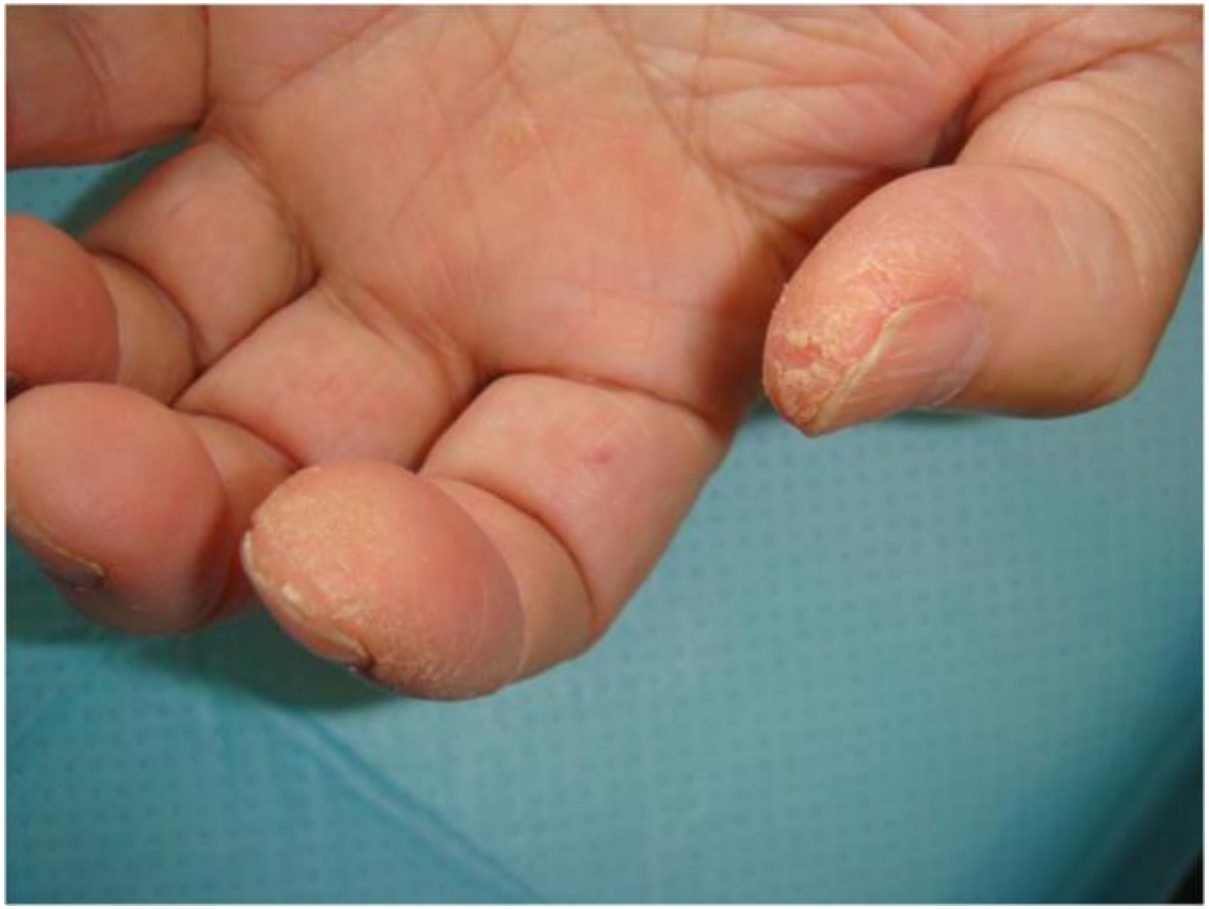
2. Cancer-associated myositis

- Anti-p155/140
  – TIF1-gamma
  – Severe cutaneous disease (calcinosis) in juvenile dermatomyositis
  – Cancer in adult dermatomyositis

3. Anti-Mi-2

– Adult & Juvenile dermatomyositis
– Skin disease (hallmark), mild muscle weakness, good response to treatment

Mechanic's Hands



Fissures and roughness with hyperkeratosis and scaling on the pulp of the thumb and the radial aspect of the index finger

BMC Res Notes. 2014; 7: 303.

Idiopathic Inflammatory Myositis - Diagnosis

C. **Inclusion Body Myositis**
   - Anti-CN-1A/Mup44

D. Myositis-**Associated** Ab
   - Anti-Ro/SSA
   - Anti-La/SSB
   - Anti-U1-RNP
   - Anti-PM-Scl
   - Anti-Ku

- Myositis overlap with CTD:
  - Sjogren's syndrome
  - SLE
  - MCTD
  - Scleroderma

Idiopathic Inflammatory Myositis - Diagnosis

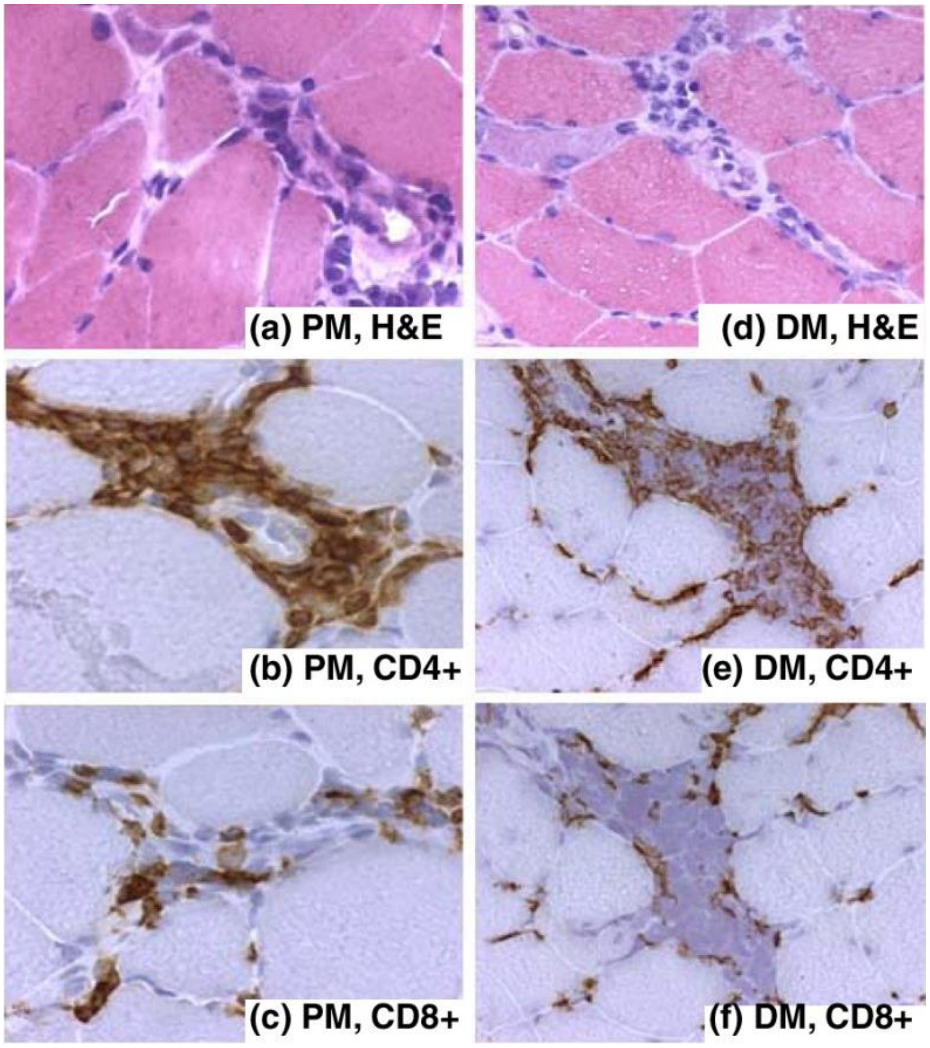
5. Electromyography (EMG)
   - increased membrane irritability +/-
   - Increased insertional activity and spontaneous fibrillations
   - AbN myopathic low-amplitude, short-duration polyphasic motor unit potential
   - complex repetitive discharges

6. MRI
   - (Noninvasive) sensitive but nonspecific
   - detects areas of muscle inflammation, edema with active myositis, fibrosis, calcification

Idiopathic Inflammatory Myositis - Diagnosis

7. Biopsy

- Muscle
  - Dermatomyositis
    - **Peri**fascicular myofibre injury, atrophy, fibrosis
    - Perimysial infiltrate CD**4**+
  - Polymyositis
    - Infiltrate CD**8**+ predominantly **intra**fascicular
- Skin



Myositis – Monitoring

i. CK

ii. LDH

iii. ALT/AST

iv. Acute phase reactants

v. Muscle strength testing (dynamometer)

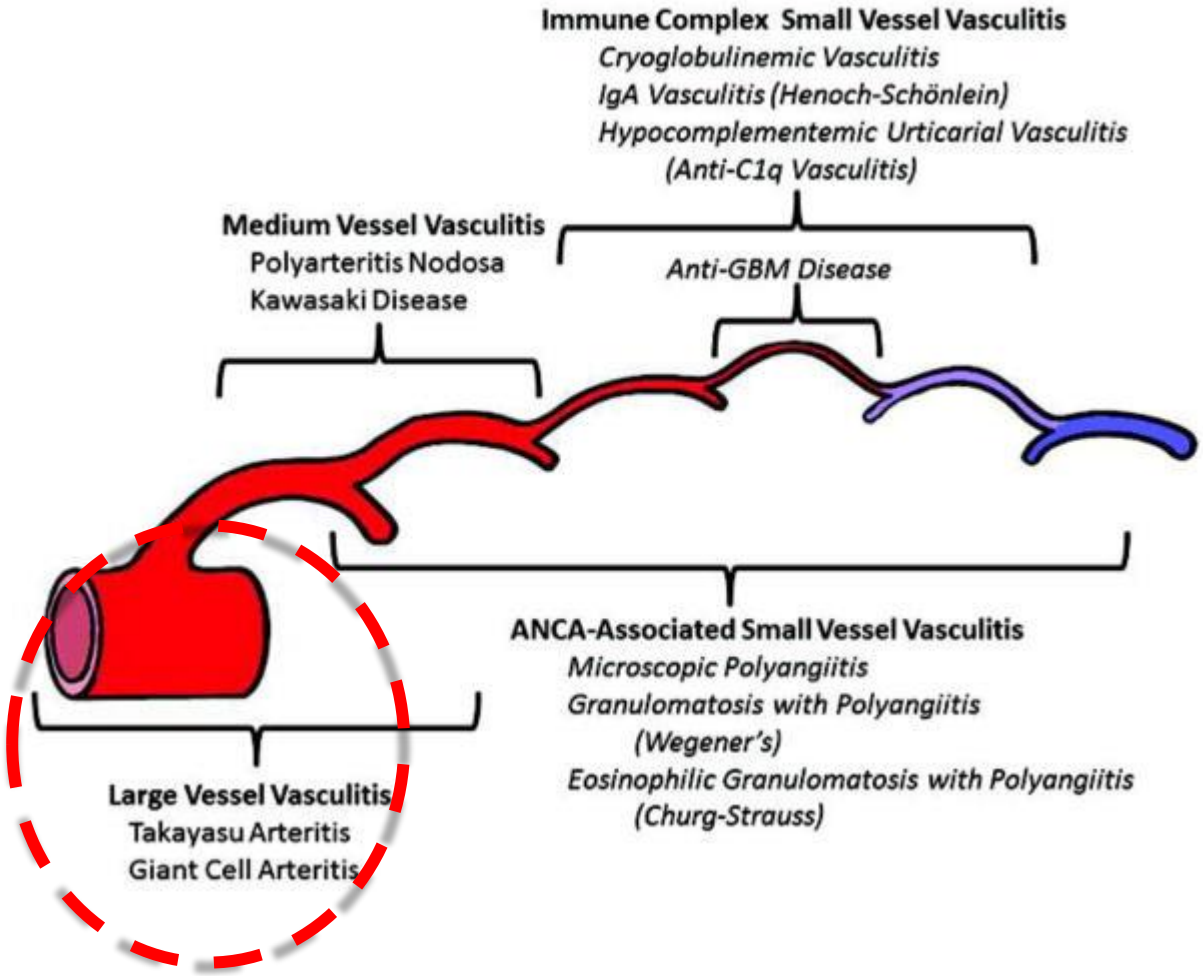
Overview

- General principles
- Inflammatory arthritis (IA)
  - Crystal, RA, SpA, infectious
- Connective tissue diseases (CTD)
  - SLE, Sjogren's, Scleroderma, IgG4RD
- Myositis
- **Vasculitis**

Vasculitis - Classification

- 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides

1. **Large** Vessel
   - Takayasu arteritis (TA)
   - Giant cell arteritis (GCA)

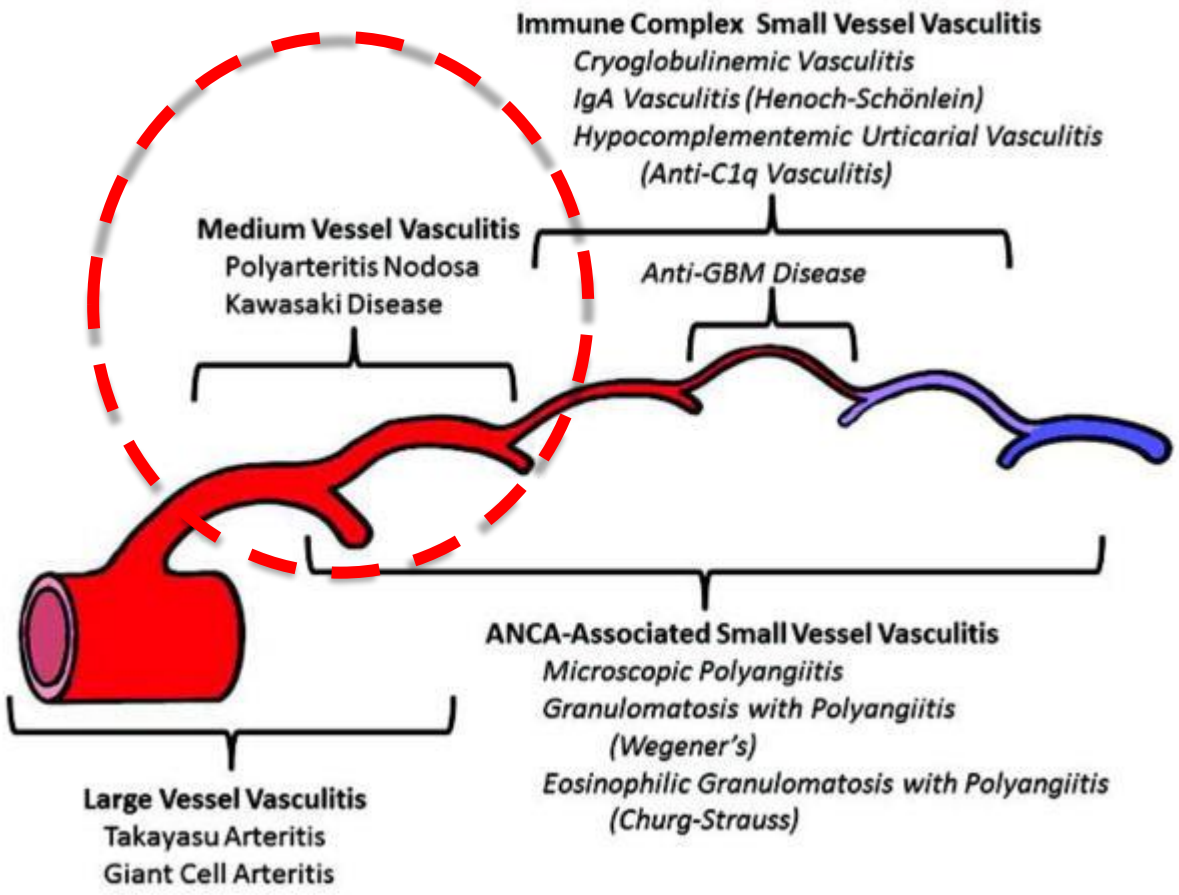


Arthritis & Rheumatism. 2013;65(1):1-11

Vasculitis - Classification

- 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides

2. **Medium** Vessel
   - Polyarteritis nodosa (PAN)
   - Kawasaki disease

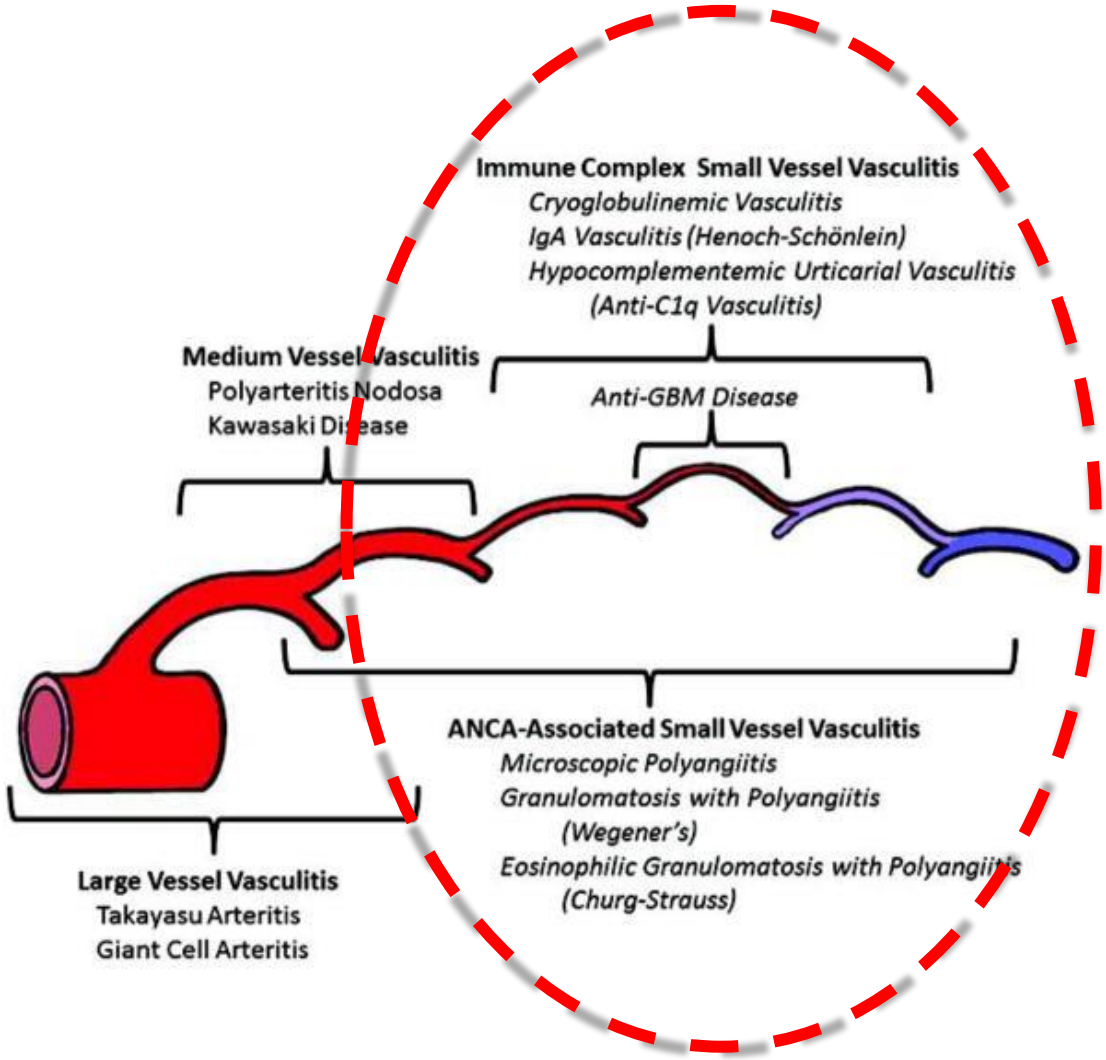


Arthritis & Rheumatism. 2013;65(1):1-11

Vasculitis - Classification

3. Small Vessel

- ANCA-associated vasculitis (AAV)
  - Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
  - Granulomatosis with polyangiitis (Wegener's)
  - Microscopic polyangiitis
  - Henoch-Schonlein Purpura (IgA vasculitis)
  - Cryoglobulinaemic vasculitis
  - Connective tissue disease related



Arthritis & Rheumatism. 2013;65(1):1-11

Vasculitis - Classification

4. **Variable** Vessel
   - Bechet's disease – any vessel size (artery/vein)
   - Cogan's syndrome – any vessel size

5. **Single-organ**
   - Cutaneous LCV
   - Primary angiitis of the CNS (PACNS)
     - medium/small vessels brain, spinal cord, meninges

6. Vasculitis assoc with systemic disease

Vasculitis - Diagnosis

1. Serology
   - ANA
   - Complement
   - ANCA
     - C-ANCA (protease-3/PR-3)
     - P-ANCA (myeloperoxidase/MPO)
   - Acute phase reactants

2. Urinary
   - protein_creatinine ratio
   - phase contrast microscopy

3. Tissue biopsy

4. Imaging
   - Angiography
     - CTA/MRA
     - GCA, TA, PAN, PACNS
   - Ultrasound
   - PET scans

5. EMG
   - Mononeuritis multiplex

Vessel Size	Condition	Tests [*denotes gold standard]
LARGE	Giant cell arteritis	**Biopsy***: temporal artery - sensitivity: unilat (86.9%), bilat (+5%) - panarteritis, internal elastic lamina fragmentation, CD4+ lymphocytes, macrophages, giant cells (not requisite) Colour Doppler US (CDUS) – "halo sign" [not conventional] • Sens 75% (95% CI, 0.67-0.82), specif 83% (95% CI, 0.78-0.88)
	Takayasu's arteritis	**MRA***, CTA – aorta & primary branches • Smoothly tapered luminal narrowing or occlusion ± wall thickening
MEDIUM	Polyarteritis nodosa	HBV, urinalysis **Biopsy*** (e.g. renal) – medium-sized artery inflamm **Mesenteric** (or renal) **angiogram** – multiple aneurysms, irreg constrictions in larger vessels, occlusion smaller penetrating arteries
	Primary Angiitis of the CNS (PACNS)	**Lumbar puncture** – AbN 80-90% - Aseptic meningitis, lymph pleocytosis, elevated protein, normal glucose **MRI**, **Cerebral angiogram** – segmental narrowing ("beading"), sensitivity 60% **Biopsy***: brain - leptomeninges & underlying cortex, sensitivity 74.7% (95% CI 64.0-84.1) • Langerhans or foreign body giant cells, necrotizing vasculitis, or lymphocytic vasculitis
SMALL - **ANCA**	• Granulomatosis with polyangiitis (Wegener's) • Microscopic polyangiitis • Eosinophilc Granulomatosis with polyangiitis (Churg-Strauss)	**ANCA** – +ve 82-94% (GPA-PR3, MPA-MPO), -ve 10% Urinalysis – glomerular haematuria, red cell casts CXR, CT chest ±sinus **Biopsy*:** • renal - pauci-immune necrotising glomerulonephritis • skin – leukocytoclastic vasculitis (nonspecific), little to no complement & immunoglobulin on immunofluorescence • lung – open or thoracoscopic (sampling error) – necrotising granulomas • nasal – high false –ve (sampling error)

Vasculitis - Monitoring

1. Acute phase reactants

2. Urinary sediment

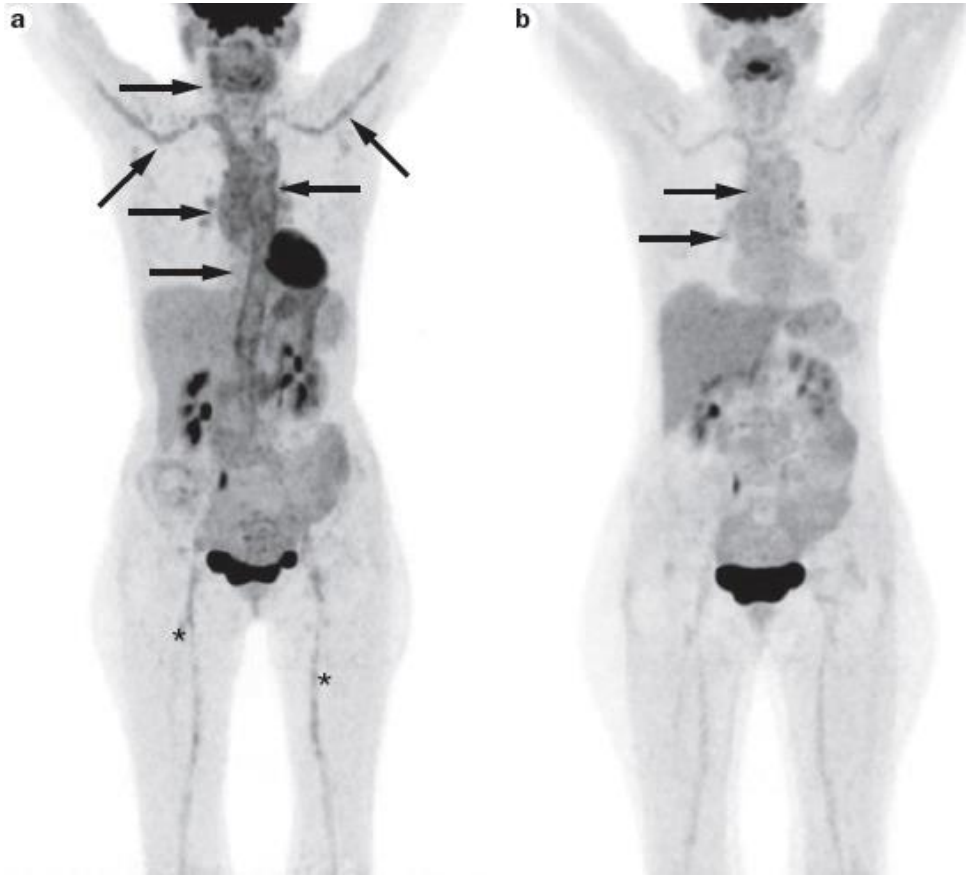
3. Levels of
   - Complement
   - dsDNA
   - Cryoglobulins
   - (ANCA)
   - Eosinophil counts

4. Imaging
   - US, MRA, CTA, PET

Nat Rev Rheumatol 2012;8:509-521

Large Vessel Vasculitis - Monitoring

- Magnetic resonance imaging (MRI)/MRA
- Conventional angiography
- Ultrasonography
- Positron emission tomography (PET)



Pre-Treatment PET **Post**-Treatment PET

Nat Rev Rheumatol 2012;8:509-521

Thank you for your attention

BEST WISHES FOR YOUR EXAMS!