



9:45 – 10:45am

Diagnostic Challenges of Rheumatologic Disease

SPEAKER

Peng Thim Fan, MD, FACP



Presenter Disclosure Information

The following relationships exist related to this presentation:

- Peng Thim Fan, MD, FACP: Speakers Bureau for AbbVie Inc.; Amgen, Inc.; Bristol-Myers Squibb Company; Genentech; Pfizer, Inc.; and Takeda Pharmaceutical Company.

Off-Label/Investigational Discussion

- In accordance with pmcME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Diagnostic Challenges of Rheumatologic Disease

Peng Thim Fan, MD, FACP

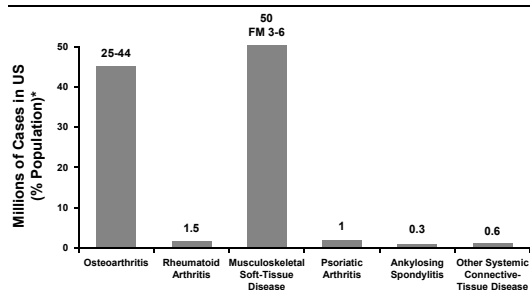
Clinical Professor of Medicine
Division of Rheumatology
David Geffen School of Medicine at UCLA

Learning Objectives

- Recognize the importance of pathophysiology in understanding rheumatic disease –target tissue and characteristic joint distribution
- Distinguish inflammatory from non-inflammatory (degenerative) arthritis and non-articular (soft-tissue) rheumatic conditions.
- Discuss the role of laboratory and imaging studies in rheumatologic diagnosis
- Review the features that distinguish fibromyalgia from other rheumatic diseases

Arthritis Care: An Increasing Burden on Healthcare Resources

Prevalence of Diagnosed Musculoskeletal Disorders



*Data updated 2008

†National Osteoporosis Foundation. www.nof.org. Dec 6, 2000.

The Arthritis Foundation Fact Book for the Media. Atlanta, Georgia. Arthritis Foundation; 1994:1-4.

The Most Common Musculoskeletal Problems Encountered in a Primary Care Office

- Degenerative: Osteoarthritis
- Inflammatory: Rheumatoid arthritis
 - Seronegative spondyloarthropathy
 - Psoriatic arthritis
 - Ankylosing spondylitis
- Non-articular: Fibromyalgia

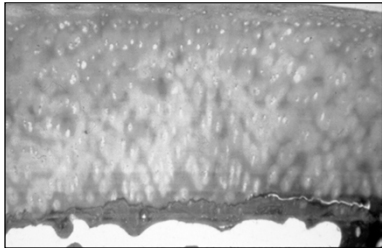
Illustrative Case

- A 50-year-old woman presents with generalized aches and pains and severe tenderness in her hands, knees, ankles and feet
- Her joints are swollen in the morning and she has several hours of morning stiffness
- Physical examination shows widespread tenderness in the neck, shoulders, hands, knees, ankles and feet
- Joints show full range of motion without swelling
- CBC, comprehensive metabolic panel, UA, ESR, CRP, RF and anti-CCP are negative; ANA positive at 1:320

Two Pragmatic Principles for Recognizing Arthritis

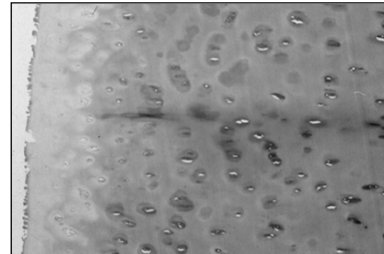
- I. Every arthritis has a specific target tissue:
 - Osteoarthritis: articular cartilage
 - Rheumatoid arthritis: synovium
 - Seronegative spondyloarthropathy: enthesis
- Fibromyalgia does **NOT** have a target tissue

Normal Cartilage

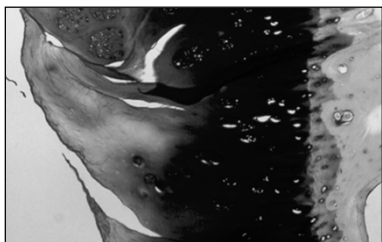


Note the smooth surface of the articular cartilage and uniform staining of the matrix with healthy embedded chondrocytes
There are no blood vessels in the cartilage, nutrients are supplied by diffusion from bone

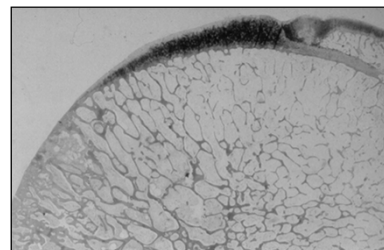
Osteoarthritis Cartilage – Early Fibrillation and Loss of Matrix



Osteoarthritis Cartilage – Late Deep Clefts in the Cartilage and Bone Hypertrophy



Osteoarthritis Late Complete Loss of Cartilage

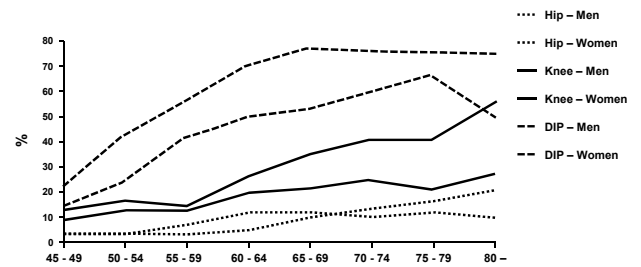


Note asymmetric cartilage loss

Two Pragmatic Principles for Recognizing Arthritis

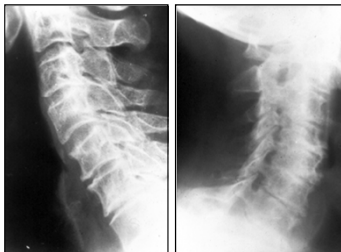
- II. Every arthritis has a specific pattern of joint distribution:
 - **Osteoarthritis:** symmetrical pattern of non-inflammatory arthritis
 - **Rheumatoid arthritis:** symmetrical synovitis
 - **Seronegative spondyloarthropathy:** axial inflammation and peripheral inflammatory arthritis

Prevalence of Radiological OA in a Dutch Population



Oxford Textbook of Rheumatology 2004.

Osteoarthritis: Cervical Spondylosis



Disc space narrowing at C5-6 and C6-7

Neuroforaminal narrowing by encroaching osteophytes

Osteoarthritis: Heberden's Nodes



Two bony prominences at the DIP joint; note irregular joint space narrowing and marginal osteophytes

Osteoarthritis: Bouchard's Nodes



Note bony enlargement of the PIP joints; she also has Heberden's nodes

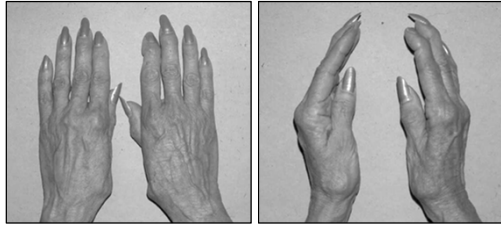
Osteoarthritis First Carpometacarpal Joint



Trapezioscapoid joint may also be affected

First Carpometacarpal joint joint space narrowing and subchondral sclerosis

Osteoarthritis: Hands

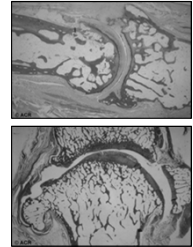


Note: Squaring at the base of the thumb due to subluxation of the CMC JOINT

Genetics of Osteoarthritis

Heberden's and Bouchard's nodes

Sisters of women with Heberden's nodes were 3x as likely to have generalized osteoarthritis as those in the general population: Stecher, 1941



Osteoarthritis: Effect of Disuse



Patient with multiple sclerosis: left hemiplegia for 30 years
Note absence of bony changes in the left hand

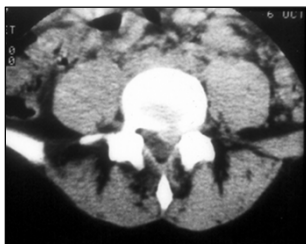
Osteoarthritis: Lumbar Spine



Acute back pain with stooping

Disc space narrowing and vacuum disc at L4-5 with Grade I spondylolisthesis

Osteoarthritis: Spinal Stenosis



CT Scan of the lumbar spine showing encroachment of degenerative disc material into spinal canal

Clinical Presentation of Lumbar Spinal Stenosis Syndrome and Neurogenic Claudication

- Extension provokes symptoms
- Pain/weakness in the legs
- Patients lean forward while walking to ambulate more comfortably
- Sitting relieves symptoms

Osteoarthritis: Hip

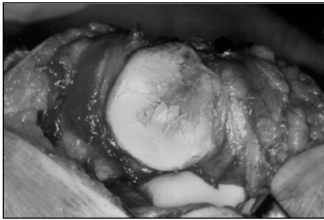
Suspect hip osteoarthritis if internal rotation <24 degrees and groin symptoms

Holla JFM, Arth Care Res 2012;64:59-65

Osteoarthritis: Hip

Progressive loss of superior cartilage and femoral head deformity

Osteoarthritis: Knee



Tri-compartmental cartilage degeneration:
Note irregular bare areas with exposed bone

Asymmetric Cartilage Loss in OA of the Knee



Asymmetric joint space narrowing causing varus or valgus deformity

Osteoarthritis of the Knees

Both valgus and varus alignment abnormalities are the principal factor in progression; nullifies effect of weight reduction. Even minor alignment changes are important.

- Felson D. Arth Rheum 2/13

Hallux Rigidus and Hallux Valgus Deformity in OA



Degenerative changes are confined to the first MTP joint

Bunion and Overlapping Toes in OA



Erosive Osteoarthritis



Note "gull-wing" appearance of the PIP joint

Charcot Arthropathy

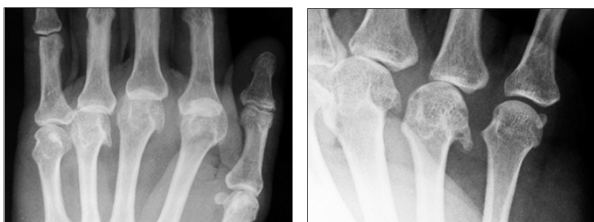


A 50-year-old Man with Painful Knuckles



Note joint space narrowing and osteophytes at the MCP joints

A 50-year-old Man with Painful Knuckles



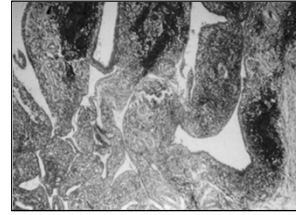
A 50-year-old Man with Painful Knuckles

- Serum iron = 75 $\mu\text{g/dL}$ (50-160)
- Iron saturation = 23% (15-50)
- TIBC = 328 $\mu\text{g/dL}$ (300-360)
- Ferritin = 1081 ng/mL (27-360)
- ESR = 11 mm/hour, C-Reactive Protein negative
- Liver function tests elevated 1.5 normal
- Diagnosis: Hemochromatosis

Osteoarthritis

- No systemic symptoms
- Morning stiffness under 30 minutes
- ESR and C-reactive protein are normal
- Very uncommon in patients under 40 except for trauma or certain inherited patterns
- No pathognomonic serologic test for OA

RA: Proliferative Synovium with Invasion of Cartilage and Bone



Note synovial proliferation and reduplication with intense lymphoid activity

Synovitis

- Swelling is confined to the area of the joint capsule
- Synovial thickening feels like a firm sponge

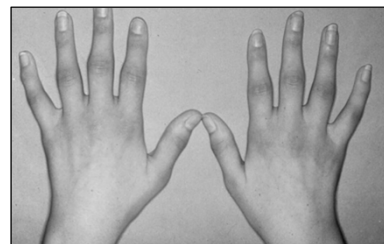
Principle

- Every arthritis has a specific pattern of joint distribution:
 - Rheumatoid arthritis: **symmetrical synovitis**

Rheumatoid Arthritis: Joint Distribution

- Symmetric polyarthritis
- Corresponds to the distribution of synovial lined joints
- Note absence of axial involvement except at C1-2

Early RA: Symmetrical Synovitis



Note fusiform swelling of the PIP joints and less obvious swelling of the MCP joints and wrists
The DIP joints are not affected

Radionuclide Scan in Early RA



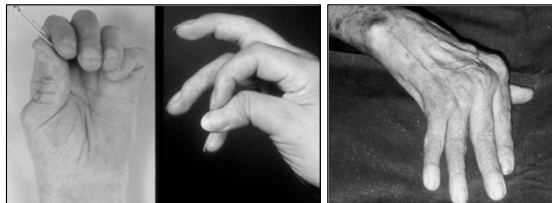
Note intense symmetric uptake at the PIP, MCP joints and wrists
Note sparing of the DIP joints

RA: Finger Deformities

Deformity of the fingers
caused by weakness of the intrinsic muscles
and slippage of ligaments

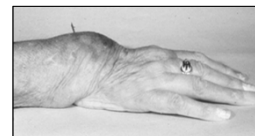


RA: Hand Deformities



Collapse of the thumb, ulnar deviation and muscle atrophy

RA: Wrist



Wrist synovitis restricts extension with weakening of grip
and trapping of the median nerve causing carpal tunnel syndrome

RA: Extensor Tendon Rupture



Painless rupture of extensor tendon typically in the morning

RA: Knee Swelling and Popliteal Cyst



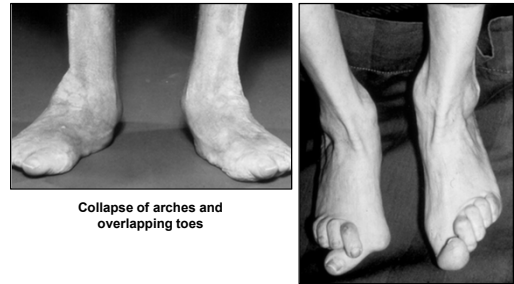
Dissection of Popliteal Cyst; Rupture causes Pseudo-thrombophlebitis

RA: Feet

Metatarsalgia, Callus Formation and Subluxation

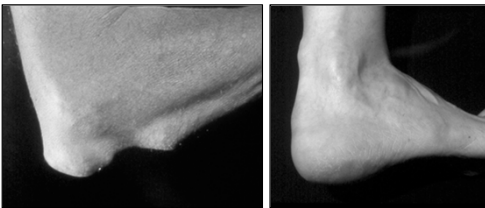


RA: Foot Deformities



Collapse of arches and overlapping toes

Rheumatoid Nodules



Prominent and Subtle painless rheumatoid nodules

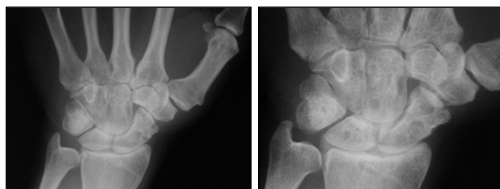
The Value of X-rays in Rheumatoid Arthritis

- For a Symmetric polyarthritis that satisfies ARA Criteria for rheumatoid arthritis:
 - Perform X-rays of the hands and feet
 - Repeat them at 1 year or sooner if the disease is not controlled



Early x-rays are normal

Radiographic Progression of Joint Erosions

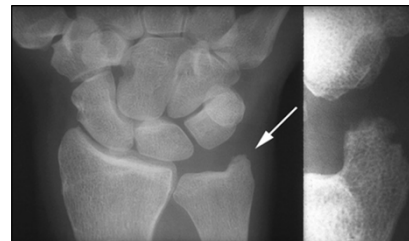


6 months:
cystic erosions at scaphoid

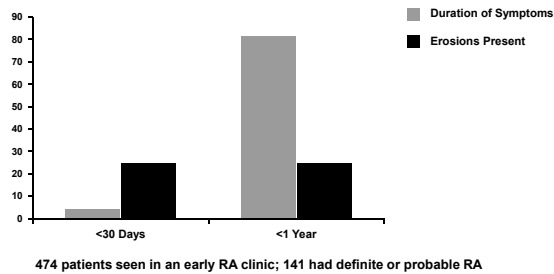
1 year:
more extensive erosions

Rheumatoid Arthritis

Early erosion at the tip of the ulnar styloid

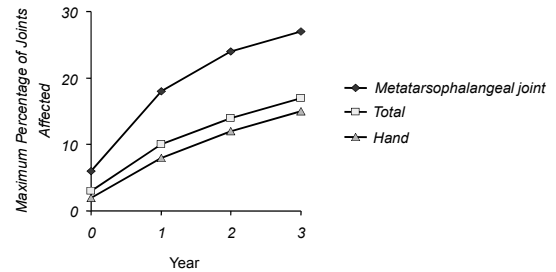


25% of Patients in an Early Arthritis Clinic Already Had Erosions at the First Visit



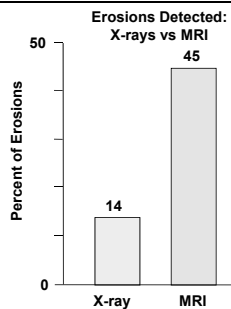
Van der Horst-Bruinsma, et al. *Br J Rheumatol*. 1998;37:1084.

Joint Erosions Occur Early in Rheumatoid Arthritis



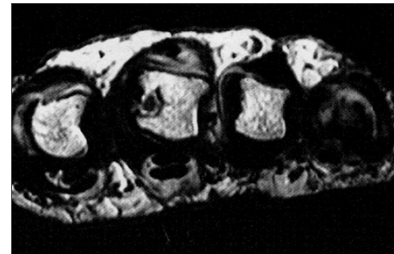
van der Heijde DM, et al. *J Rheumatol*. 1995;22:1792-1796. Fuchs HA, et al. *J Rheumatol*. 1989;16:585-591. McQueen FM, et al. *Ann Rheum Dis*. 1998;57:350-356.

Magnetic Resonance Imaging as a Diagnostic Tool



McQueen FM, et al. *Ann Rheum Dis*. 1999; 58:156-163; McQueen FM, et al. *Ann Rheum Dis*. 1998; 57: 350-356

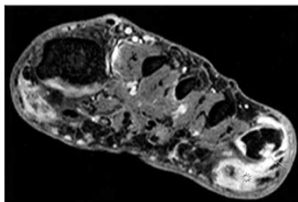
MRI Scan of the MCP Joints as an Index of Disease Progression in RA



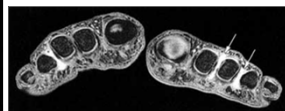
An MRI of metacarpophalangeal joints 2-5 shows synovial hypertrophy and flexor tenosynovitis

MRI scan of the feet in Early RA

High sensitivity: 97% synovitis, 80% erosions



Erosions at 5th MTP



Tenosynovitis between toes

Useful Tests in Inflammatory Arthritis

- ESR and CRP reflects general systemic inflammation
- Rheumatoid factor is positive in 80% of RA patients
- Anti-CCP antibody is positive in 70+% of RA patients
- ANA needs to be interpreted with great caution in patients with musculoskeletal pain.
 - It does NOT imply a diagnosis of SLE

RF: van Zeben D, et al. *Ann Rheum Dis* 1992; 51:1029
Anti-CCP : Zendman AJ, et al. *Rheumatology (Oxford)* 2006; 45:20.
ANA: Abeles AM, et al. *Am J Med*. 2013 Apr;126(4):342-8.

Anti-CCP Antibody (cyclic-citrullinated peptide)

- A better and more specific assay than RF
- Sensitivity 60-70 (66.4)%, specificity ?100(98.3)% (active TB – 7-39%)
- Present in early and preclinical disease (up to 14 years)
- Correlates with increased risk for progressive joint damage
- Does not correlate with fluctuation of RF

Peoples C, Valiyil R, Davis RB, Shmerling RH. J Clin Rheumatol 2013; 19:351.

Co-Morbidities in RA

- Osteoporosis
- Chronic pulmonary disease
- CV
 - Preclinical atherosclerosis (Carotid US)
 - Myocardial Infaction
 - All strokes and ischemic strokes
 - Congestive heart failure
 - Metabolic syndrome
- Malignancy – NM skin cancer, lung, lymphoma

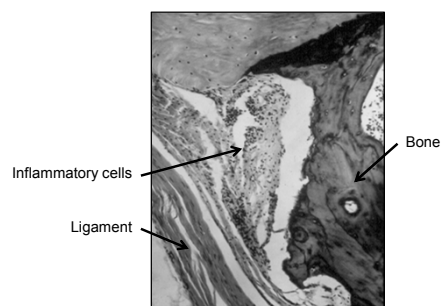
Seronegative Spondyloarthropathies

- Ankylosing spondylitis
- Psoriatic arthritis
- Reactive arthritis
- Arthritis of inflammatory bowel disease
- **Characteristics:**
 - Negative rheumatoid factor
 - spinal involvement and sacroiliitis
 - Asymmetric oligoarthritis
 - Sausage digits

Principle

- Every arthritis has a specific target tissue:
 - Osteoarthritis: articular cartilage
 - Rheumatoid arthritis: synovium
 - **Seronegative spondyloarthropathy: entheses and synovium**

Enthesopathy



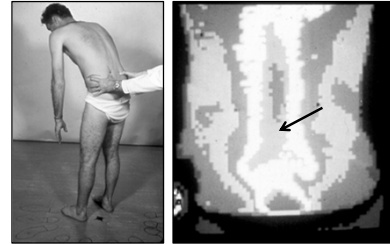
Two Pragmatic Principles for Recognizing Arthritis

- **II.** Every arthritis has a specific pattern of joint distribution:
 - **Seronegative spondyloarthropathy:** axial inflammation and peripheral inflammatory arthritis

Seronegative Spondyloarthropathy

- Axial Involvement
- Common targets highlighted
- Pattern is symmetrical in ankylosing spondylitis and asymmetric in psoriatic arthritis

Spinal Inflammation



Limited flexion. Thermogram shows increased spinal temperature

Spinal Inflammation



Restricted lateral flexion and pectoral muscle wasting

When Should You Suspect Inflammatory Back Pain?

- Young male
- Morning stiffness greater than 30 minutes
- Back pain is worse with rest and better with movement
- Unable to sleep through the night: usually awakens in the early hours of the morning
- Alternating buttock pain but no true radicular symptoms

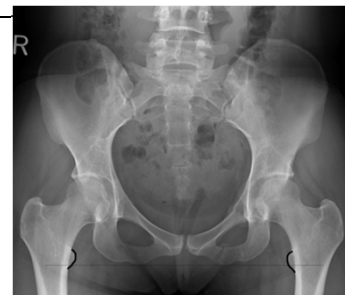
Hamilton L, et al. Rheumatology (Oxford). 2014 Jan;53(1):161-4.

Sacroiliitis – Ferguson Projection



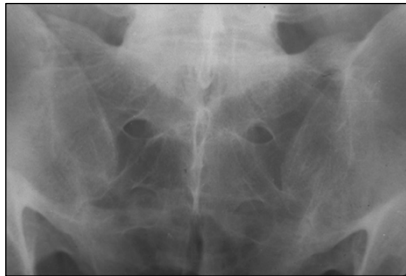
Sclerosis, irregular joints and pseudowidening

Pelvis regular projection



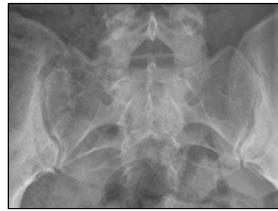
Normal sacroiliac joints

Sacroiliac Joint Fusion

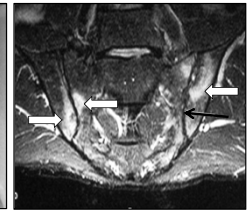


Fusion of sacroiliac joints in late sacroiliitis

MR Imaging of Sacroiliac Joints: Most Sensitive Way to Detect Sacroiliitis



X-rays show normal
sacroiliac joints



White areas on T2 imaging
indicate bone marrow edema

Spinal Fusion: Syndesmophytes

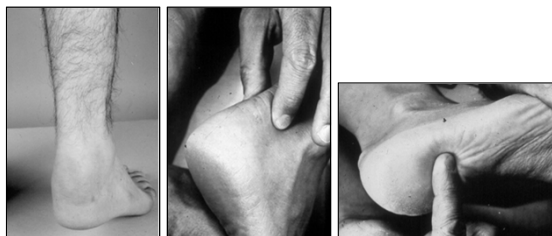


The Bamboo Spine



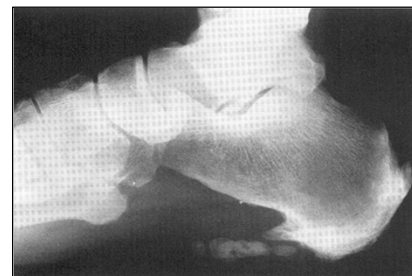
Complete fusion of the spine

Peripheral Arthritis: Enthesopathy



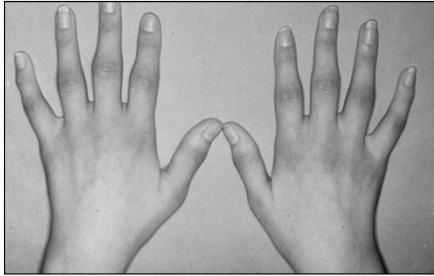
Regions of tenderness

Peripheral Arthritis: Enthesopathy

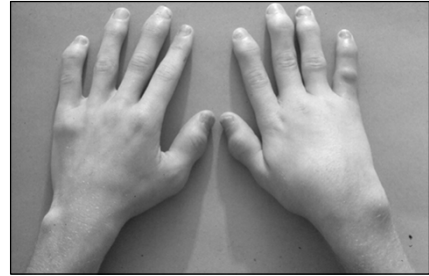


Note sclerosis, fluffy periostitis and new bone formation

RA Symmetrical Synovitis



Peripheral Arthritis: Asymmetry



Rheumatoid Arthritis: Synovitis



The Sausage Digit



Psoriasis: Nail Pitting, Onycholysis



What Distinguishes Psoriatic Arthritis from Rheumatoid Arthritis?

- Asymmetry
- Spine involvement
- Sausage digits
- Absence of nodules
- Psoriasis may be subtle and easy to miss

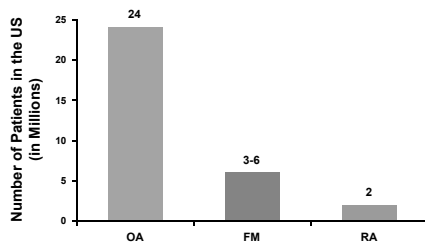
Fibromyalgia

- A clinical syndrome characterized by chronic widespread pain and tenderness to palpation at specific body sites
- Fibromyalgia has no target tissue but an easily recognizable clinical presentation

The Paradox of Fibromyalgia: No Target Tissue

- Normal passive range of joint motion
- Minimal mechanical disability
- Absence of muscle weakness or atrophy
- Normal ESR
- Normal radiographs, electromyogram, etc

Fibromyalgia More Prevalent than Rheumatoid Arthritis



ACR Fibromyalgia Criteria

- From History: widespread pain of 3 months duration
- From Examination: tender points defined by digital palpation with a force of 4 kg pain experienced in at least 11 of 18 tender point sites

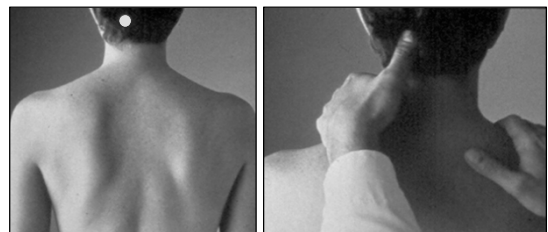
Wolfe F, et al. *Arthritis Rheum.* 1990;33:160-72.

The Tender Point: Key to Fibromyalgia Diagnosis

- Excessively tender, discrete area of soft tissue
- Palpated with thumb or first two fingers
- Palpation pressure: ~4 kg/cm, enough to whiten nail

Wolfe, et al. 1990.

Tender-Point Palpation: I. Head



● Insertion of suboccipital muscle

Tender-Point Palpation: IV. Neck and Chest



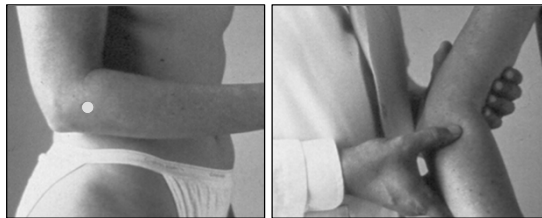
- Lower sternomastoid
- ▲ Second costochondral junction

Tender-Point Palpation: II. Upper Back



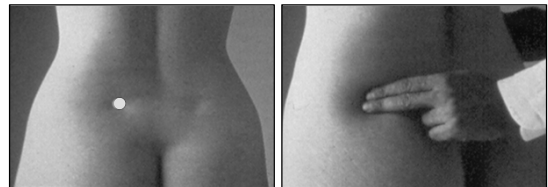
- Mid upper trapezius
- ▲ Origin of supraspinatus

Tender-Point Palpation: V. Arms



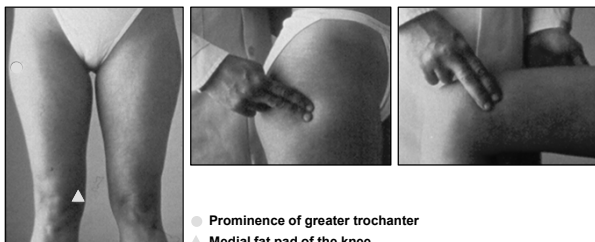
- Lateral epicondyle

Tender-Point Palpation: III. Lower Back



- Upper outer buttock quadrant

Tender-Point Palpation: VI. Legs



- Prominence of greater trochanter
- ▲ Medial fat pad of the knee

Fibromyalgia Patients Have Widespread Somatic Symptoms

| Criterion | % Positive |
|-----------------------------------|-------------|
| Widespread Pain | 97.6 |
| Tenderness 11 of 18 tender points | 90.1 |
| Fatigue | 81.4 |
| Morning stiffness > 15 minutes | 77.0 |
| Sleep disturbance | 74.6 |
| Parasthesias | 62.8 |
| Headache | 52.8 |
| Anxiety | 47.8 |
| Dysmenorrhea | 40.6 |
| Sicca symptoms | 35.8 |
| Prior depression | 31.5 |
| Irritable bowel syndrome | 29.6 |
| Urinary urgency | 26.3 |
| Raynaud's phenomenon | 16.7 |

Syndromes That Overlap with Fibromyalgia

The neurologist sees chronic headache,
the gastroenterologist sees IBS,
the otolaryngologist sees TMJ syndrome,
the cardiologist sees costochondritis,
the rheumatologist sees fibromyalgia,
and the gynecologist sees PMS.

Don't use ANA as a screening test

Sensitivity 99+ %, specificity 85%

Lupus is a rare disease: highest prevalence (AA women) is 400/100,000 (or 4/1000)
= *base rate*

If 1000 women were screened,

4 would be true positive (all SLE positive)

But 150 would be false positive (15% false positive)

A patient with a positive ANA has $4/154 = 2.59\%$ chance of having lupus

In a primary care setting 232 patients referred with positive ANA and widespread pain – 2.1% had lupus, 9.1% had any ANA-associated rheumatic disease; no patient with ANA < 1:160.

Abeles, Abeles. Am J Med 126:342, 2013.

Illustrative Case

- A 50-year-old woman presents with generalized aches and pains and severe tenderness in her hands, knees, ankles and feet
- Her joints are swollen in the morning and she has several hours of morning stiffness
- Physical examination shows widespread tenderness in the neck, shoulders, hands, knees, ankles and feet
- Joints show full range of motion without swelling
- Fibromyalgia may be the most likely diagnosis

Conclusions

- Examine the whole patient
- Identify the target tissue and joint distribution
- Recognize synovitis
- Interpret laboratory studies in the context on the clinical picture