Rheumatology for the PCP

Understanding the Basics of Degen/Autoimmune Syndromes: OA, RA, Psoriatic Arthritis (PsA), Systemic Lupus Erythematosus (SLE)

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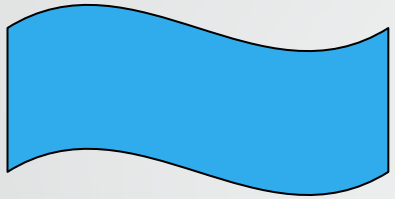
Special Thanks

To my PA friends:

I have NO relevant commercial relationships to disclose



Rick Pope, PA-C, DFAAPA
Ben Smith, PA-C, DFAAPA

For their slides and support

Discussion Outline

Arthropathy Evaluation

Degenerative Joint Disease (OA)

Inflammatory Arthritis (RA, Psoriatic Arthritis)

Systemic Lupus Erythematosus

NOTE: PANCE/PANRE Summary Slides are at the end of this lecture

What is Rheumatology?

A medical science devoted to the study of rheumatic diseases and musculoskeletal disorders, affecting the connecting or supporting body parts, some diseases even affect organs.

Rheuma refers to "a substance that flows", and probably was derived from phlegm, an ancient primary humor, believed to originate from the brain and flow to various parts of the body causing ailments.

There are over 120

rheumatic/musculoskeletal disorders

Health Impact of the Rheumatic/MS Diseases

- **30% of the population** has symptoms of a musculoskeletal condition, **OA** being the **most common**
- When analyzing the 30 most common autoimmune diseases, **about half will have Rheumatoid Arthritis** and half will have one of the others (SLE, polymyositis, etc)
- **One out of every 5-10 office visits** to a primary care provider **is for a musculoskeletal disorder.** 66% of the these patients are <65 years old

Why Rheumatology?

Students seem confused

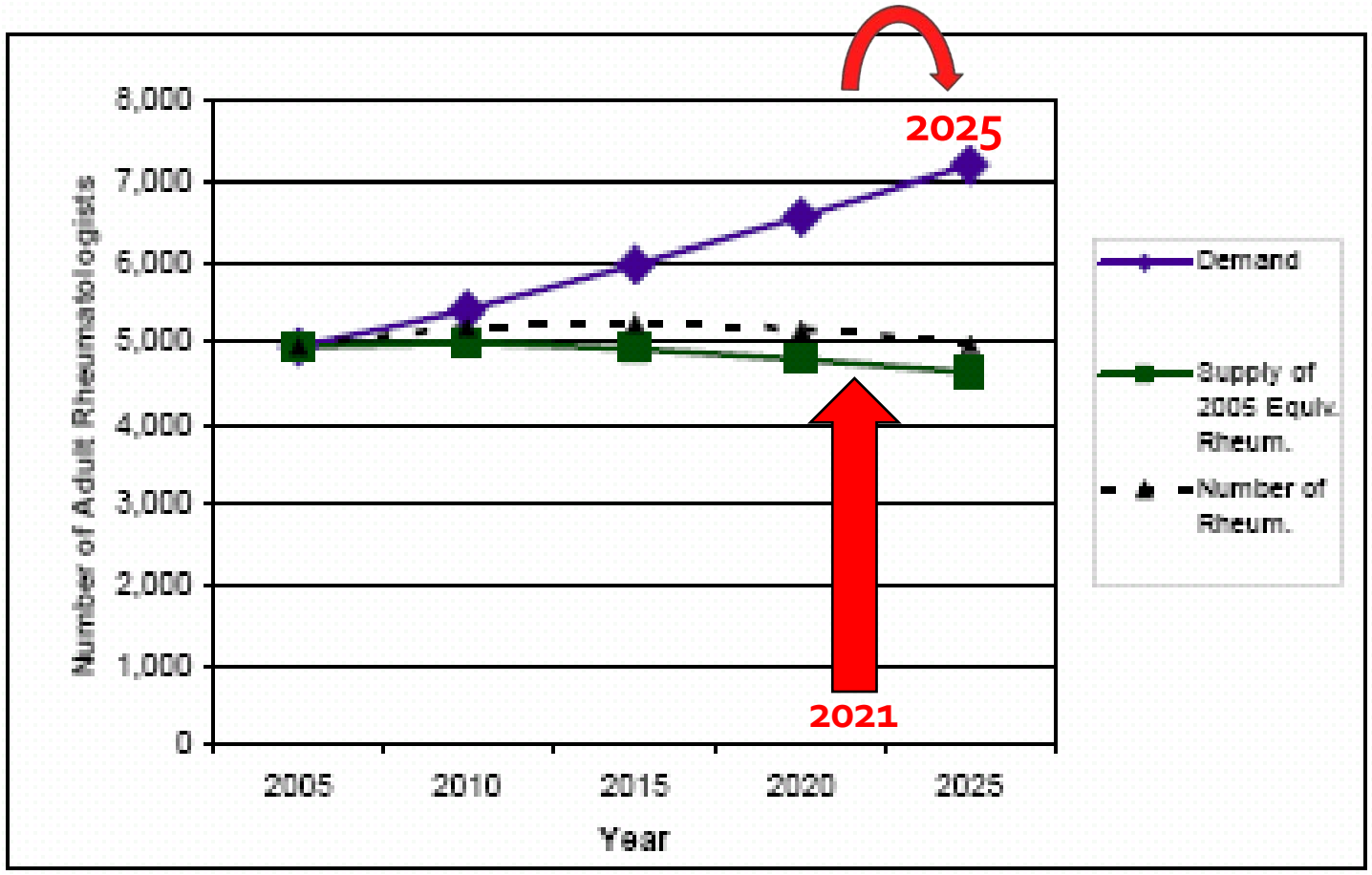
Air of mystery, medical frontier

Misconceptions about medications

Relevance to Primary Care

Speed bump to graduation

Stop and Think Slide: What if you Dx Lupus in a young woman and could not get them in to a Rheumatology practice for one year. What would you do?



Suppy/Demand curve, similar for Pediatric Rheumatologists

This presents PAs with an excellent opportunity to choose Rheumatology as a Specialty workplace

2006 Workforce Study of Rheumatologists: Final Report (www.rheumatology.org)

Deal CL, **Hooker R**, Harrington T, Birnbaum N, Hogan P, Bouchery E, et al. The United States rheumatology workforce: supply and demand, 2005-2025. *Arthritis Rheum* 2007; 56: 733-9

Learning Objectives

1. Apply a higher level of confidence in diagnosing and communicating with patients regarding Rheumatic diseases
2. Practice improved diagnostic skills for the presented common Rheumatologic conditions
3. Appraise variations in Rheumatologic presentations in the primary clinical setting
4. Specify what labs/xrays to order and interpret what they mean
5. Name treatment categories such as NSAIDs, DMARDs, Biologics and Janus Kinase Inhibitors

Discussion Outline

"**Specialism** is a natural and necessary result of the growth of accurate knowledge, inseparably connected with the multiplication and perfection of instruments of precision. It has its drawbacks, absurdities even… A few years ago a recent graduate and ex-hospital intern asked me, apparently seriously, to give him the name of a specialist in rheumatism. We can afford to laugh at these things…"

~ Frederick Shattuck, 1897
Professor of Medicine
Harvard Medical School

- Arthropathy Evaluation
- Degenerative Joint Disease (OA)
- Inflammatory Arthritis (RA, Psoriatic)
- Systemic Lupus
- Pance/Panre Review (If Time Allows)

Rheumatology For The PCP

A Brief Overview:

Joint Evaluations

History of Present Illness

"A good evaluation starts with a good history"

Location	Record Joints (mono, oligo(2-4), poly)
Quality or Character	Dull, Achy, Burning, Stiff, Red
Chronology	Acute, Chronic, Intermittent, Migratory, Morning stiffness *
Severity	Mild, Moderate, Intense
Aggravating or Alleviating Factors	Activity vs Rest, Night pain*
Associated Sx	Constitution, CV, Resp, GI, GU, Derm
Disability	ROM, Gait
Attributions	Patient's perception of the cause (family, job, stress, recent illness, etc.)

Review of Symptoms… And PMH/Social

General:
- Fatigue
- Fever
- Weight Loss
- Raynauds
- Sleep Disturbance
- Lymphadenopathy
- Health Maint. UTD?

Nervous System:
- HA
- Numbness
- M. Weakness
- Seizure

Heent:
- Inflamm eye sxs
- Sicca
- Oral Lesions
- Tinnitus
- Viz Changes
- Scalp tenderness
- Jaw claudication

Menstrual:
- Pregnancies
- Miscarriages
- LNMP
- Contraception

Cardio-Pulm:
- Chest Pain
- SOB
- Pleurisy
- Cough

Gastro:
- Abdm Pain
- Dyspepsia
- Dysphagia
- Diarrhea
- Blood

Social:
- Marital Status
- Occupation
- Travel
- Cigs
- ETOH

Family:
- Connective Tissue Disorder (CTD)
- Arthritis
- Other

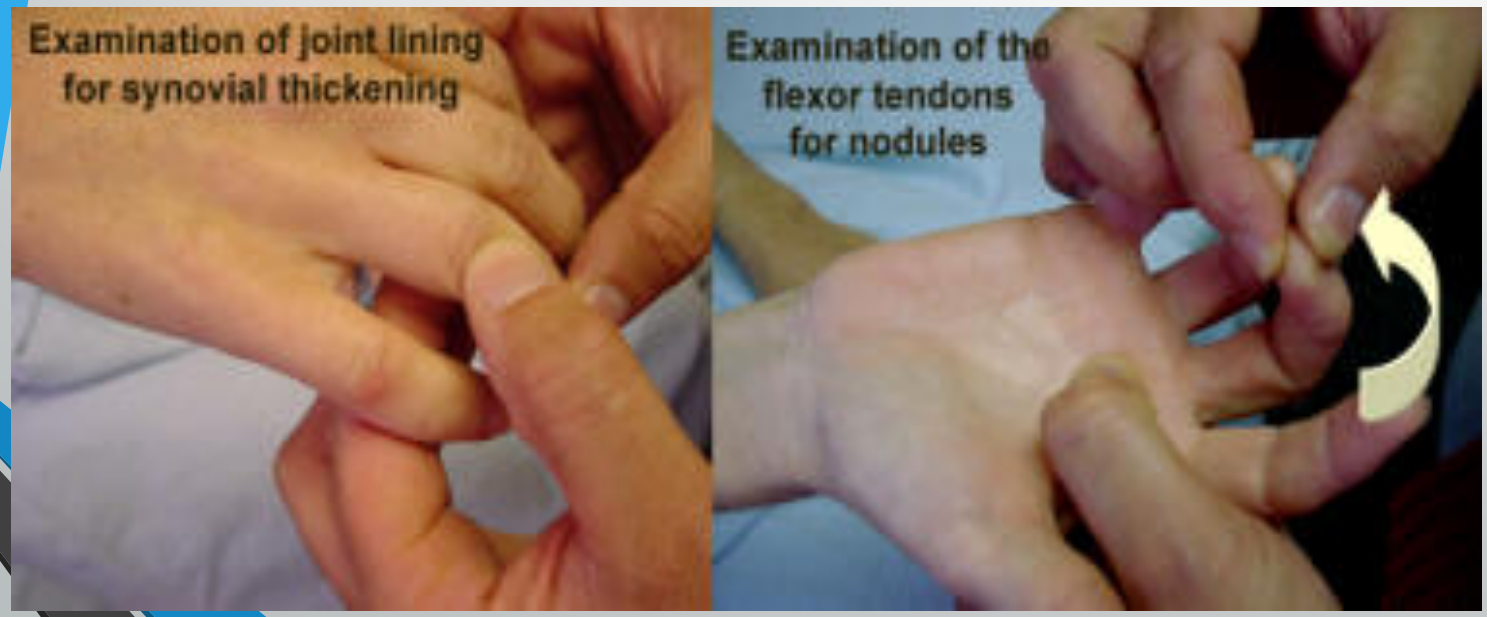
Past Medical HX:
- Child
  - Rh Fever
- Adult
  - DM
  - HTN
  - ASCVD
  - COPD
  - Cancer
  - Hepatitis/ Cirrhosis
  - TB
  - DVT
  - PUD
  - Transfusions

Genito- Urin- Renal:
- Change Urine Color
- Discharge
- Dysuria
- Vaginal Dryness
- Rash
- Ulcers
- Stones

Social History is unfortunately one of the more important Histories…

Physical Exam

- First and foremost, use enough pressure to blanch ones thumb (4kg/cm^2)
- Note: Fibro points require the same amount of pressure
- Be keen to signs of fluid shifts, crepitus, foreign bodies, nodules, scratches/wounds

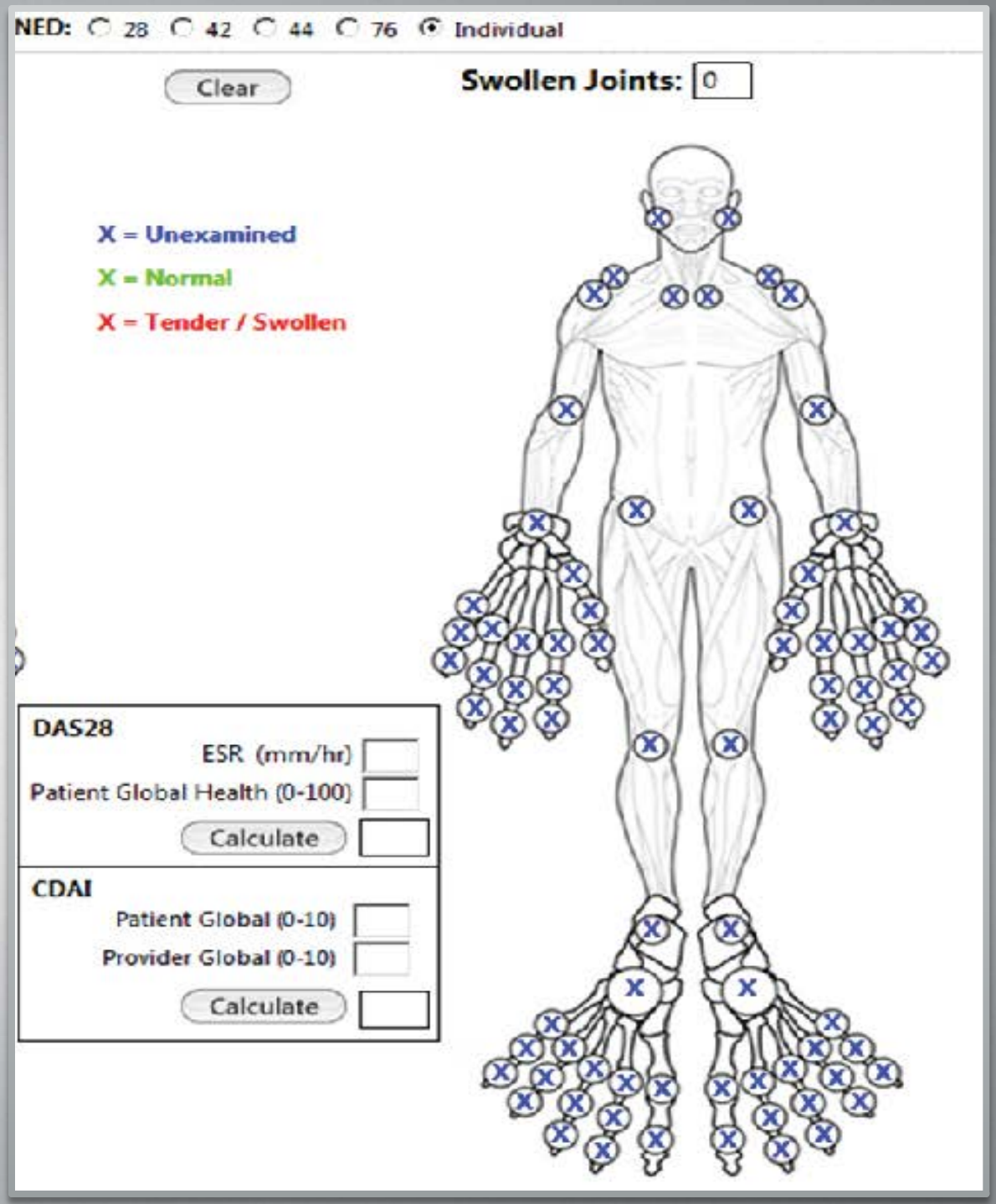


- Direct palpitation and resistive maneuvers causing pain indicate a "Peri" articular source
- Cardinal signs to always look for inflammation:
  - Swelling *
  - Erythema
  - Warmth
  - Pain
  - Loss of ROM *

Homunculus

Latin- “Little Man”

- Differentiate between tender, swollen
- Differentiate between acute and chronic



Summary Tables of differences in Mechanical Vs Inflammatory

History	Inflammatory Prototypical (RA)	Non-Inflammatory Prototypical (OA)
Swollen Red Tender Joints	+++	+
AM Stiffness	+++	+
Aggravating Sxs	Rest	Activity
Alleviating Sxs	Activity	Rest
Extra-articular Manifestations	+++	-

*** > 1 hour for stiffness, Fatigue is included in extra articular

Exam		
Swelling, Warmth, Redness, Tenderness	+++	+
ROM	+	+
Extra-Articular Manifestations	+++	-

X-Ray Evaluation

	Inflammatory (RA)	Non-Inflammatory (OA)	Other
Ankylosis	Rare	-	+(Seronegative Spondylo-arthropathy)
Alignment	++	+(Irregular)	
Bone Density	++	-	
Sclerosis	-	++	
Osteophyte	-	++	
Periosteal	-	-	+(Seronegative)
Cartilage Space	++ (Sym)	+(Asym)	
Calcification (Soft Tissue)	-	-	+(CPPD)
Cysts	Pseudocystic	Subchondral	
Distribution	PIP/MCP/Carpal	DIP/PIP/ 1st CMC	
Erosions	+++	-(Erosive OA)	
Swelling	+++(Fusiform)	++(H&B Nodes)	

Rheumatology For The PCP

A Brief Overview:

Osteoarthritis and Treatment:

Case One

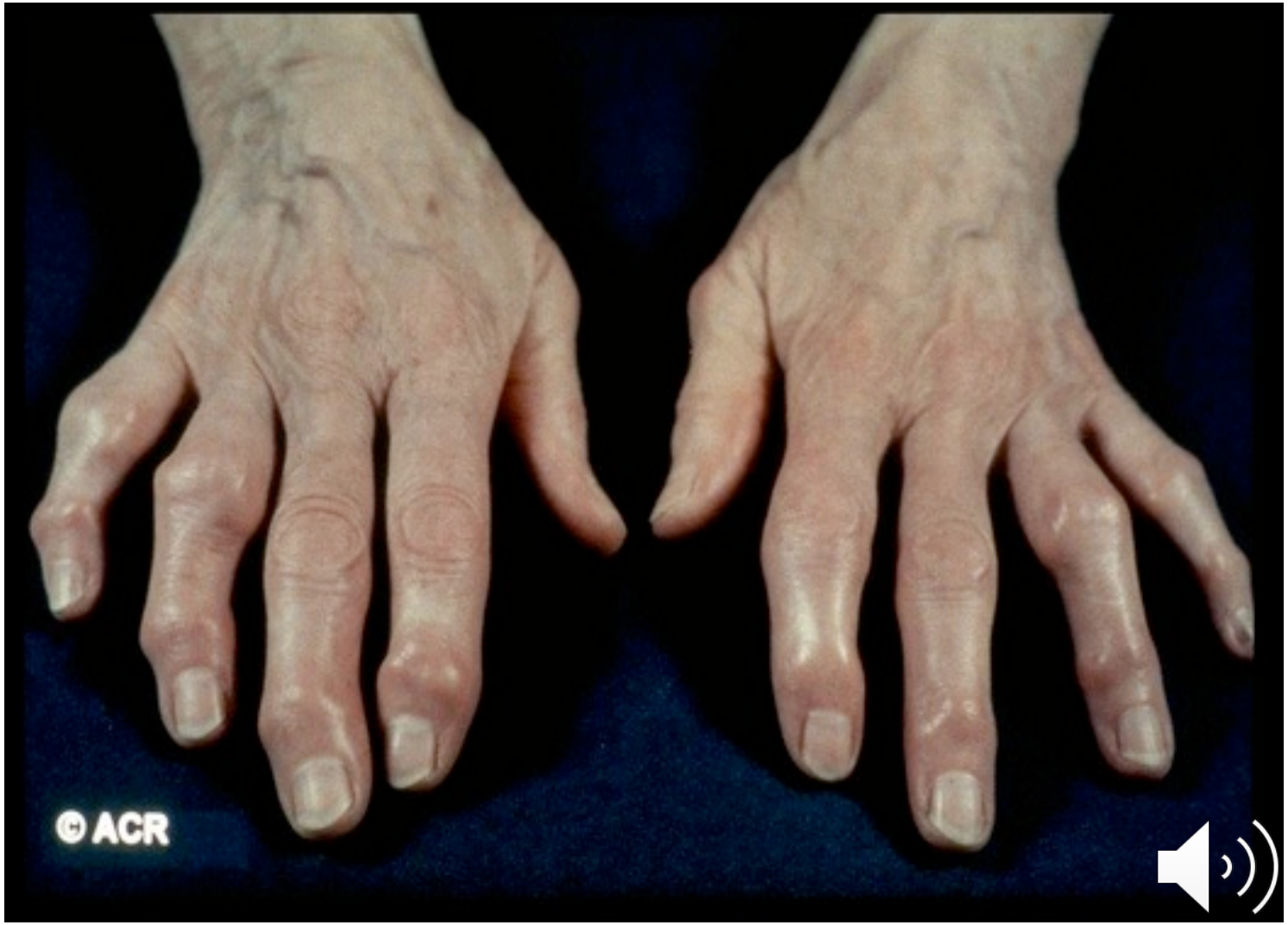
HX: 50 y/o Female

- Hard to open Jars
- Pain better after exercise/movement
- Mother and Grandmother had similar issues later in life as well.

AM Stiffness = 15 mins

PE: Small joint pain/ stiffness, thickening

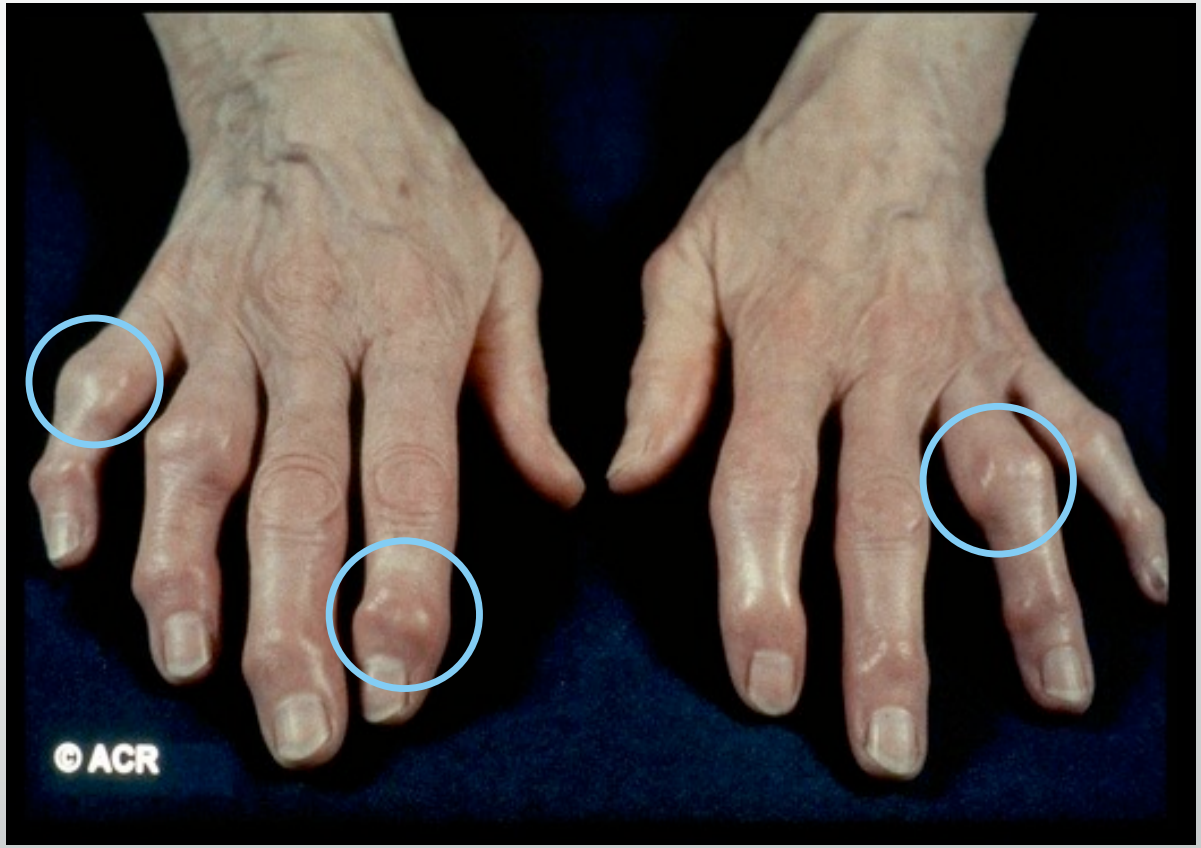
Lab: ESR 10 (Normal)



Understanding the Basics

Osteoarthritis: Degenerative Joint Disease

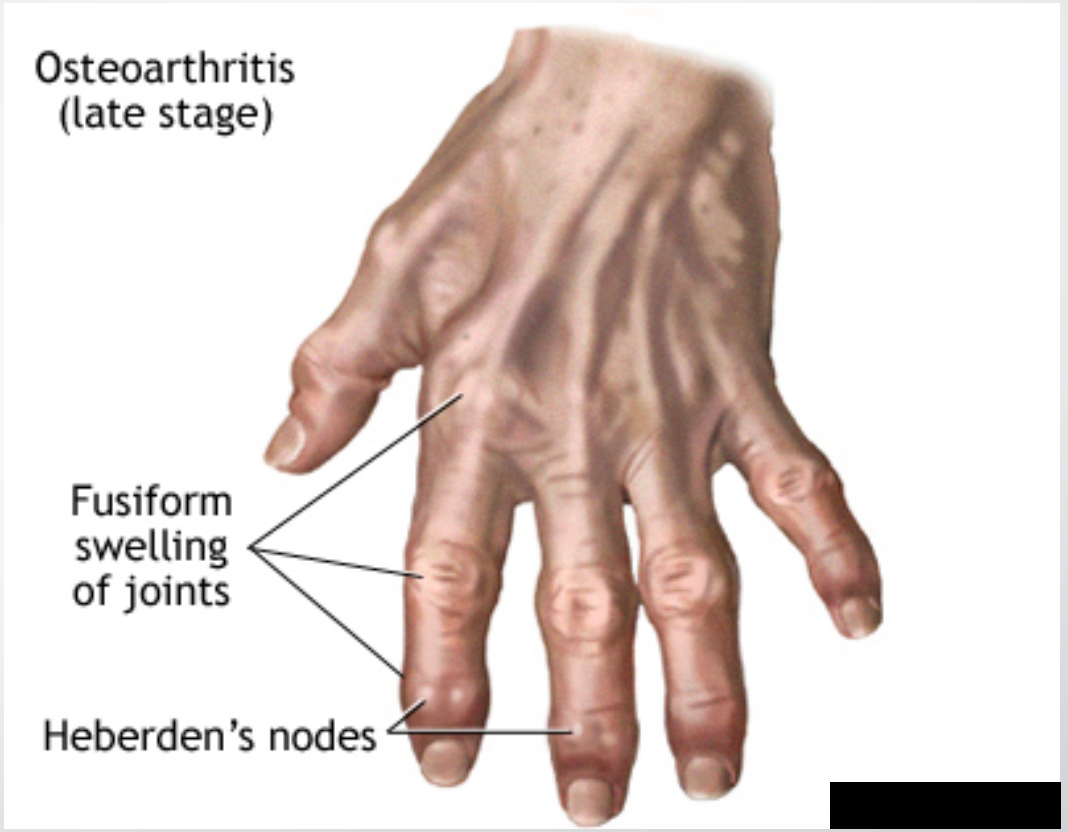
- Hard boney enlargements
- **Heberden's** nodes at the DIP joints
- **Bouchard's** nodes at the PIP joints
- Often have "squared first CMC joint due to osteophytes at that joint
- **Can't stop it's Progress!**
- Limit NSAID use if possible

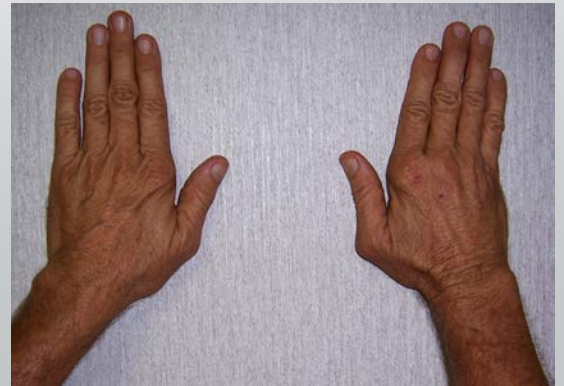


Osteoarthritis

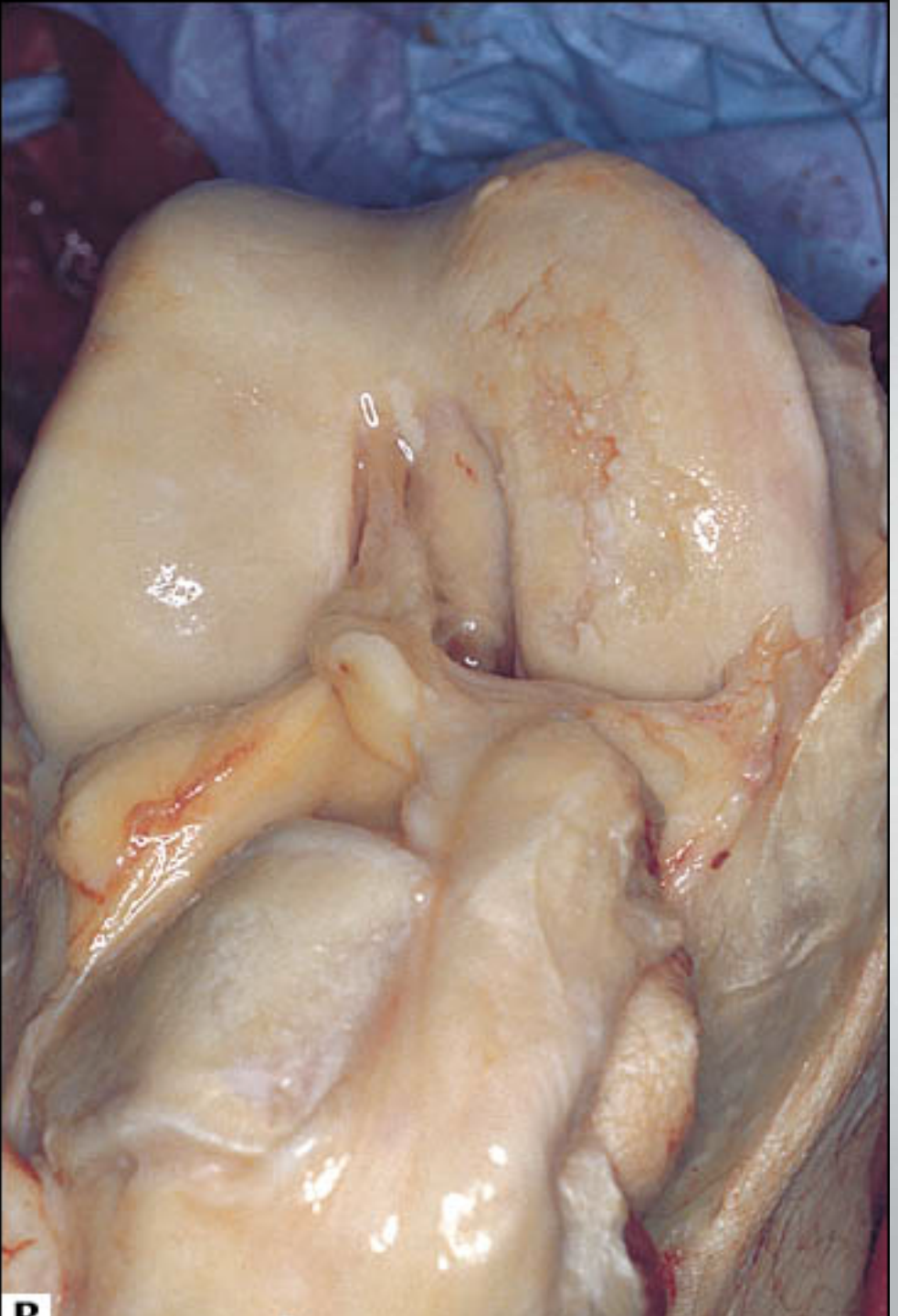
Clinical Features

- Reduced range of motion*, joint pain, crepitus
- Pain worse with activity, relived with rest
- Morning Stiffness < 30mins
- Gelling / Theatre Sign- Stiffness after period of rest
- Bony Hypertrophy most obvious in hands
  - **Bouchard's** Nodes: PIP Joints
  - **Heberden's** Nodes: DIP Joints





CMC OA
"Squaring Off"



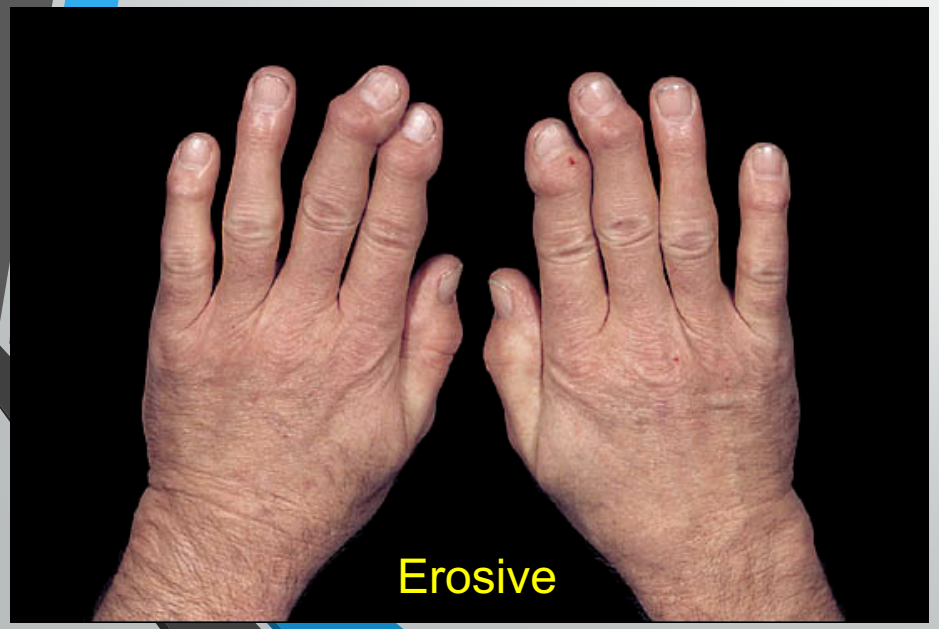
Primary Osteoarthritis

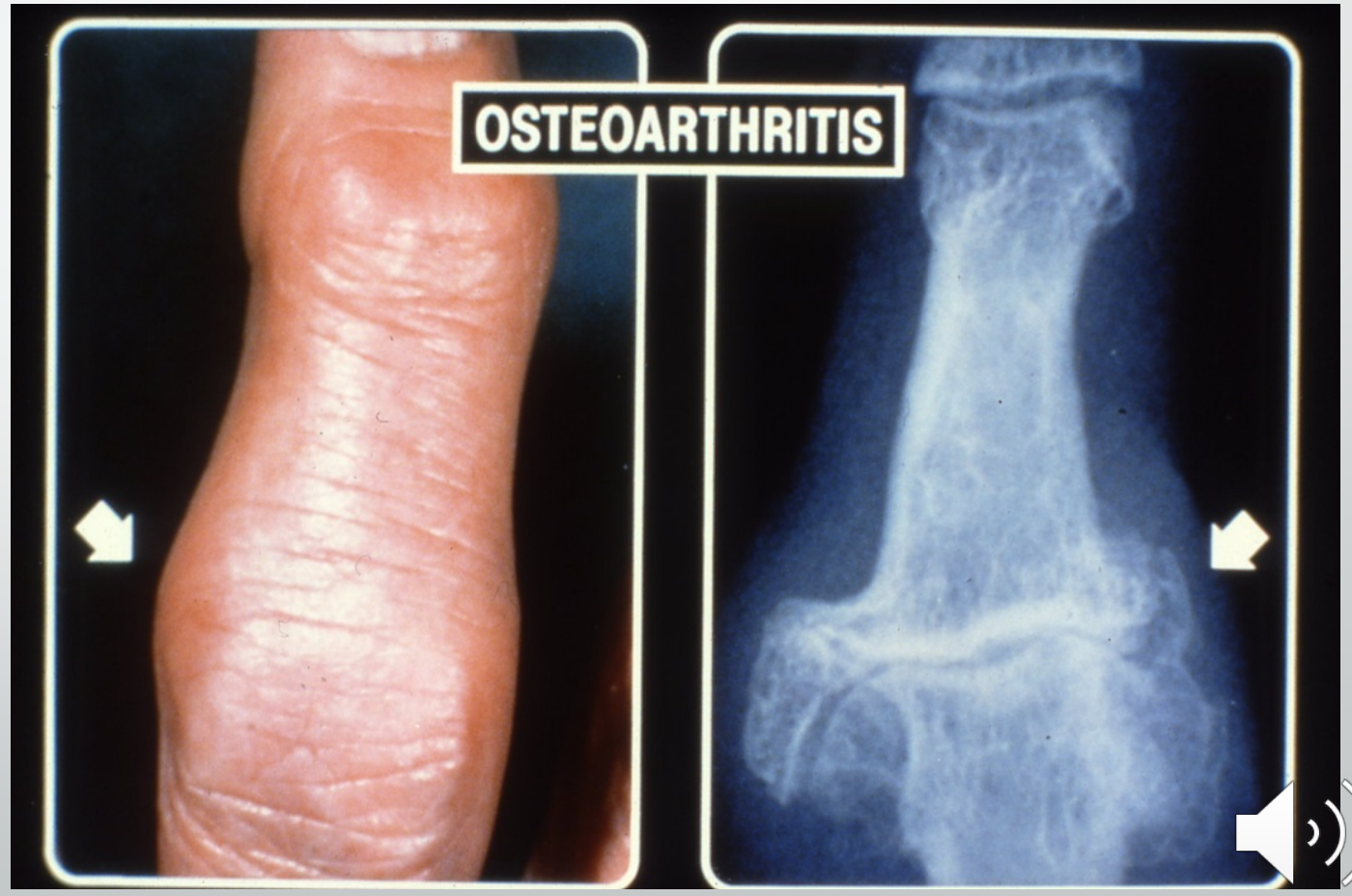
- Cartilage Functions are protective to the underlying bone and nerves
- Cartilage functions include shock absorption and mechanical range of motion
- Functions also include nourishment and maintenance of the fluid viscous layer between the joints as well
- Cartilage replacement preceded the 1980s significantly, but despite bold claims and cutting edge surgical methods and technolog

Primary Osteoarthritis

The Process:

- As the cartilage degrades new bone formation occurs
- Interferes with function and causes pain

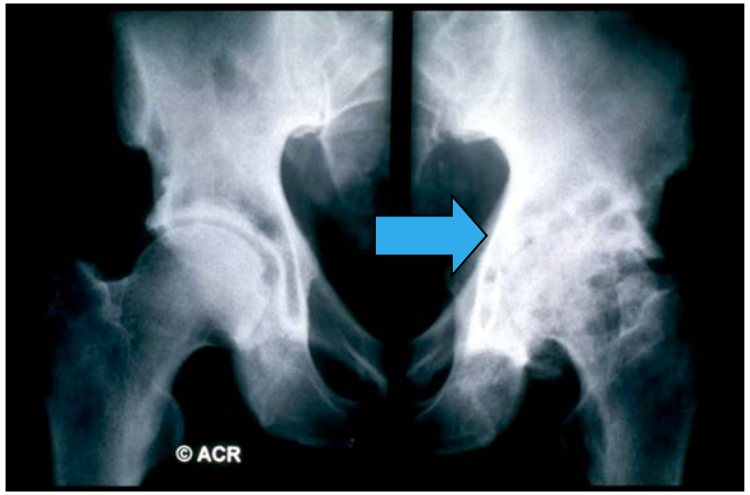


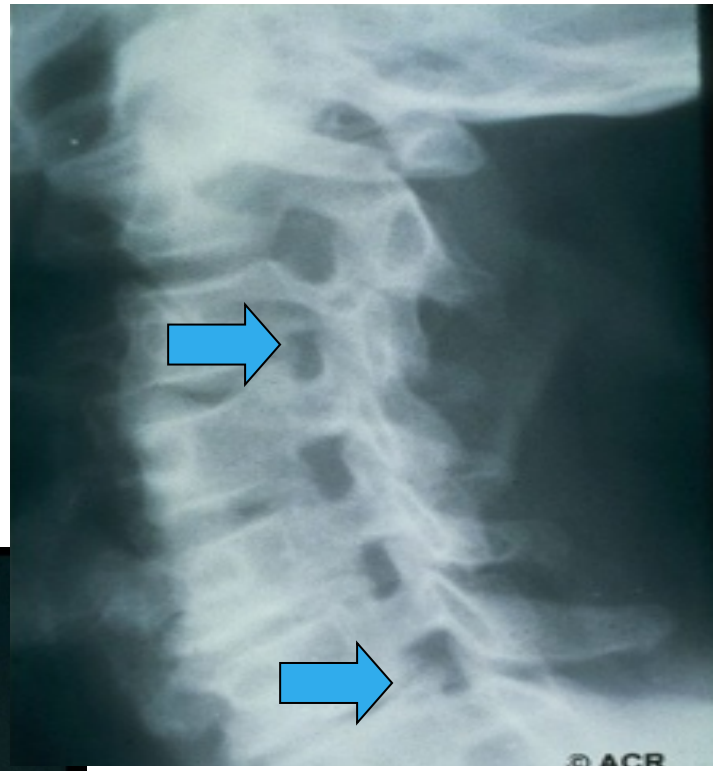


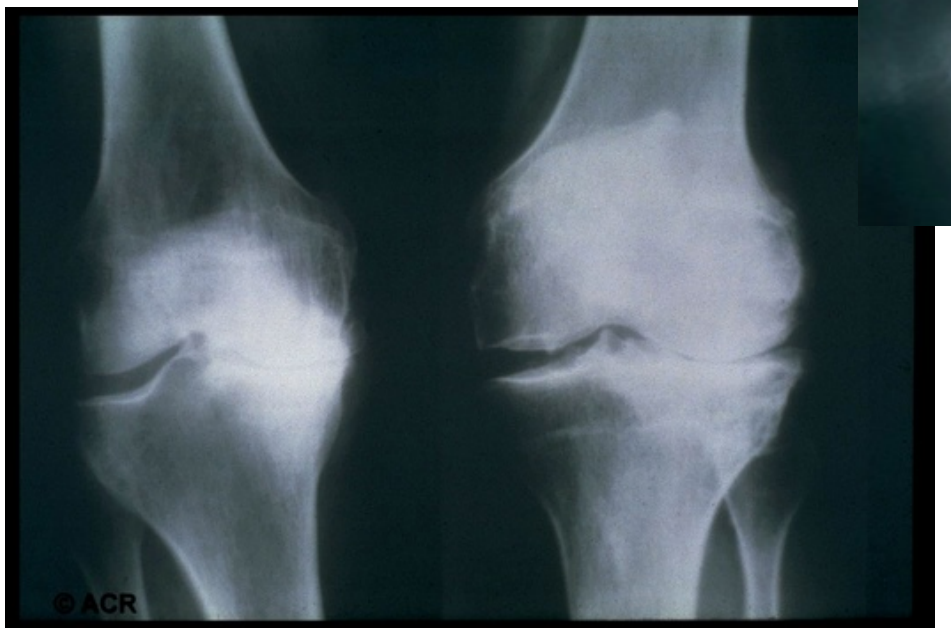
X-Ray Changes of OA

THE KEY IS IN THE X-RAY

- Non-uniform joint space narrowing
- Subchondral Cysts
- Osteosclerosis (Dense Bone) on both sides of joint space
- Osteophytes







GET STANDING KNEE (WEIGHTBEARING) ***

Osteoarthritis: Differential DX

- Osteonecrosis / Avascular Necrosis
- Psoriatic Arthritis
- Gout / Pseudo gout
- Hemochromatosis
- Reiter Syndrome
- Other unlikely diseases IA, Fibromyalgia, Lead / heavy metal poisoning, Poor diet (High Fructose Corn Syrup)

OSTEOARTHRITIS: Analgesics/Procedures

Pain Meds

Must know regulations & dosages (some less toxic than NSAIDS)

1. acetaminophen (max 3000 mg)
2. tramadol
3. codeine
4. hydrocodone (Class II)
5. oxycodone
6. others (narcotic class I and II)

Viscosupplementation (HYALURONIC ACID)

Hyalgan - 5 weekly injections
Synvisc - 3 weekly injections
Synvisc One – Single injection
Supartz- 3 weekly injections
Orthovisc-3 weekly injections
Euflexxa- 3 weekly injections
Durolane- Single injection

Some insurances are no longer paying for this !!

Steroid Injections

Methylprednisolone acetate (Depomedrol) 60–80 mg q 3-4 months

Triamcinolone Acetonide Extended-Release Injectable Suspension (TA-ER) (Zilretta *)
NEW 32 mg of TA embedded in biodegradable polymer microspheres q 3 months

* Data on File. Flexion Therapeutics, Inc

Structural Classes / Risks of NSAID's

Propionic Acid
Ibuprofen
Fenoprofen
Naproxen*
Oxaprosyn
Ketoprofen
Flurbiprofen
*No Cardiac Risk

Acetic/Fenamic Acid
Sulindac
Indomethacine
Diclofenac
Etodolac
Tolmetin
Meclofenamate

Salisalates
ASA
Na Salic
Salsalate
CholMgTrisal
Diflunisal

Risks
Previous GI NSAID
Complications
Previous Ulcer
Smoking
Use with Corticosteroids
Use with Anticoagulants
Age
Hypertension
Edema
Renal

Cox-2 Inhibitors
Celecoxib
Etoricoxib*
Lumiracoxib*
*not FDA approved

Enolic / Carboxylic Acid
Piroxicam
Meloxicam
Ketorolac

Nonacidic Comp
Nabumetone

Alternative, Therapies?

Prolotherapy*, Platelet Rich Plasma, Stem Cell Injections

Naturopathy

Diet, Exercise, PT/OT?

Stop and Think Slide… The number one cause of long term disability…

Rheumatology For The PCP

A Brief Overview:

IA and Treatment

Case Two

HX: 52 y/o female

- Gradual onset joint swelling, stiffness x 3 months, MS > 1hr
- No recent infections
- Sister and Great Uncle had some sort of Arthritis that crippled them

PE:

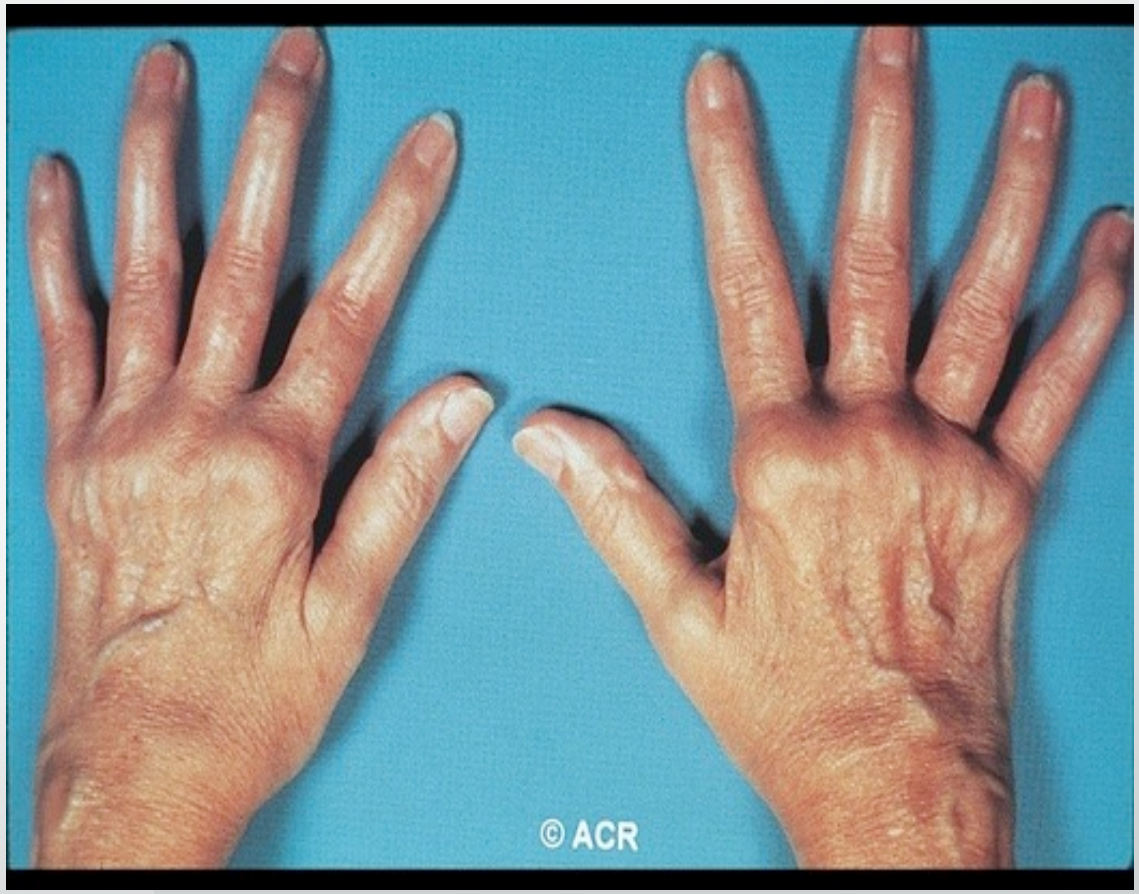
- Soft MCP synovial swelling
- Synovitis and volar subluxation at the MCP joints
- Synovitis of the wrists
- Synovitis of the PIP joints with early **Swan Neck Deformities**

LAB: ESR 40 , RF mildly elevated at 17 IU/mL

Understanding the Basics

Inflammatory Arthritis

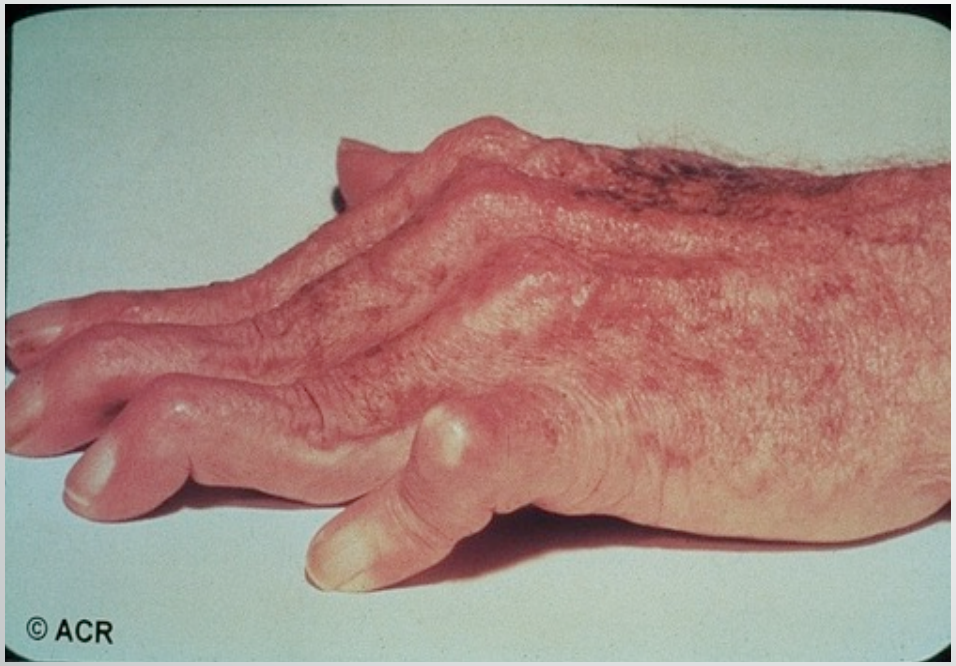
- Rheumatoid Arthritis most common, However SLE, Spondyloarthritis, and PSA collectively will show up more often
- **Exam:** Symmetrical distribution often hands/wrists
- **Lab**:+ RF, and possible the CCP AB if ordered, SED, CRP, and Protein electrophoresis are contributory but not specific
- Need Rheumatology referral to sort out Diff Dx



What We Want To Prevent

Permanent Joint Changes
Extra Articular Manifestations
Limited Activities of Daily Living

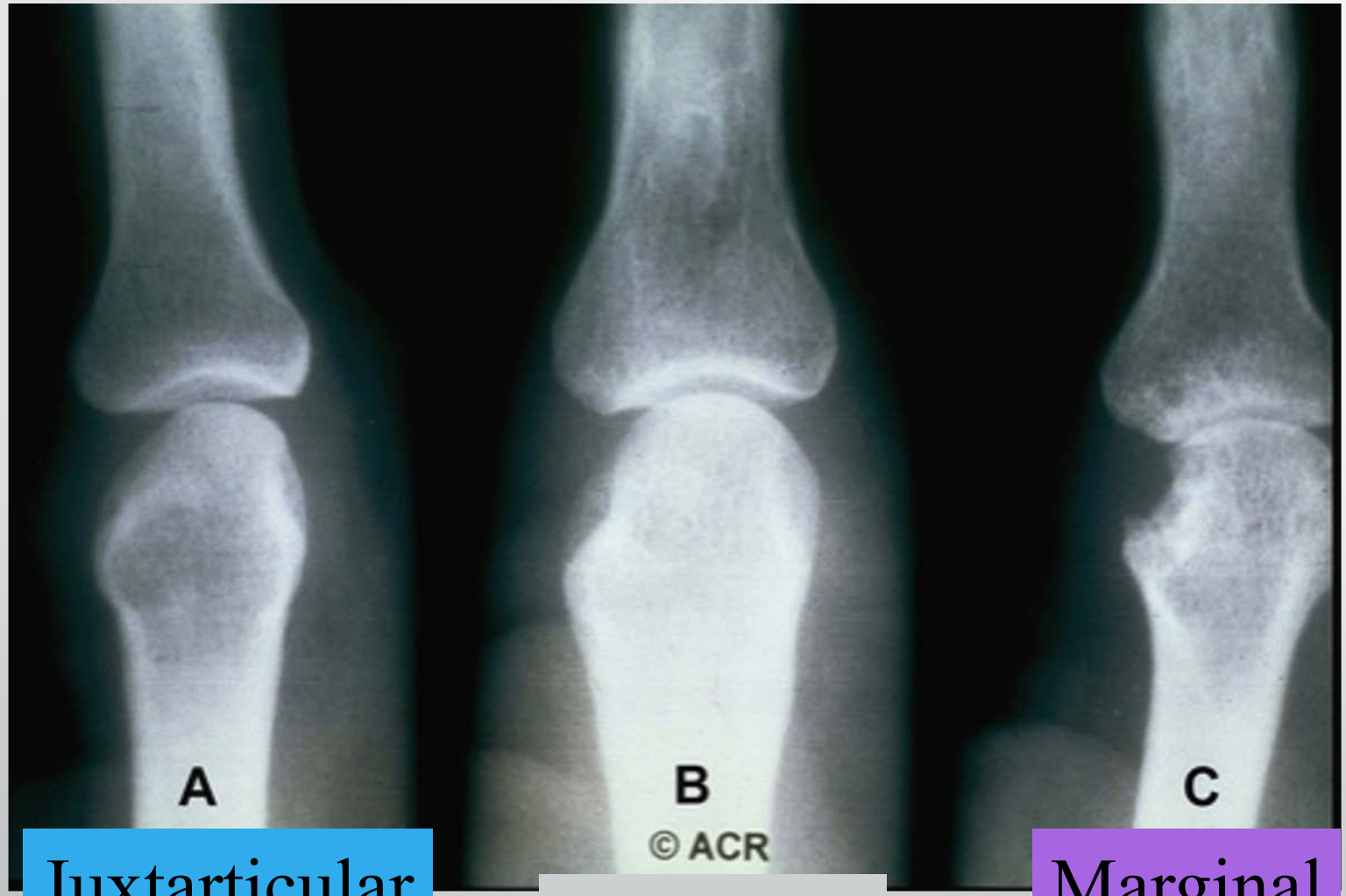
Swan Neck and Boutonnière Deformities



RA if left untreated

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

Xray Changes in RA



Juxtarticular osteoporosis

Soft tissue swelling

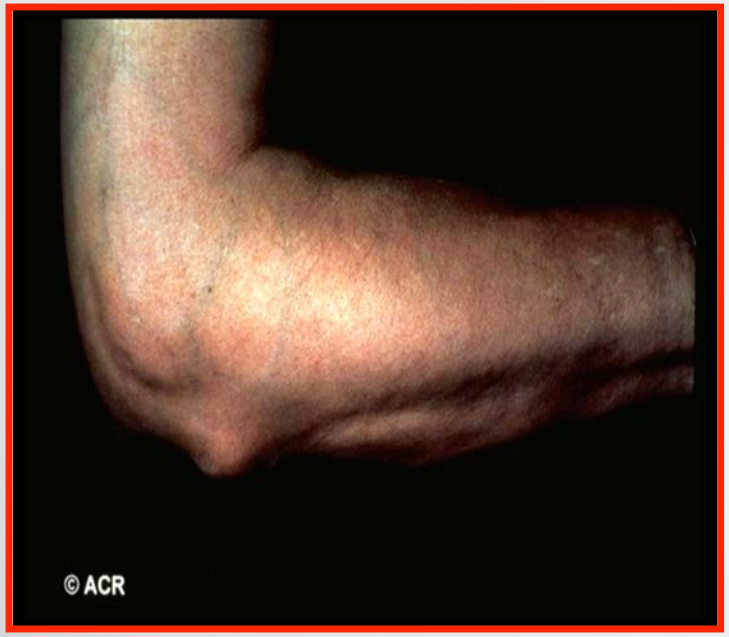
Marginal erosions

Uniform joint space narrowing

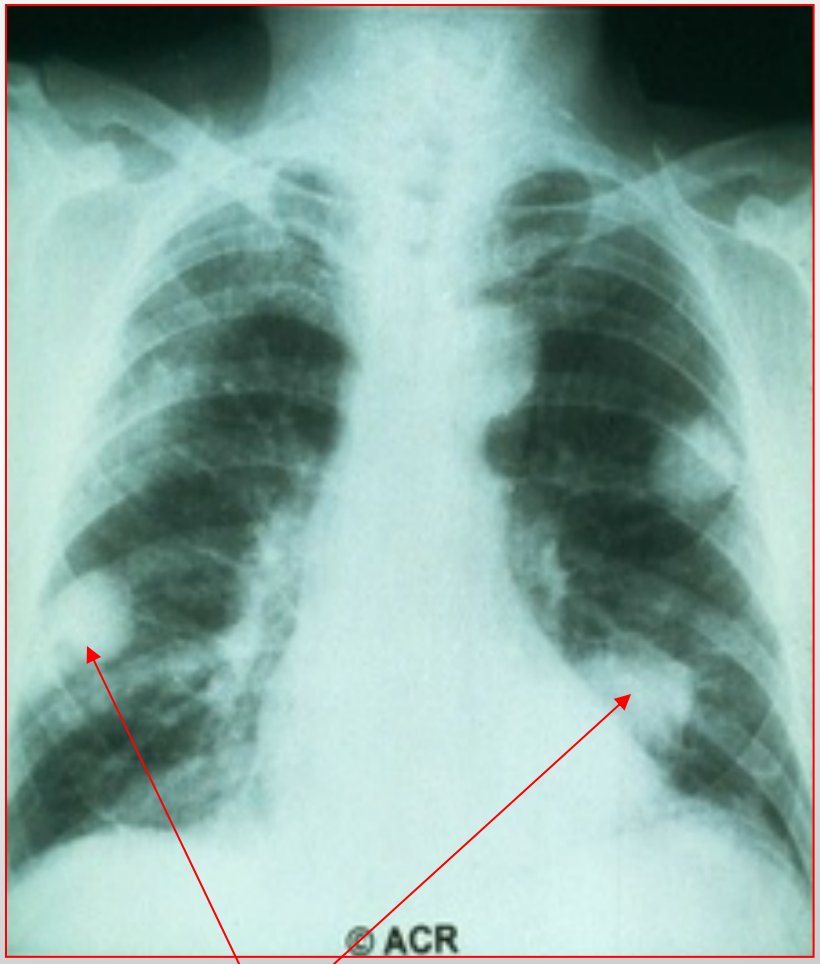
Bilateral
Hands/Feet

Involves all synovial joints except T & LS spine

RA Nodules and Lung Disease

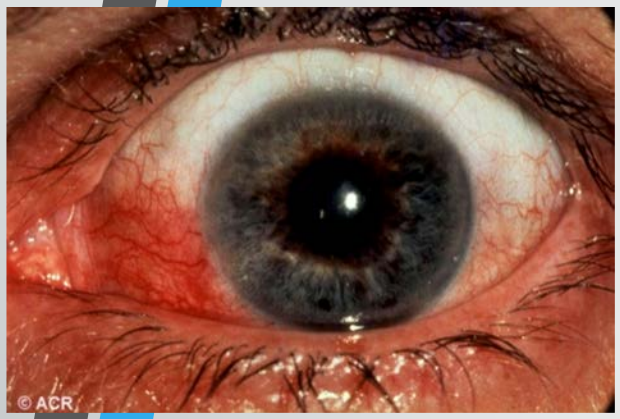


- Hard to distinguish from gouty tophi or other subcutaneous nodules
- Characteristic histology
- Occur at pressure points-elbows, heels
- **Associated with + RA factor, + CCP, and poorer outcome**



Pulmonary Nodules
Pleuritis
Interstitial Fibrosis

RA Eye Involvement and Vasculitis



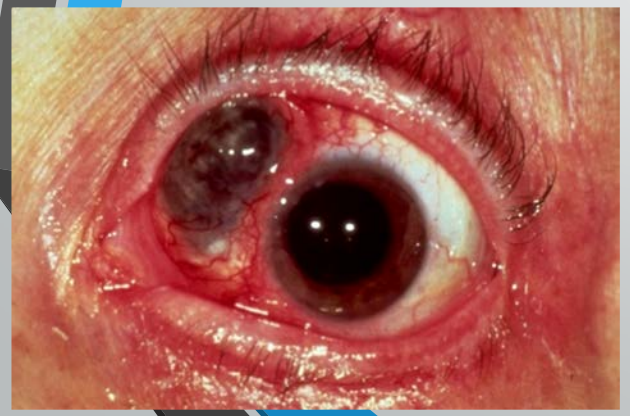
Episcleritis

Painful redness in sclera

Not Unique to RA

Not usually an emergency

Topical and underlying cause treatment



Scleritis

Aggressive Granulomatous process

Can perforate

Vasculitis

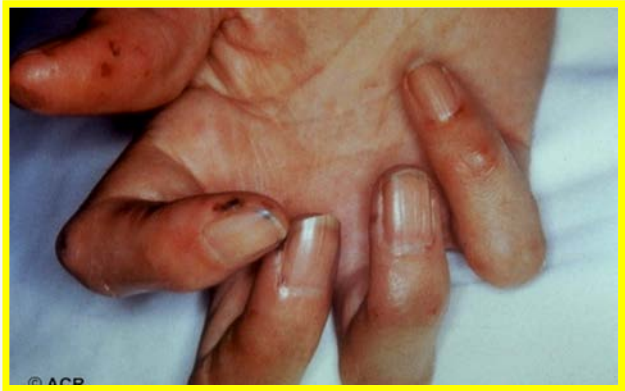
Usually longstanding RA

RF +, Nodular disease

Fever, Neuropathy, Rash, GI, Cardiac

Spares kidneys and lungs

Poor prognosis !!!

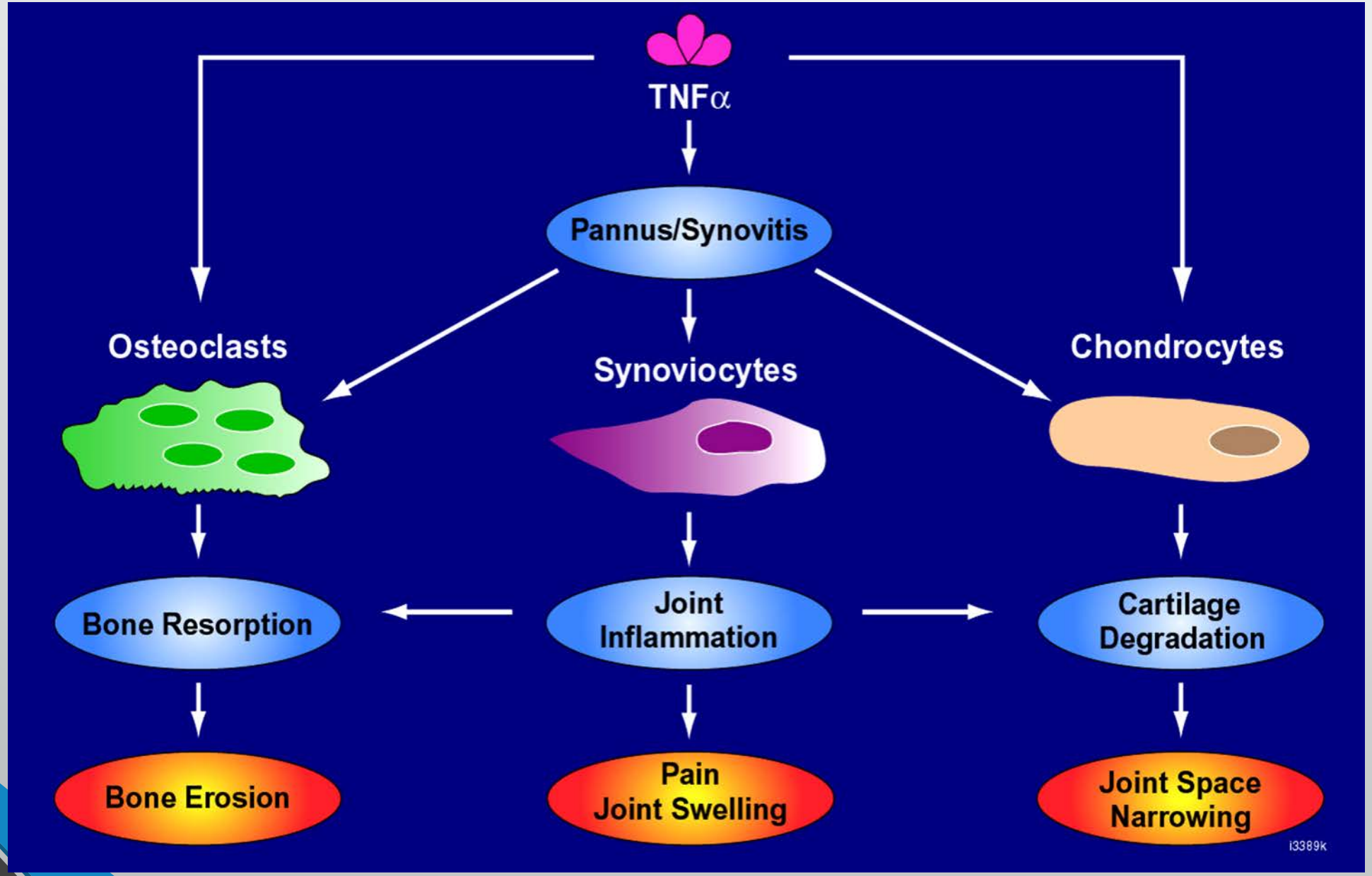


Felty's Syndrome

A rare manifestation of extra articular RA
Think "SANTA" when Identifying
Patients will be very ill, and will likely suffer multiple infections, require hospitalization
Often due to long term uncontrolled RA… But not always

S	**S**plenomegaly
A	**A**nemia
N	**N**eutropenia
T	**T**hrombocytopenia
A	**A**rthritis (Rheumatoid)

Central Role of TNFα in RA



Kirwan JR, *J Rheumatol.* 1999; 7:720-725.

Common Rheumatology Lab

ANA, ENA, RF, CCP AB (Serology)

HLA-B27 (Gene test – Spondyloarthropathy)

C-Reactive Protein

Male = age / 50

Female = age / 50 + 0.6

Rises and falls more quickly than ESR

SPEP

The most sensitive test for inflammation

Ordered to look for chronic inflammation and Multiple Myeloma

Erythrocyte Sedimentation Rate

Normal Calculations

Male = age / 2

Female = (age + 10) / 2

Causes of Elevated ESR/CRP

- **Infection**
- **Connective Tissue Disorder**
- **Malignancy**
- **Pregnancy**
- **Anemia**
- **Obesity / PCOS**

Other Miscellaneous tests:

Ferritin – Gen inflammation, Adult stills disease

CBC – Anemias of different sorts

Met. Panel – Inflammation in liver, renal dysfunction

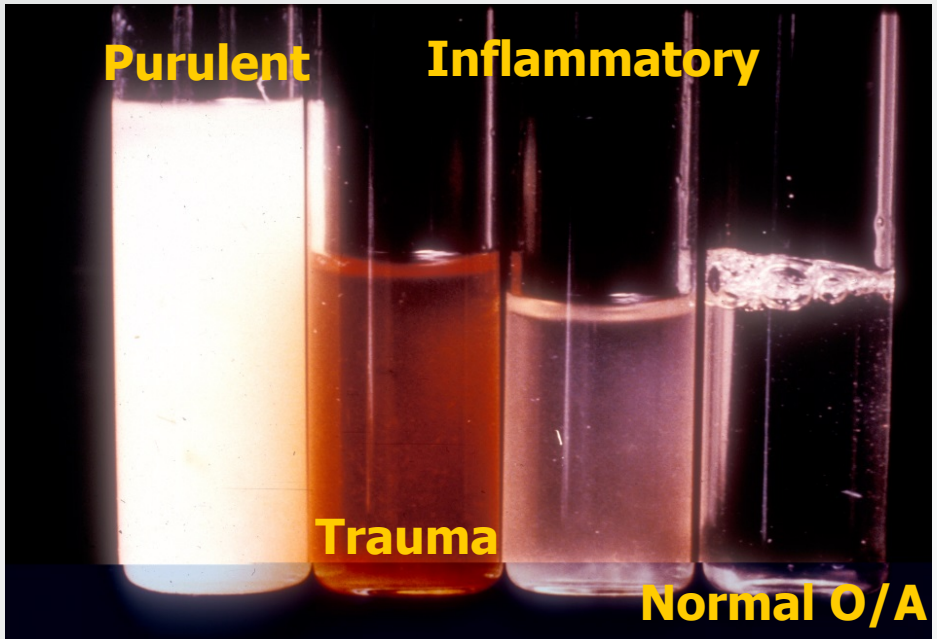
Complement Levels – SLE and complement driven diseases

Immunoglobulins – a WIDE variety of disorders

Rheumatoid Arthritis Lab Notes

- ESR and CRP usually elevated
- **Rheumatoid factor (RF)** positive in ~ 80% of pts
  - **(+) RF Can occur in active TB, SLE, Sjogren's, Polymyositis, Dermatomyositis, Vasculitis, Scleroderma, Cryoglobulinemia, Juvenile rheumatoid arthritis**
- **Anti-CCP antibody:** A most unusual time bomb
  - High specificity
  - Correlated with aggressive, erosive disease
  - Practically diagnostic with suggestive physical exam and Hx

SYNOVIAL FLUID ANALYSIS



Synovial Fluid Analysis Characteristics

	Volume (mL)	Viscosity	Clarity	Color	WBC/mm³
Normal	< 3.5	**High**	Clear	Colorless/ Straw	< 150
Noninflammatory	> 3.5	**High**	Clear	Straw/ Yellow	< 3000
Inflammatory	> 3.5	Low	Cloudy	**Yellow**	> 3000
Septic (purulent)	> 3.5	Mixed	**Opaque**	Mixed	> 50,000
Hemorrhagic	> 3.5	Low	Mixed	**Red**	**Similar to blood level**

Additional Positive Rheumatoid Factor in <u>Non-Rheumatic</u> Diseases

Frequency: Normal individuals (< 5%)

Population: Elderly

<u>Special populations:</u>

Bacterial infections

- Endocarditis
- Leprosy
- Syphilis
- Lyme disease
- Periodontal disease
- TB

Viral infections

- Hepatitis C (also A & B)
- Parvovirus
- Rubella
- CMV
- HIV
- EBV

Other

- Lymphoproliferative disease (Lymphoma, Leukemia)
- Lung disease (Interstitial fibrosis, (Silicosis, Asbestosis)
- Chronic liver disease (Hepatitis C)
- Sarcoidosis
- Post-vaccination
- Primary Biliary Cirrhosis
- Malignancies

Parasitic Infections

RA Medications

- OTC Analgesics
- Centrally Acting Analgesics
  - Narcotics, Tramadol, SNRIs
- Prescription NSAIDS
  - Nonselective, Cox-2 Selective
- Corticosteroids
  - Oral, Injectable, Intraarticular
- **Disease Modifying Antirheumatic Drugs**
  - Immunosuppressive, Nonsuppressive, Biological (Rapidly Expanding + Biosimiliars)
  - Janus kinase (JAK) inhibitors (intracellular enzyme modulators) (Expanding)

Disease Modifying Antirheumatic Drugs (DMARDs) for RA

Non-immunosuppressive

Plaquenil
Gold products*
D-Penicillamine*
Minocycline*
Azulfidine

Immunosuppressive*

Methotrexate
Imuran
Arava
Cytoxan
Prednisone

Adalimumab
Infliximab (TNF)
Etanercept
Rituximab (B Cell)
Abatacept (T Cell)

DMARDs and Biologic/JAK agents can increase risk of infection !

Evidence suggest aggressive early treatment is unarguably superior for safety and long term morbidity and mortality outcomes

Biological * & JAK Agents (Tofacitinib, Baricitinib)*

*** Partial List**

Types of Biologic Agents and Enzyme Inhibitors for RA Currently in Use

TNF inhibitors:

Etanaercept (Enbrel Injection)

Adalimumab (Humira Injection)

Certilizumab (Cimzia Injection)

Infliximab (Remicade IV)

Golimumab (Simponi Injection and IV)

IL-6 inhibitors:

Tocilizumab (Actemra Injection and IV)

Sarilumab (Kevzara Injection)

T Cell inhibitor:

Abatacept (Orencia Injection and IV)

B Cell inhibitor:

Rituximab (Rituxan IV)

Janus kinace (JAK) Inhibitor(Small molecule):

Tofacitinib (Xeljanz, Oral)

Olumiant

Renvoq

(Newer type of treatment category)

JAKs are intracellular enzymes which transmit signals on cell membrane to influence immune cell function

What is a Biosimilar?

- **Lower priced copies of first to market biologics**
- Hard to replicate
- Highly similar but not exact copies
- Estimated to save US $47 Billion over next 10 years (or less)
- In Europe since 2006, cost 10-15% less
- Ex: Zarxio (for Neupogen) but not yet released

- Has FDA approval
- Concerns about potential efficacy, safety and convenience
- Biotech drugs account for 22% of US annual expense on Rxs
- 15+ new biotech drugs may be approved soon
- Example of uses: RA, DM, cancer
- They are not the same as as competitive drugs of similar class, Enbrel Vs. Humira, Xeljanz Vs. Olimiant

Ex: Infliximab (Remicade) and Infliximab-dyyb (Inflectra)

Article in WSJ March 7-8, Vol CCLXV No 54

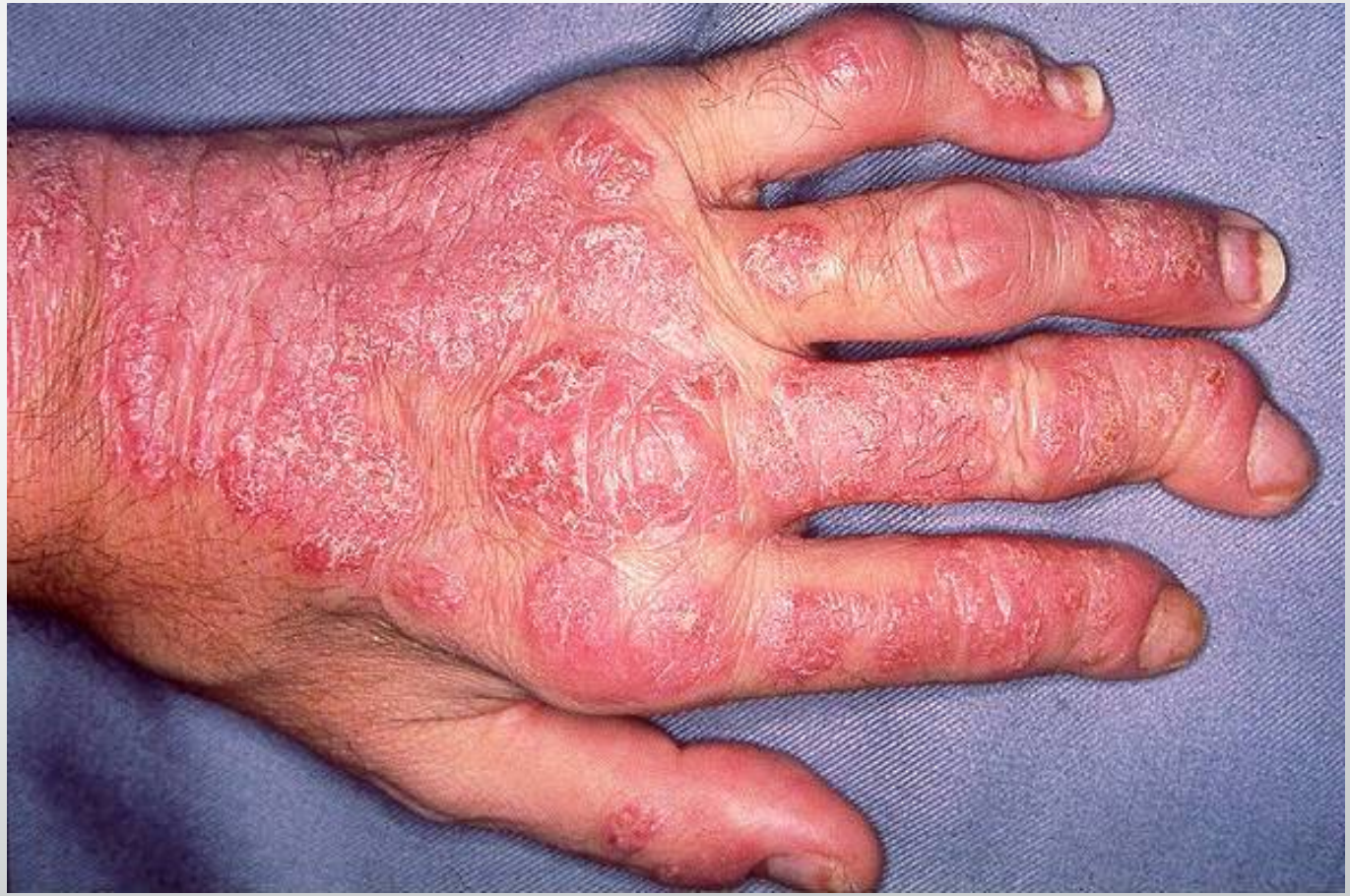
Case Three

Hx: 35 y/o female gradual onset episodic, asymmetric joint pain and swelling, 1 or 2 joints x 6 months, can resolve spontaneously, Psoriasis on hands, elbows, scalps, knees

FHx: of psoriasis

PE: Nail pitting, 3 swollen fingers, 1 swollen toe

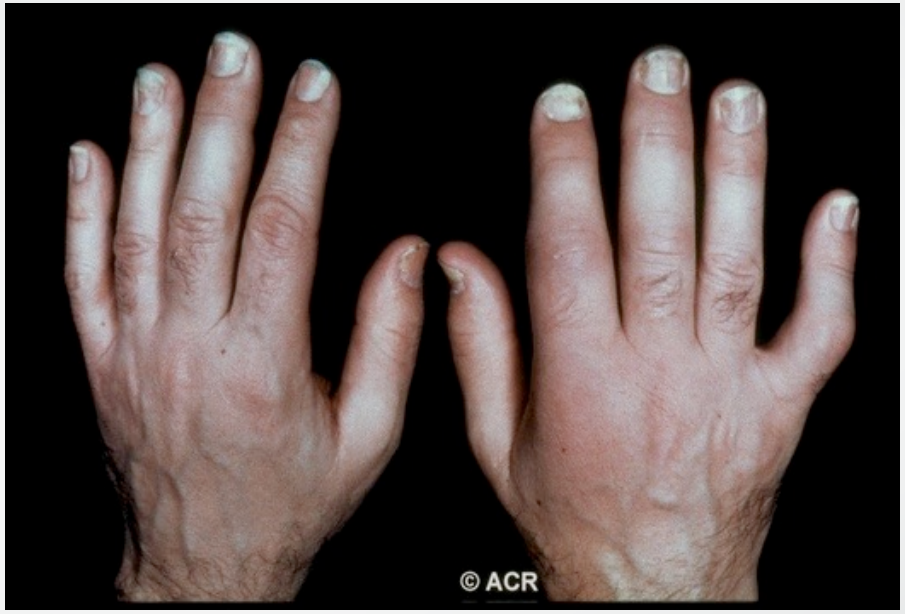
Lab: Neg ANA, RF,
ESR 56

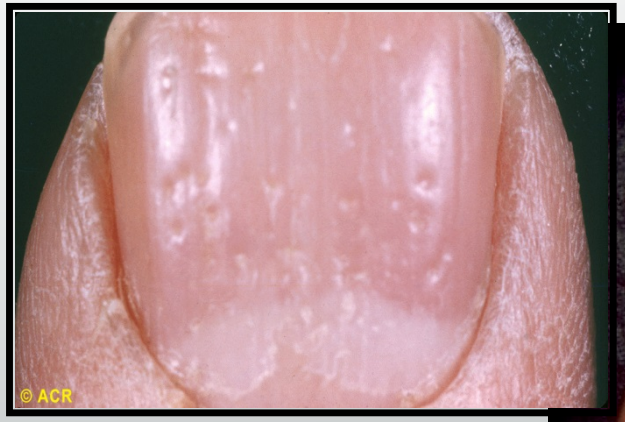


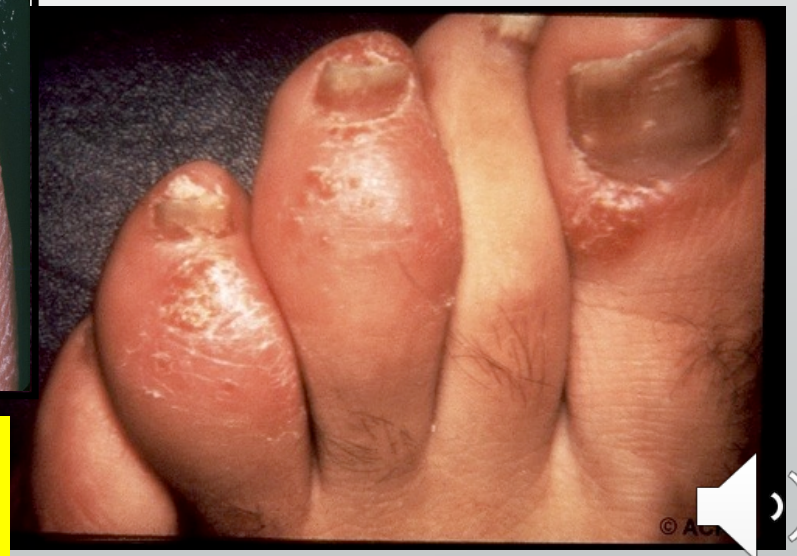
Understanding the Basics

Psoriatic arthritis (6 Domains)

- **"Sausage"** fingers/toes
- Inflammation of the DIP joints common (**Asymmetric)**
- Nail changes often present, pits, crumbling, oil spots, onycholysis
- Psoriatic patches (10-60%)
- Heel/Plantar pain
- Back/neck pain
- Arthritis may start before the skin







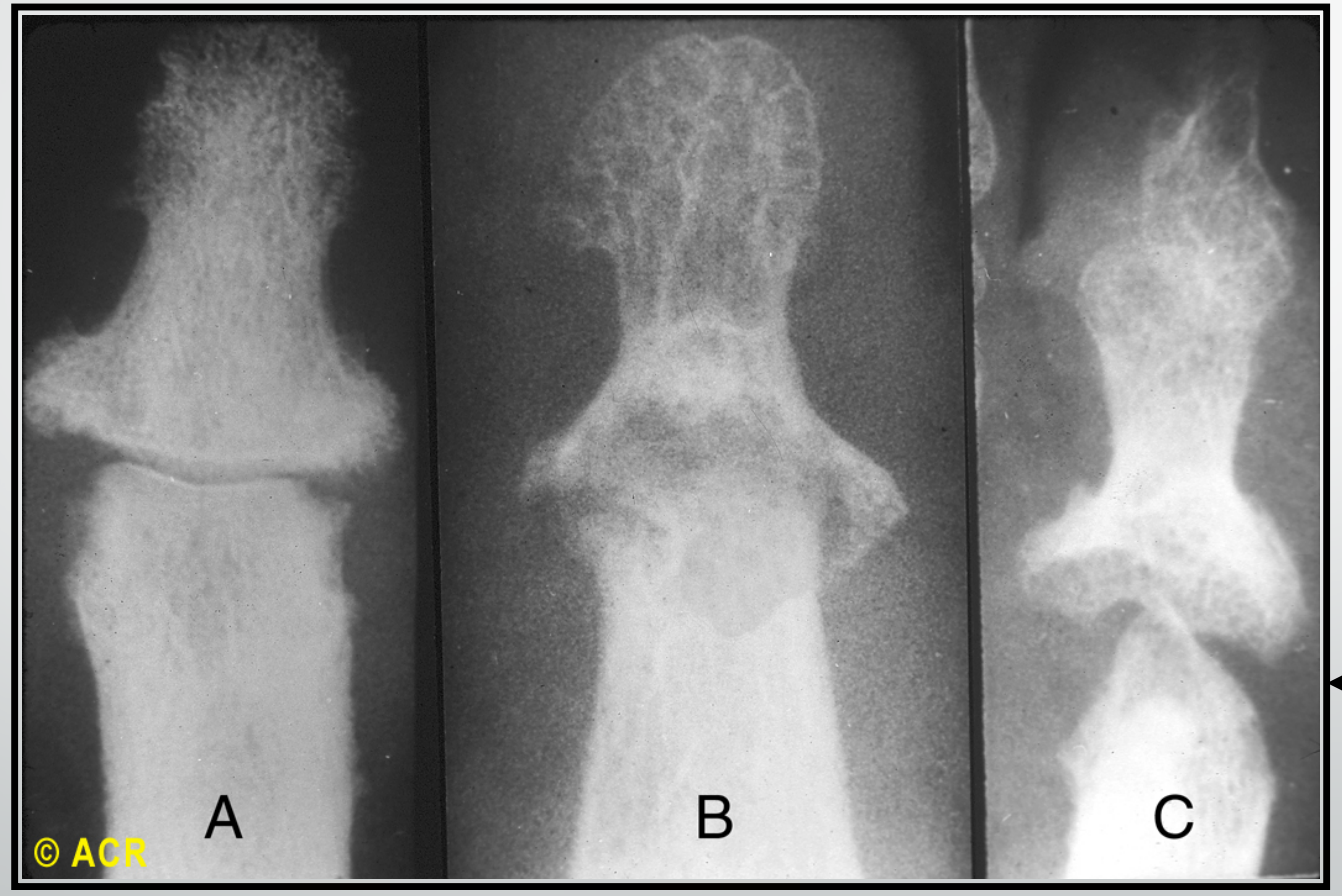
A Review for Physician Assistants and Nurse Practitioners on the Considerations for Diagnosing and Treating Psoriatic Arthritis, Antonio Giannelli

Rheumatol Ther https://doi.org/10.1007/s40744-018-0133-3 Dec, 2018

Psoriatic Arthritis Cont.

- **Enthesitis often present**
- CAN look exactly like RA early on (up to 16%)
- Severity of arthritis does not correlate with extent of rash
- Nail involvement with pitting and (nail detaches from nail bed)
- **Characteristic** findings on xray
- Is part of Inflammatory bowel, Spondyloarthritis, Psoriasis, Reactive arthritis, super family
- Psoriasis can be inverted/internal or hidden in hair line, or transient and confused with eczema

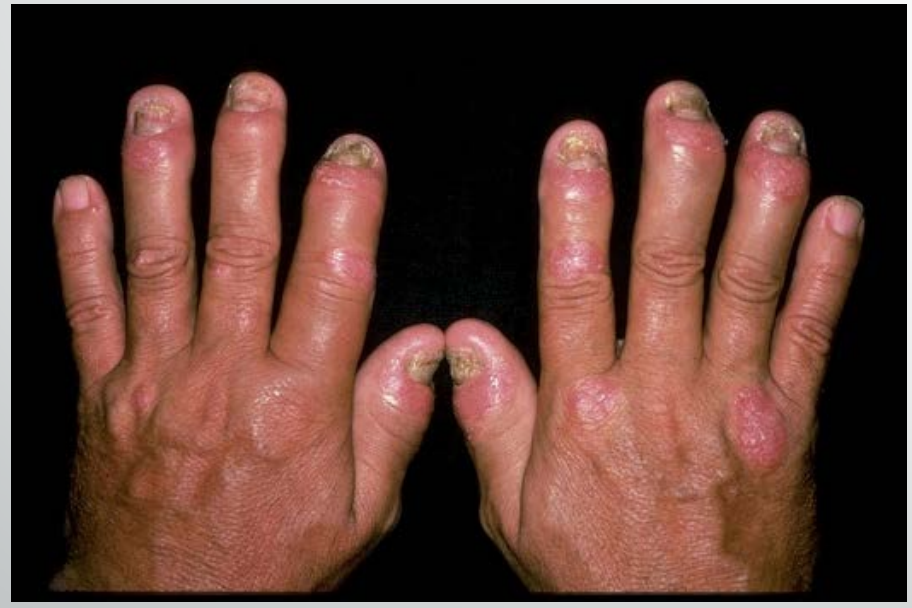
Psoriatic arthritis: progressive joint changes

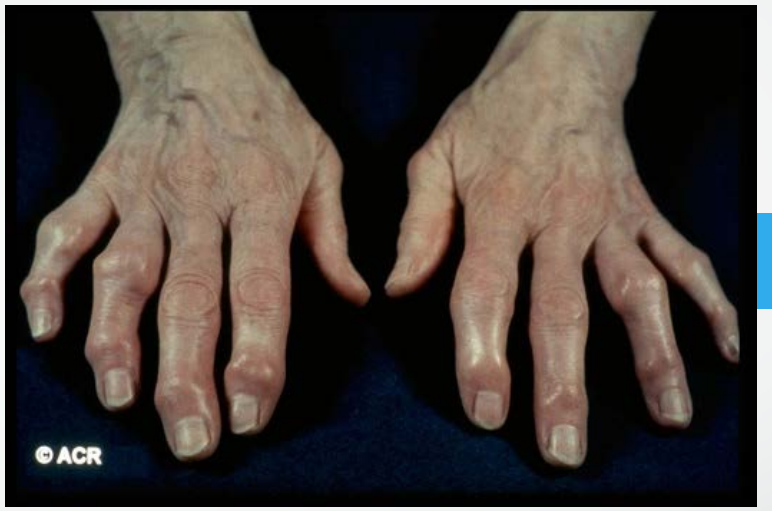


Pencil- in- cup deformity

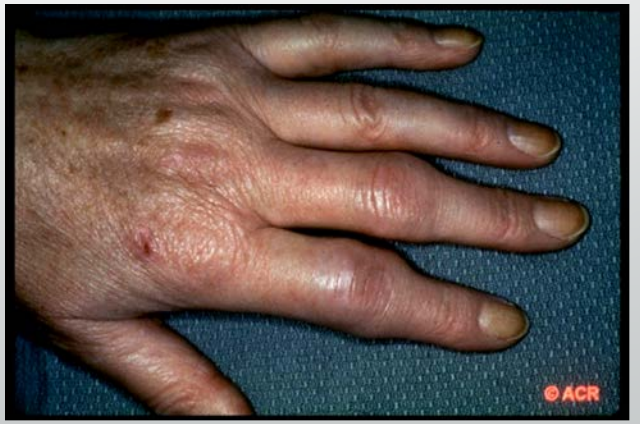
The Big Three:
Psoriatic Arthritis, OA and RA

Psoriatic





OA



RA

You will see this in your Practice. Learn the Patterns !!

Sometimes the diagnosis is made with just a visual inspection

Psoriatic Arthritis Treatment

- Sulfasalazine (Azulfidine)
- Methotrexate
- NSAIDs
- Steroids
- Biologic Agents

Note: Psoriasis can be treated with topical agents and/or Ustekinumab (Stelara) SC, or Ixekizumab (Taltz) Injections (now also for Psoriatic Arthritis)

Stop and Think Slide – If Psoriatic Arthritis (or other Rheum diseases) manifests just like RA sometimes, how can I differentiate?

Rheumatology For The PCP

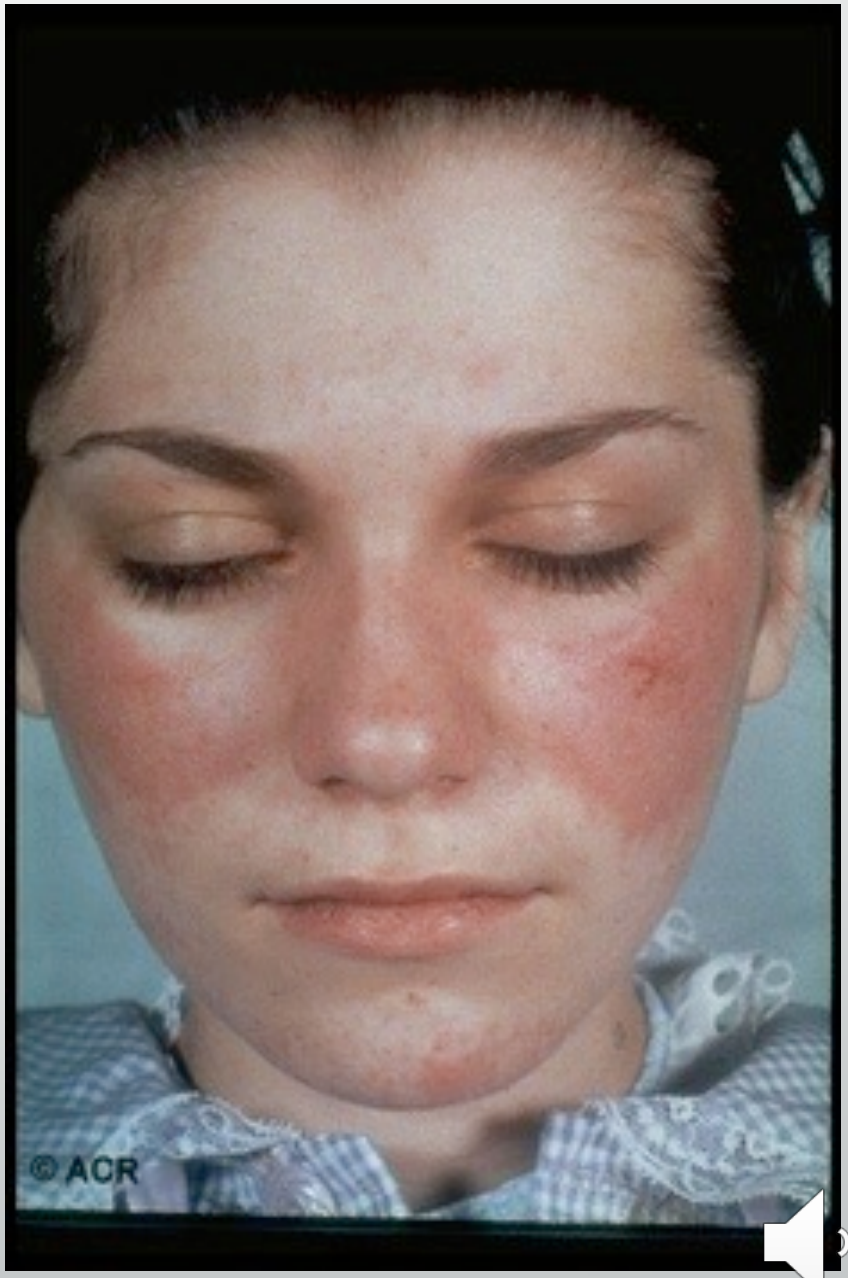
A Brief Overview:

SLE and Treatment

Case Four

- 22 y/o female
- **Hx:** joint pain, rash
- **PE:** facial rash (spares nasolabial folds), joint tenderness
- **Lab:** + ANA, **proteinuria**, low WBC

Don’t forget to get a UA !!



Understanding the Basics

Systemic Lupus Erythematosus

Definition:

An autoimmune disorder characterized by:

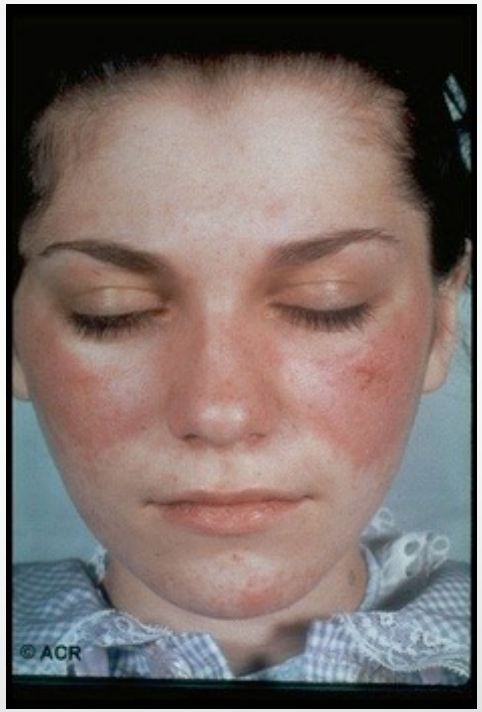
antinuclear antibodies (ANA)

and

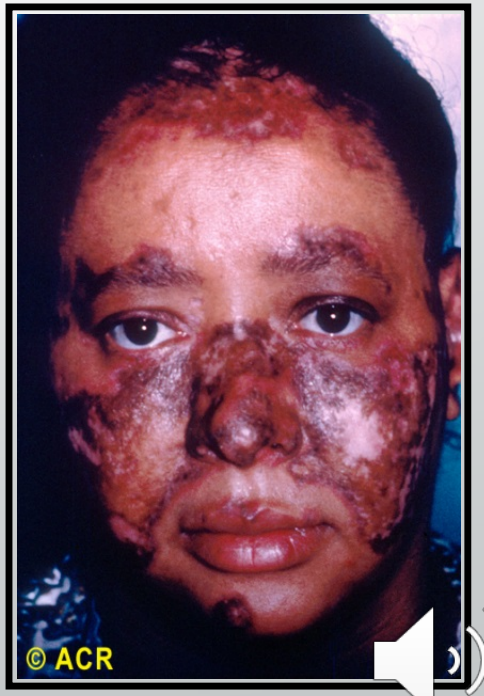
involvement of multiple organ systems

Commonly affects women,

ages 15 – 40 y/o



Malar Rash



Discoid Rash

SLE Clinical Manifestations

- **Constitutional** – fever, fatigue, weight loss, anorexia
- **Skin** – malar and discoid rash, photosensitivity, mouth/nose ulcers, dry eyes/mouth (Sicca symptoms consistent with Sjogren's syndrome)
- **MS** – muscle and joint pain/inflammation, osteonecrosis
- **Renal** – glomerulonephritis, cystitis
- **Blood** – Low WBCs, lymphocytes, anemia, lymphadenopathy, splenomegaly
- **Neuropsych** – headache, seizure, psychosis, CVA, neuropathy, depression, cognitive dysfunction

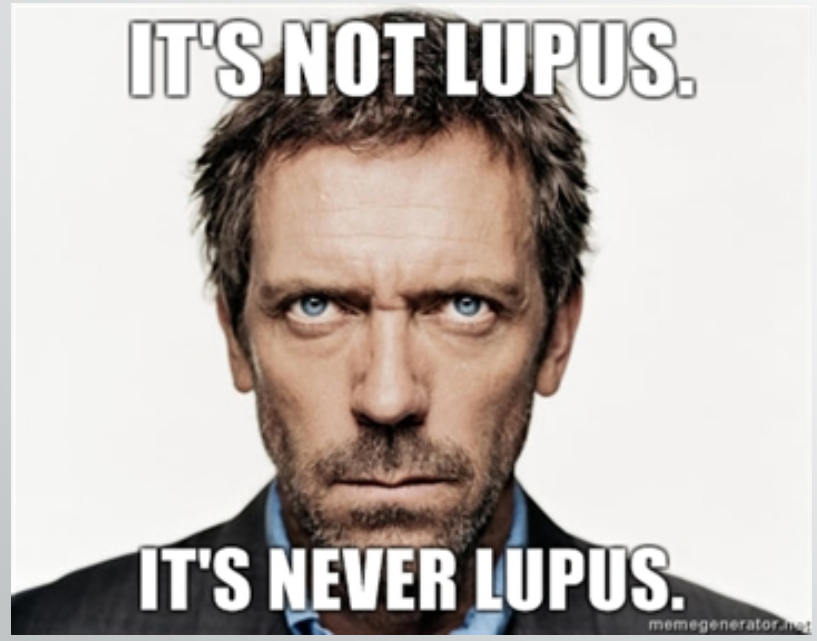
Need 4 out of 11 areas for Dx

SLE Clinical Manifestations - cont

- **Serosal** – pleuritis, pericarditis, peritoneal
- **Cardio/Vascular** – Raynaud's phenomenon, vasculitis, hypertension, myocarditis, endocarditis, thromboembolic events (clots)
- **Pulmonary** – pulm. hemorrhage, pulm. hypertension, interstitial lung disease
- **GI** – hepatitis, pancreatitis
- **Immunologic labs** – False pos VDRL, elevated immune complexes, low serum complements (C_3, C_4)

Need 4 out of 11 areas for Dx

Old Awful Pneumonic



Diagnostic criteria in SLE

S	• Serositis [pleuritis, pericarditis]
O	• Oral ulcers
A	• Arthritis
P	• Photosensitivity
M	Malar rash

B	• Blood [all are low - anemia, leukopenia, thrombocytopenia]
R	• Renal [protein]
A	• ANA
I	• Immunologic [DS DNA, etc.]
N	• Neurologic [psych, seizures]
D	Discoid rash

Likelihood of Lupus Manifestations

- Diagnosis early on and getting treatment is paramount
- Long term high dose steroids is no longer considered acceptable treatment
- The younger the patient is, the more likely Morbidity or death will occur
  - Reasons include Hormones, lack of medical compliance, and idiopathic

Cutaneous manifestations	*Frequencies (%)*
Malar rash	60.5
Photosensitivity	54.5
Discoid lupus	49
Hair loss	47
Erythema	35
Oral ulcer	28
Facial eruption	27.5
Dermal vasculitis	22
Alopecia	23
Raynaud's phenomenon	21
Telangiectasia	19
Bullae	11.5
Hives	11
Purpura	10
Lupus hair	6
Skin ulcer	4.5
Vaginal ulcer	2

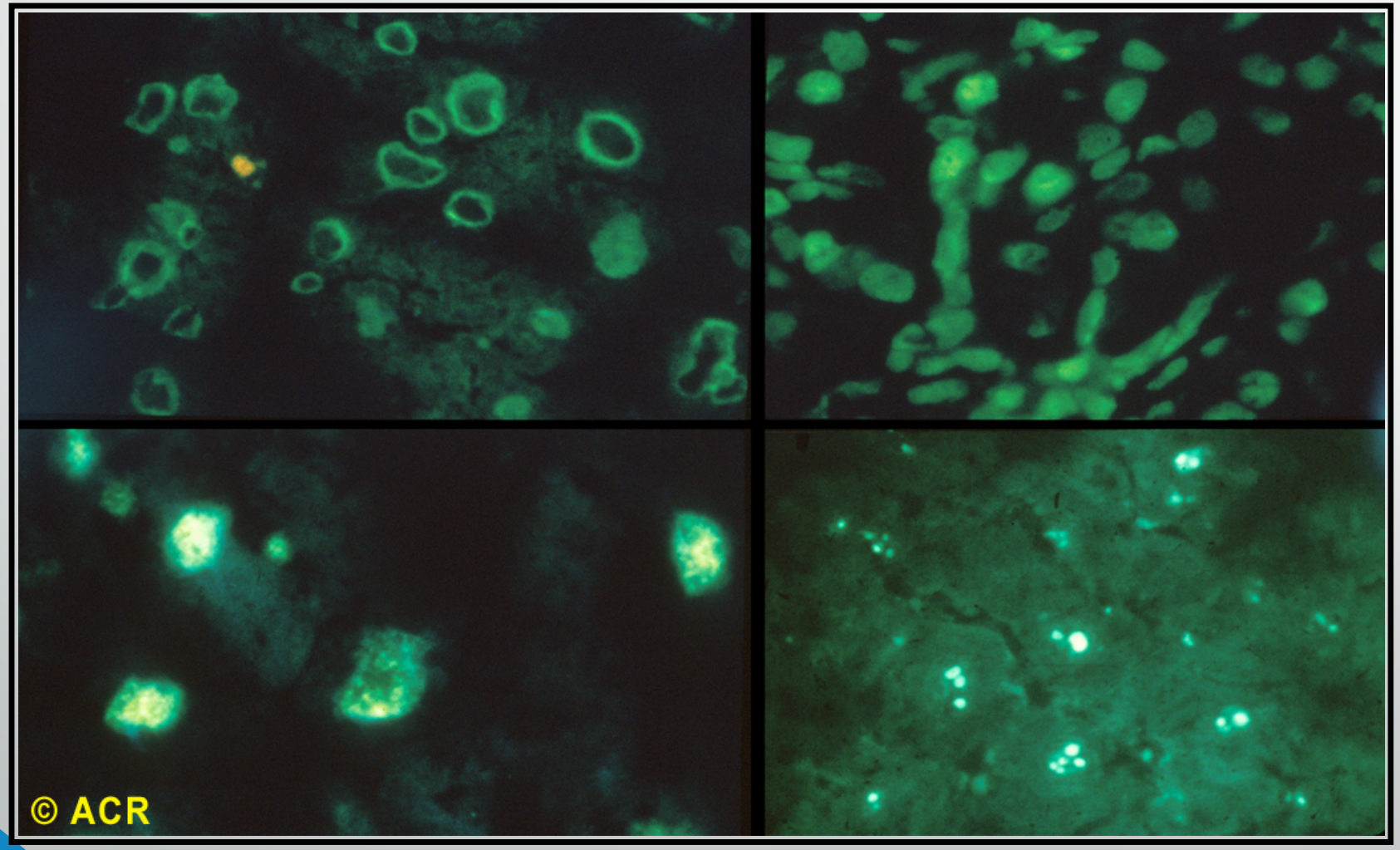
Anti Nuclear Antibody (ANA)

- Performed by Indirect immunofluorescence or ELISA methods (reported as Titer and Pattern)
- 95 - 99% sensitivity (true positive) for Lupus activity (need to do dsDNA lab)
  - There are only a few situations where this will be negative
- <1:160 titers less clinically significant
- Titer not a measure of disease activity, rather disease presence

Antinuclear AB Nuclear Staining Patterns

Peripheral or "rim" (associated with dsDNA AB)

Homogeneous (non-specific, drug induced)



Speckled (least specific, do ENA lab*)

Nucleolar (Sclerosis, SLE, myositis)

*Always do an ENA lab

ANA in Other Conditions

- Drug Induced Lupus
- Mixed Connective Tissue Disease
- Autoimmune Liver Dz (autoimmune hepatitis, Primary Biliary Cirrhosis) – antimitochondrial ABs seen
- Progressive Systemic Sclerosis
- Polymyositis
- Sjogren's Syndrome
- RA
- Multiple Sclerosis
- Silicone Breast Implants ***
- Healthy relatives of SLE patients
- Neoplasia
- Elderly – progressively more common as we age

Additional Autoantibodies

*Anti-ds DNA (SLE) – RENAL / Vasculitis

ENA:

Anti-SS-A (Ro) (Sjogren's)

Anti-SS-B (La) (Sjogren's)

Anti-Smith (SLE)

Anti-RNP (mixed CTD)

Jo-1 (myositis, interstitial lung disease)

SCL-70 (Scleroderma)

Complements

(C_3, C_4, CH 50) (low in active SLE)

PM-Scl (myositis, scleroderma)

Anti-Histone AB (drug induced) *

Antiphospholipid Antibodies

(Hypercoagulable states)

The presence of specific autoantibodies correlates with particular organ involvement and prognosis

International Society of Nephrology 2003 classification of lupus nephritis

Class I	Minimal mesangial	Normal light microscopy findings, abnormal electron microscopy findings
Class II	Mesangial proliferative	Hypercellular on light microscopy
Class III	Focal proliferative	<50% of glomeruli involved
Class IV	Diffuse proliferative	>50% of glomeruli involved
Class V	Membranous	Predominantly nephrotic disease
Class VI	Advanced sclerosing	Chronic lesions and sclerosis

Drug-induced Lupus: drug associations

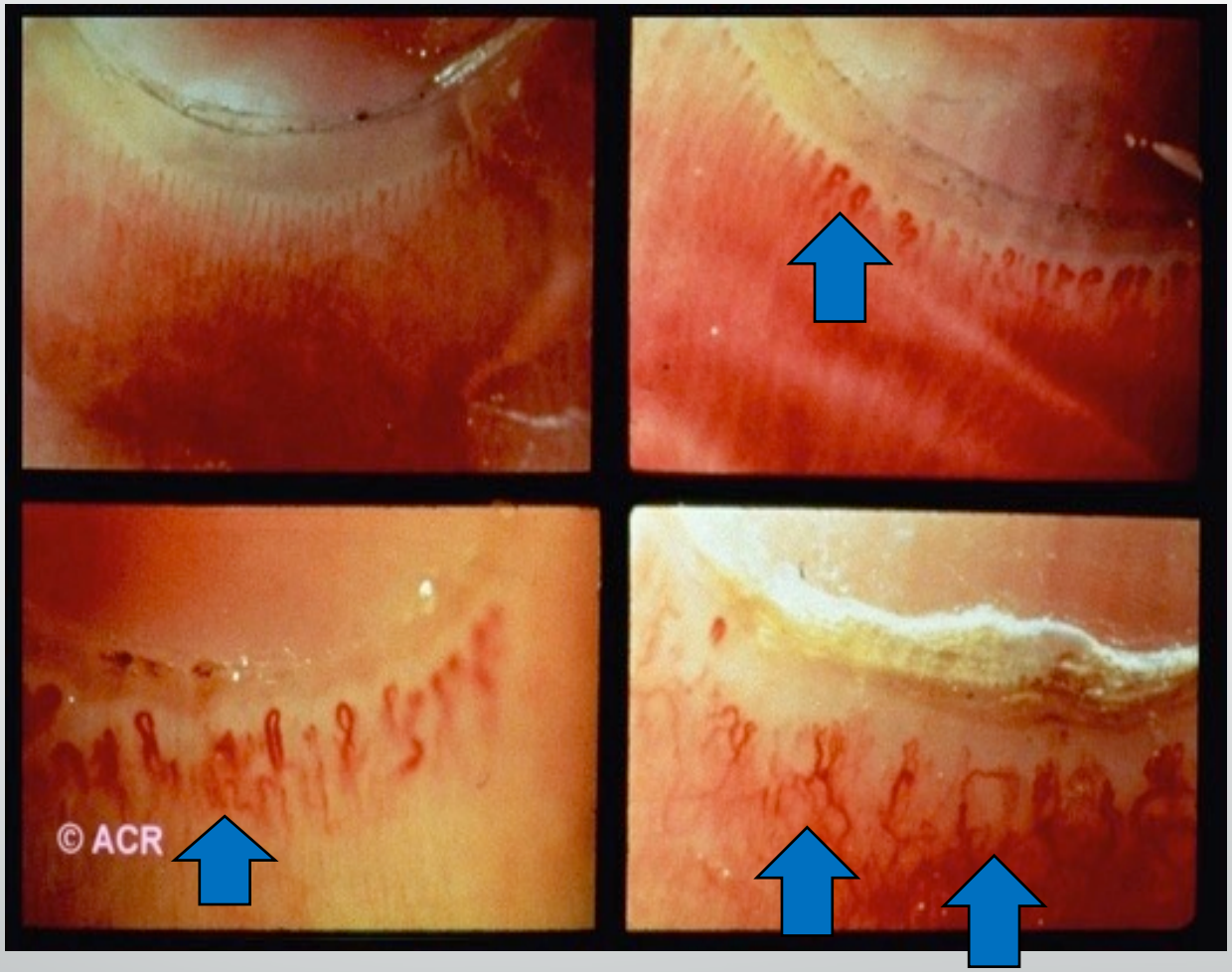
- Hydralazine
- Procainamide
- Minocycline
- Chlorpromazine
- Isoniazid
- Penicillamine
- Methyldopa
- Interferon-alpha

- Anticonvulsants
- Quinidine
- Propylthiouracil
- Sulfonamides
- Lithium
- Beta-blockers
- Nitrofurantoin
- Sulfasalazine
- Diltiazem
- Hydrazine
- Interferon-gamma
- TNF inhibitors

Understanding the Basics

Close-up views of Periungual changes

Normal



Dilated loops

Dilated loops with dropout

Dilated loops with branching

View with ophthalmoscope and drop of mineral oil or KY Jelly

Systemic Lupus Erythematosus

Some are MUCHO BENJAMINS !!

Treatment:

- NSAIDS
- Hydroxychloroquine (Plaquenil)
- Steroids – high or low dose*
- Disease Modifying Drugs (ie, Imuran, Leflunamide, Cellcept, Cytoxan/Rituxan*)
- Belimumab (Benlysta IV) – BLyS attenutor / promotes apoptosis (newest Tx 7+ years old)
- ACTHAR – ACTH and melanocortins
- Treat associated diseases – (ie, HTN, skin, lung involvement)
- Many experimental agents being tested now, many more have failed

Take Home Points

1. Early recognition of basic autoimmune disease patterns by the Primary Care provider will help in preventing a delay in diagnosing and establishing an effective treatment plan
2. Osteoarthritis, Rheumatoid Arthritis and Psoriatic Arthritis diagnosis' will be on the increase due to an aging population
3. **Knowing the difference between inflammatory and mechanical back pain is key in the prevention of chronic joint changes in diseases like Psoriatic arthritis, and in most cases the unnecessary use of chronic pain meds**
4. Rheumatology referral is important early in the diagnosis of an autoimmune disease such as Rheumatoid and Psoriatic Arthritis, but is especially true for SLE

Question One

An extra-articular manifestation of RA that demonstrates a <u>poor prognosis</u> of the disease is:

1. A positive Rheumatoid Factor
2. Episcleritis
3. Interstitial fibrosis
4. Vasculitis

Question Two

Which Xray finding is indicative of erosive destruction associated with Psoriatic Arthritis?

1. Bilateral metacarpophalangeal erosive change
2. Pencil-in-cup deformity
3. Joint space narrowing, sclerosis and osteophyte formation
4. Squaring of vertebral bodies

Question Three

Which lab test can be the most telling and one of the first signs of <u>early</u> Lupus activity?

1. A urinalysis for proteinuria
2. Serum complements
3. dsDNA
4. SPEP

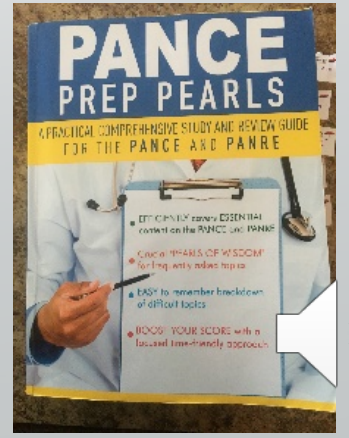
Slides and Text Supplied By

AAPA Annual Conference
Las Vegas, NV

- American College of Rheumatology (ACR) Slide Series
- West, Sterling, M.D., Jason Kolfenbach, M.D. Rheumatology Secrets, 4th Edition. Philadelphia: Elsevier, Mosby, Inc.; 2020
- Joshua June, DO
- Ben Smith, PA-C, DFAAPA
- Rick Pope, PA-C, DFAAPA
- Thomas Ignaczak, MD
- PANCE-PANRE Slide Info from

  PANCE Prep Pearls

  2st ED (Williams) 2017



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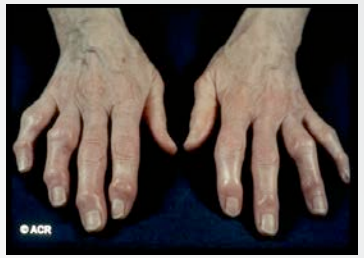
- **Giannelli, Antonio, MsA, PA-C, DFAAPA *A Review for Physician Assistants and Nurse Practitioners on the Considerations for Diagnosing and Treating Psoriatic Arthritis*, Rheumatology and Therapy 6(1), 5-21 https://doi.org/10.1007/s40744-018-0133-3 Dec, 2018**

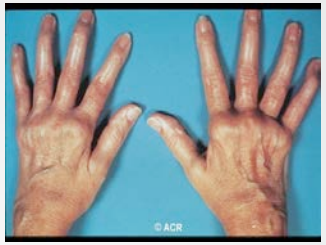
PANCE/PANRE Review

Osteoarthritis: Degenerative Joint Disease



- ✓ Articular cartilage damage; Obesity is risk factor; Common in weight bearing joints; Morning Stiffness < 30 mins (better with rest, worse as day progresses
- ✓ Hard bony joint. **Bouchard's** nodes at the PIP joints **Heberden's** nodes at the DIP joints; Sclerosis and osteophytes on xray
- ✓ Often have "squared" first CMC joint due to osteophytes at that joint
- ✓ Can't stop it's progress !
- ✓ TX: Exercise,Tylenol (in elderly), NSAIDs (limit use if possible), steroid and/or Hyaluronic acid joint injections

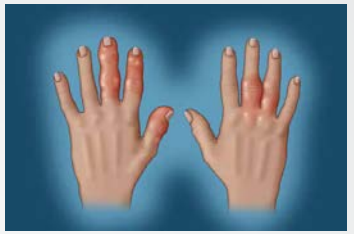
PANCE/PANRE Review



Reumatoid Arthritis: Inflammatory Joint Disease

- ✓ Systemic Disease (fevers, fatigue, eye/lung/blood vessel involvement); Symmetric polyarthritis with bone erosion, cartilage destruction and joint structure loss; T- Cell mediated; Pannus formation (erodes cartilage/bone) Common in small joints(but hips, knees, shoulders also); Morning Stiffness > 60 mins (worse with rest, improves as day progresses
- ✓ Positive Rheumatoid Factor (Best initial test); elevated ESR, CRP; Positive anti-citrullinated (CCP) antibody (most specific for RA); Xrays: osteopenia/erosions, subluxation deformities, ulnar deviation
- ✓ TX: Prompt initiation of DMARD (ie, methotrexate),Tylenol (in elderly), NSAIDs (limit use if possible), steroid PO and joint injections; Biologics (ie, infliximab)

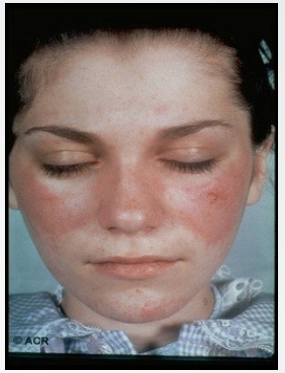
PANCE/PANRE Review 2



Spondyloarthropathies: Psoriatic Arthritis

- Inflammatory arthritis (asymmetric) of the PIP/DIP, sacroiliac joints, Dactylitis (sausage digits – fingers/toes), nail pitting, onycholysis, chronic uveitis, at 40-50 y/o. Chronic LBP and morning stiffness (> 1 hour), decreased ROM, stiffness decreases with exercise/activity. Psoriasis (silvery white scales) may precede arthritis.
- **Dx:** Elevated ESR, Positive HLA B27, X-ray of chronic, long-standing disease shows “Pencil in Cup” deformity
- **TX:** NSAIDs (first choice), steroids, Methotrexate after anti-inflammatories, Biologics (ie Infliximab)

PANCE/PANRE Review

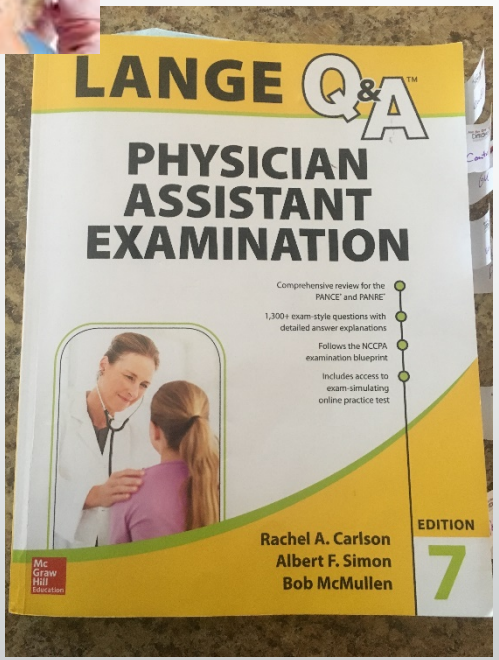


SLE: Systemic Lupus Erythematosus

- ✓ Chronic systemic multiorgan autoimmune disease, often affects young females (onset 20-40's), black and native Americans
- ✓ Drug induced: procanimide, hydralazine, INH, Quinidine (Lab: + anti-histone ABs)
- ✓ Joint pain, fever, malar (butterfly) rash sparing nasolabial folds, serositis (pericarditis, pluritis); Discoid lupus: annular, scarring; systemic: oral ulcers, alopecia, renal, CV, CNS, eye
- ✓ Dx: ANA best initial test, + anti-double stranded DNA AB
- ✓ TX: sun protection, Hydroxychloroquine (Plaquenil), NSAIDs or Tylenol for arthritis, steroids, DMARDs (Methotexate – for swollen joints, cyclophosphamide)

Thank You for Your Time and Interest

Remember:
Autoimmune disease affects all age groups



"A good PA treats the disease -
A great PA treats the patient who has the disease"

(Modified from) Sir William Osler (1849 – 1919), Physician

Great Lakes Center of Rheumatology, Lansing, MI

gnle852@gmail.com