MAYO CLINIC | School of Continuous Professional Development

32ND ANNUAL

INTERNAL MEDICINE BOARD REVIEW 2023

June 5-9, 2023

MAYO CLINIC | School of Continuous Professional Development

RHEUMATOLOGY

ARTHRITIS

Ashima Makol, MD
Associate Professor of Medicine
Division of Rheumatology

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

- Advisory Board: Boehringer Ingelheim, Sanofi-Genzyme

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

All relevant financial relationships have been mitigated.

LEARNING OBJECTIVES

At the end of this lecture, you will be able to

1. Utilize physical exam and laboratory studies to diagnose and manage Rheumatoid Arthritis
2. Diagnose and manage symptomatic Osteoarthritis
3. Diagnose and treat Fibromyalgia

OUTLINE
A CASE BASED REVIEW

- Clinical presentation of Rheumatoid arthritis (RA)
  - Key physical exam findings
  - High yield laboratory tests/ imaging
  - New classification criteria
- Approach to managing early & established RA
  - Initiate, monitor and intensify treatment
  - Manage RA in the pregnant patient
- Review Osteoarthritis diagnosis and management
  - Primary, Secondary, Erosive, “DISH”
- Review new criteria for Fibromyalgia and multi-pronged approach to management

QUESTION 1

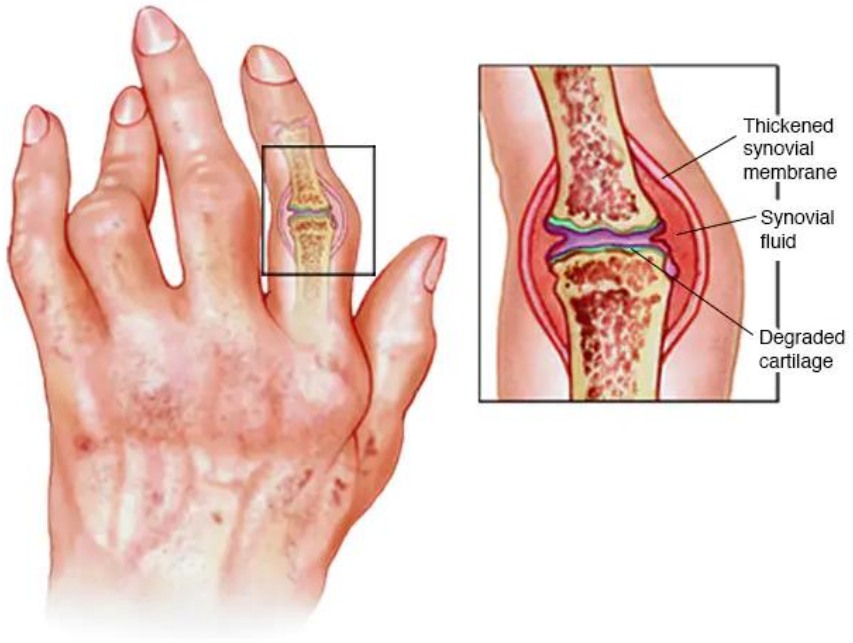
- History : A 48 y/o woman
  - 2 months of hand pain and swelling
  - 1 hour of morning stiffness
  - Manages a home day care with 7 children attending
  - Smokes 1 PPD (10 years)
- Physical Exam
  - Tender and swollen
    - Wrists and Ankles
    - 2nd- 5th metacarpophalangeal (MCP)
    - 2^{nd}-4^{th} proximal interphalangeal (PIP) joints
- Laboratory testing:
  - Hemoglobin **11 g/dl** MCV 90 fL
  - WBC 9.2
  - Platelet **400**
  - ESR **50 mm/h** (normal <29)
  - CRP **25 mg/L** (normal <8)
  - Rheumatoid factor Negative
  - ANA Negative
  - TSH Normal

WHICH OF THE FOLLOWING IS THE MOST APPROPRIATE TEST TO DIAGNOSE THIS PATIENT?

A. Parvovirus IgM and IgG
B. Anti-CCP antibody
C. Lyme Screen
D. Anti-dsDNA antibody

RHEUMATOID ARTHRITIS

- Systemic inflammatory autoimmune disorder
- Prevalence: 1% of the population
- Females > Males ; 30-60 y
- Boggy, joint swelling in small-medium joints
  - Morning stiffness > 30 min (>60 min)
- Duration of symptoms > 6 weeks



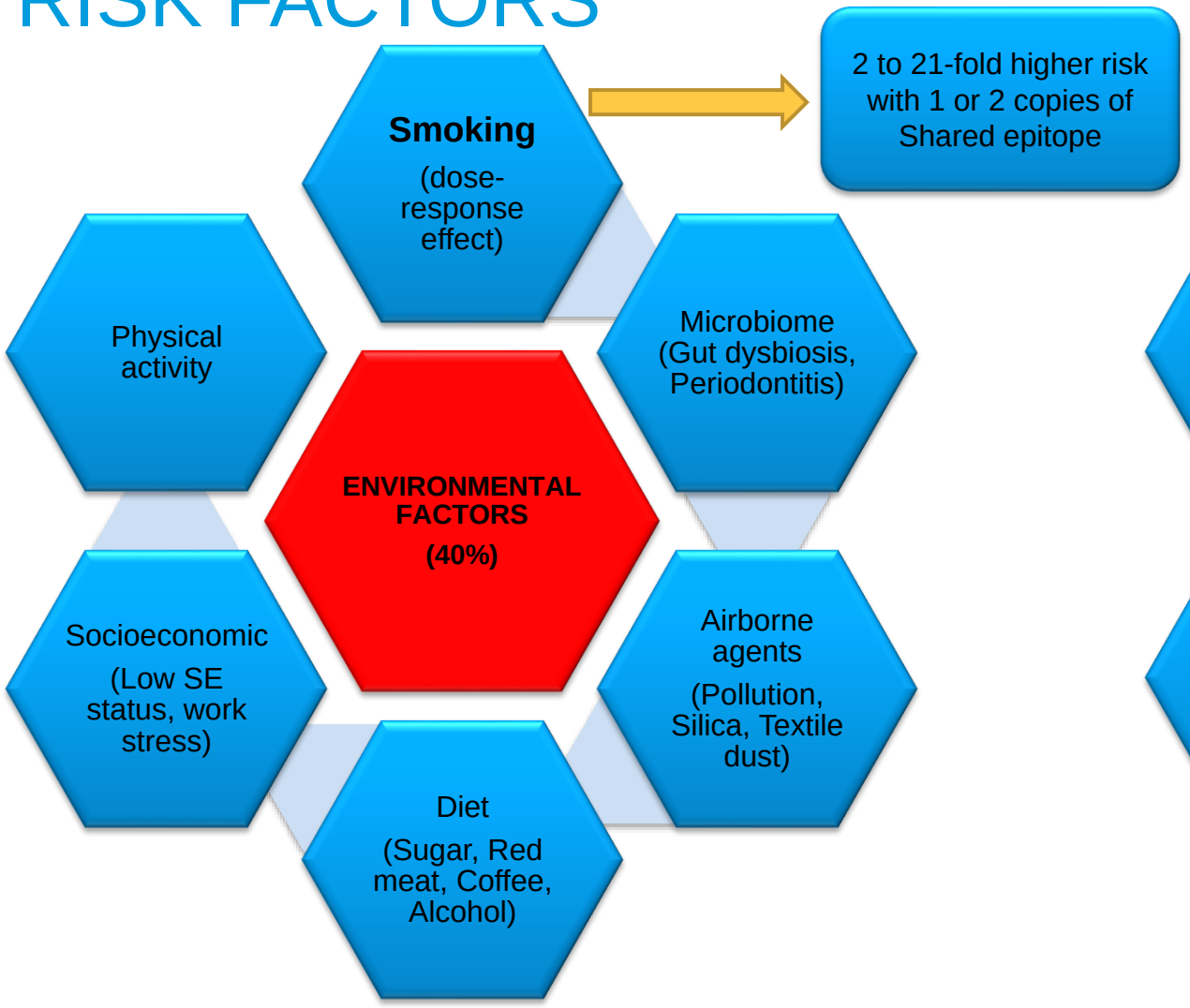
- Lifetime risk of developing RA :
  - 3.6% (1 in 28) for women,1.7% (1 in 59) for men

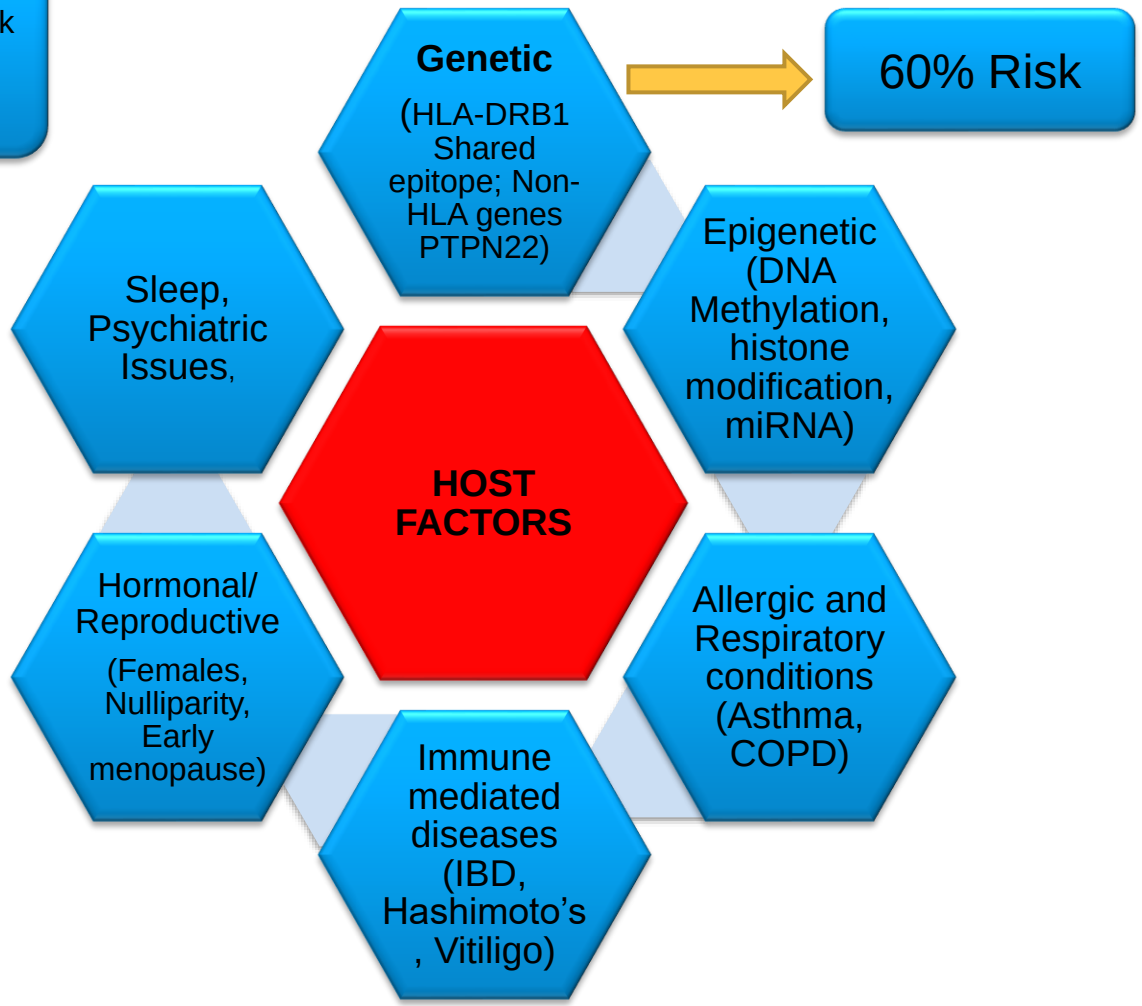
Crowson et al. Arthritis Rheum. 2011

RHEUMATOID ARTHRITIS

RISK FACTORS

Arginine → (PADI) → Citrulline (immunogenic)



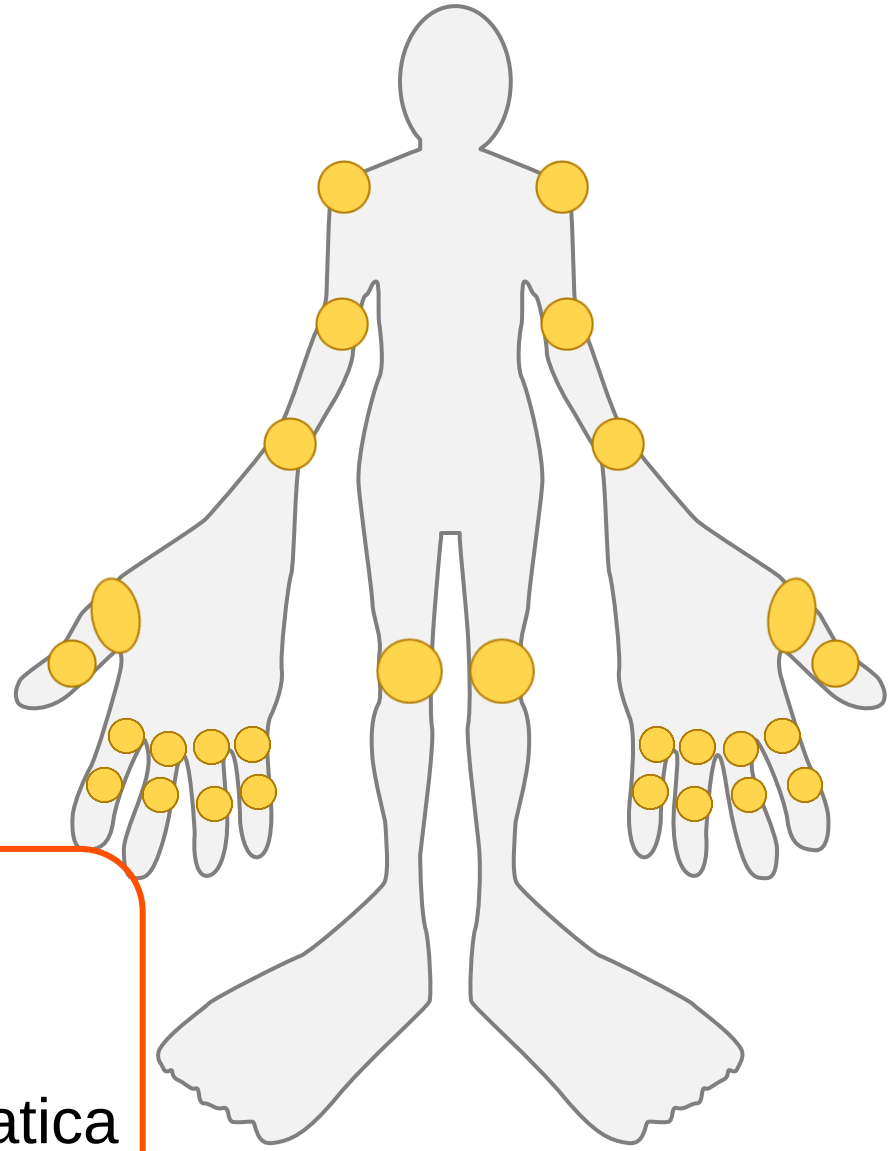


1

Utilize **physical exam** and **laboratory studies** to diagnose and manage rheumatoid arthritis

PHYSICAL EXAM IN RA "PATTERN RECOGNITION"

- Symmetric inflammatory **polyarthritis**
  - ✓ Small-medium joints
- Other joints – feet, ankles (MTPs, PIPs)



Pearl

Elderly onset – RA

- Hips and Shoulders
- Can mimic Polymyalgia Rheumatica

RA: EARLY

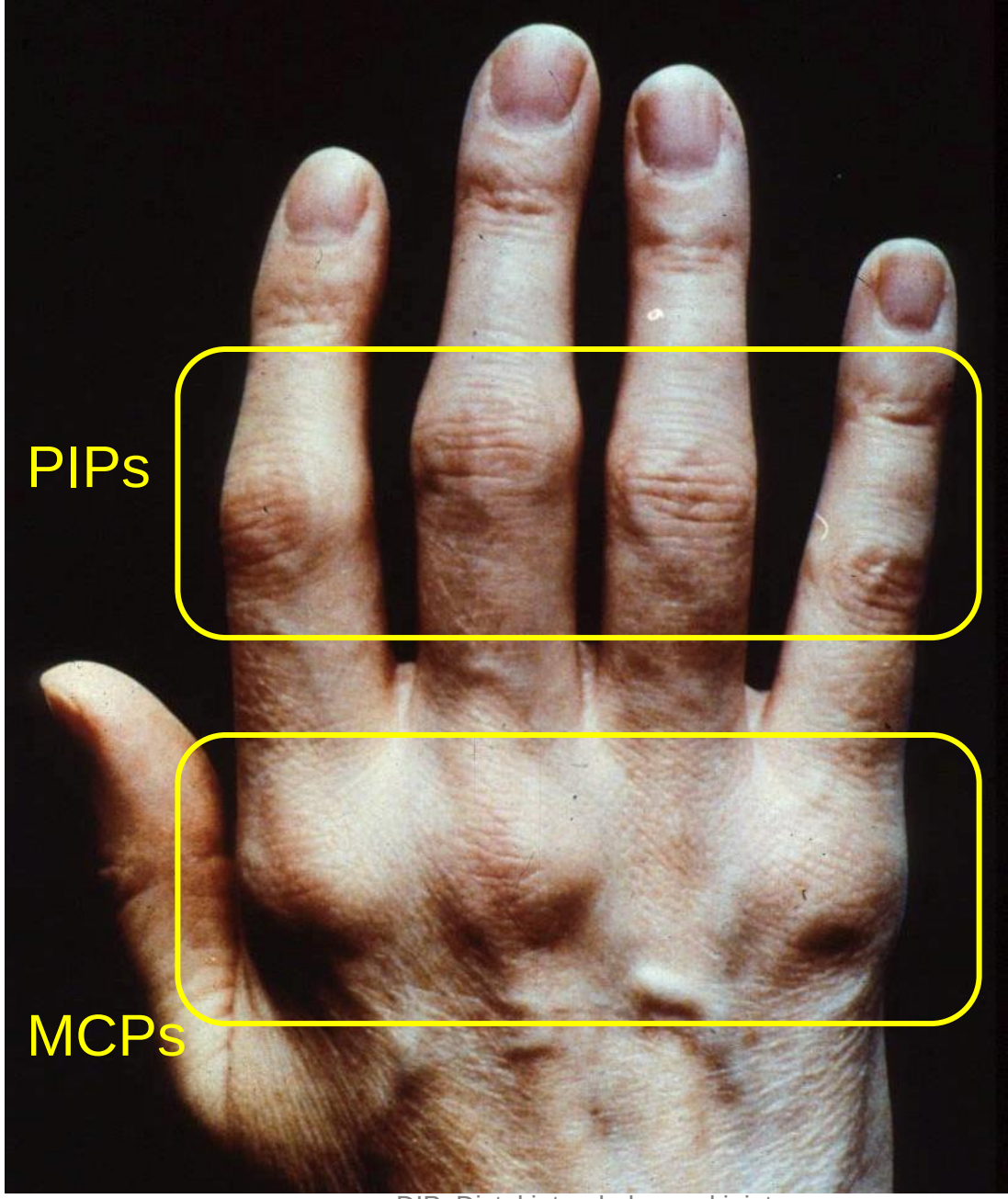
- ✓ PIPs
- ✓ MCPs

DIPs spared

Pearl: If DIP synovitis

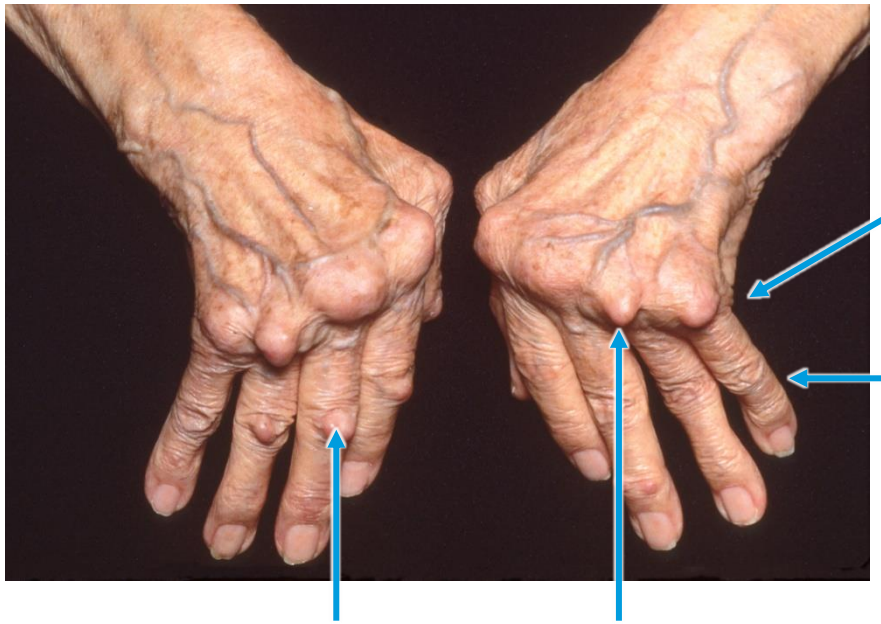
Think

- Inflammatory (erosive) Osteoarthritis
- Psoriatic arthritis



DIP: Distal interphalangeal joint
PIP: Proximal interphalangeal joint
MCP: Metacarpophalangeal joint

RA: LATE COURSE – DEFORMITIES



Subluxation at MCPs

Ulnar deviation of digits

Rheumatoid nodules

Swan neck deformity

Boutonniere's deformity

Pearl

- Swan neck and Boutonniere's deformity pathognomonic of RA

RA

Peripheral joints

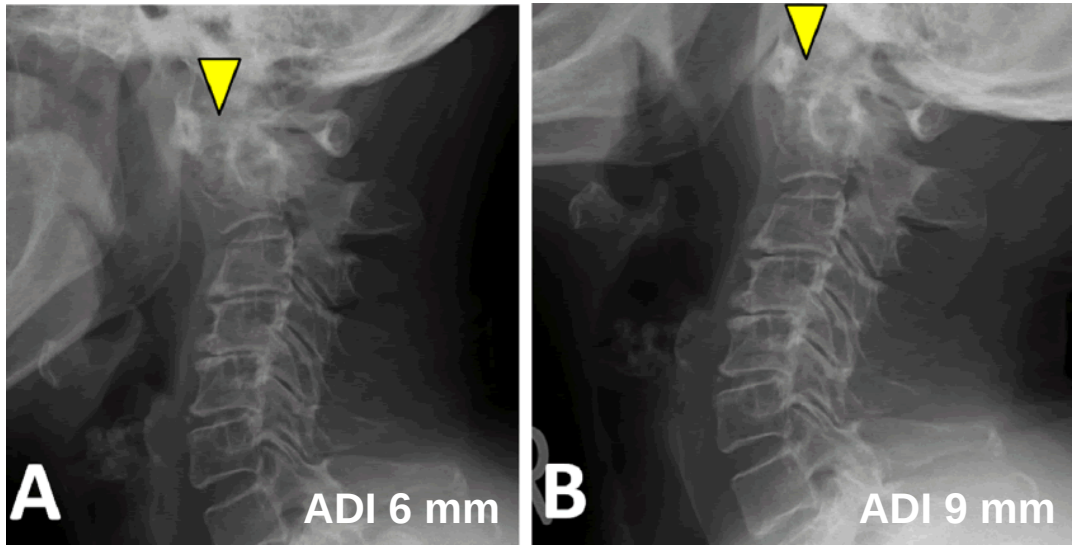
- Periarticular osteopenia
- "marginal erosions" on X ray

Spine

- Spared – except C1-C2
- Atlanto-axial subluxation in long standing, severe, erosive disease – cervical myelopathy

Pearl

- Cervical-spine radiographs flexion-extension views prior to general anesthesia



RA: EXTRA-ARTICULAR MANIFESTATIONS – SKIN

Pyoderma gangrenosum

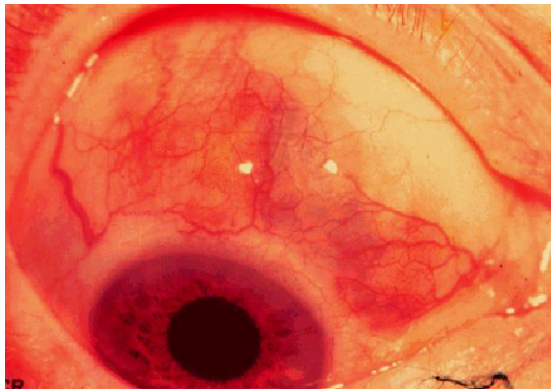
Rheumatoid vasculitis

.A. Watts, D.G.I. Scott . Best Practice & Research Clinical Rheumatology 30 (2016) 916-931

RA: EXTRA-ARTICULAR MANIFESTATIONS – EYE

Keratoconjunctivitis sicca (most common) 10-15%

Episcleritis



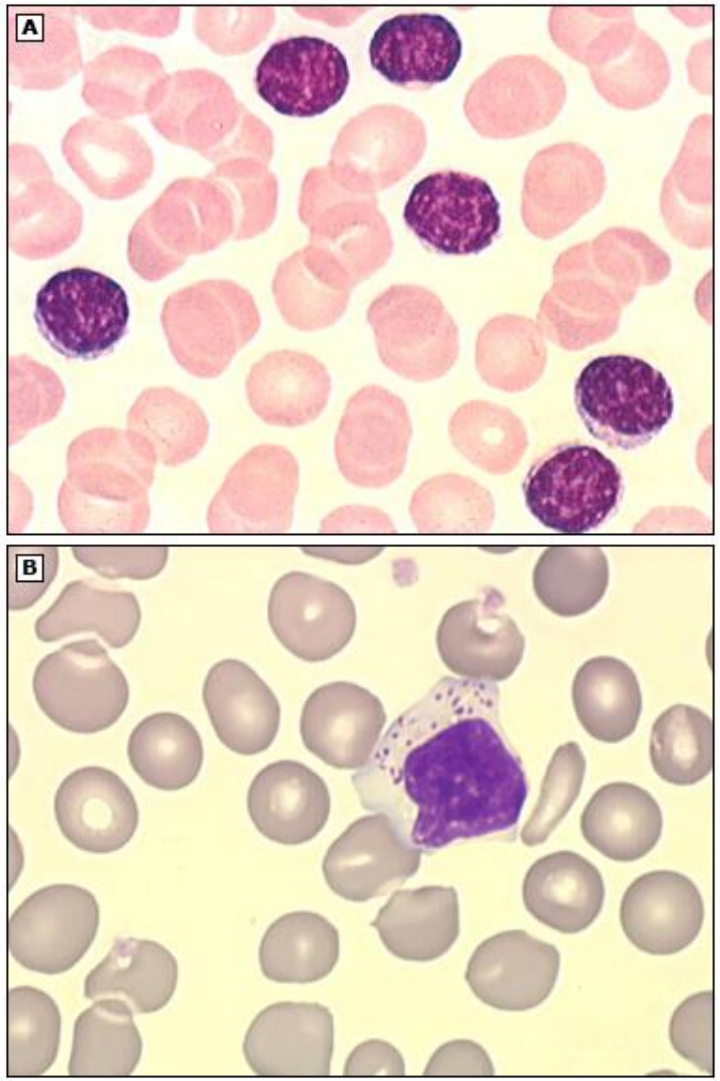
Scleritis

Scleromalacia perforans

Peripheral ulcerative keratitis, corneal melt

RA: EXTRA-ARTICULAR MANIFESTATIONS – HEMATOLOGICAL

- FELTY's syndrome
  - neutropenia + splenomegaly + leg ulcers
- LGL (Large Granular Lymphocyte) Leukemia
  - Pancytopenia
  - clonal proliferation of LGLs
    - larger than most circulating lymphocytes, characteristic azurophilic granules containing acid hydrolases
  - They may be either T cells (T-LGL), the more common type, or natural killer cells (NK-LGL)
- Diffuse large B-cell Lymphoma
  - Risk correlates with disease activity



RA: EXTRA-ARTICULAR MANIFESTATIONS

Heart

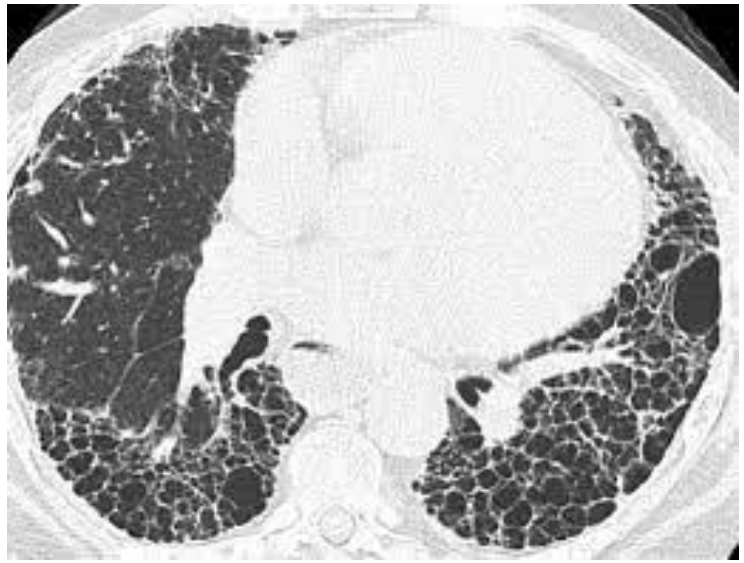
- Pericarditis, Myocarditis

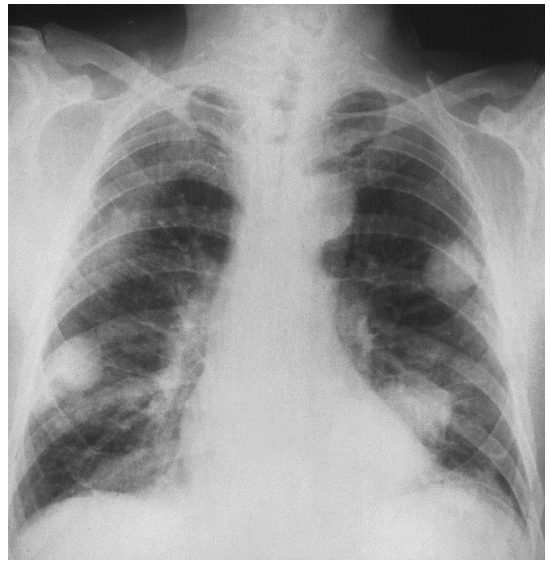
Lungs

- Interstitial lung disease (UIP pattern) 10%
- Pulmonary nodules
- Effusions (exudative, low glucose and pH)
- Caplan' syndrome
  "coal worker's pneumoconiosis"
- Upper airway involvement-rare
  - Cricoarytenoid arthritis – sore throat, hoarseness, dysphagia, stridor

Neurologic

- Peripheral neuropathy – vasculitic
  "mononeuritis multiplex" (wrist and foot drop)





RA: LABORATORY STUDIES FOR DIAGNOSIS
NON-SPECIFIC TO RA

CBC

- Anemia of Chronic Disease
- Thrombocytosis
- Leukocytosis

Elevated inflammatory markers

- ESR and/or CRP

Exclude mimics

- Viral infections (more likely in patients with symptoms <6 weeks)
  - Parvovirus B19 (IgG/IgM), Hepatitis B/C, HIV, Chikungunya

Pearl

RA: LABORATORY STUDIES

SPECIFIC TO RA

Rheumatoid factor (RF)

- Antibody to Fc portion of IgG
  - Positive in 70-80%
  - **Specificity of 86%**
  - High titer associated with severe disease

Pearl

Non-specific

- SLE, Sjogren's
- TB, Endocarditis, Hepatitis C
- Ageing:10-20% over age 65

Anti-CCP antibodies

- Antibody to citrullinated peptides
- Positive in 65%
- More common in smokers
- ✓ **High specificity of > 95%**
- Associated with radiographic progression
- Increases risk for extra-articular disease

Positive ANA can be seen in 1/3rd – low titer, not Ag specific

RF and/or CCP are Neither Necessary nor Sufficient alone for RA diagnosis

Pearl

- ✓ Patient can have RA without a + RF or CCP **"Seronegative Rheumatoid Arthritis"**
- ✓ Not all patients with positive RF and/or CCP have RA

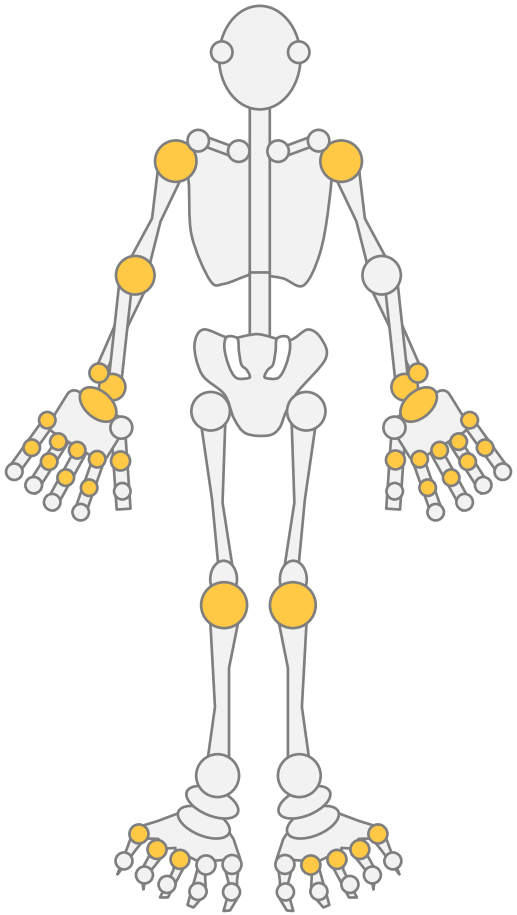
ACR/EULAR (2010) CLASSIFICATION CRITERIA FOR RA

	Points
Symptom duration (as reported by patient)	
<6 weeks	0
>6 weeks	1
Joint distribution	
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
Serology	
RF- and CCP-	0
Low RF+ or CCP+	2
High RF+ or CCP+	3
Acute phase reactants	
Normal ESR or CRP	0
Abnormal ESR or CRP	1

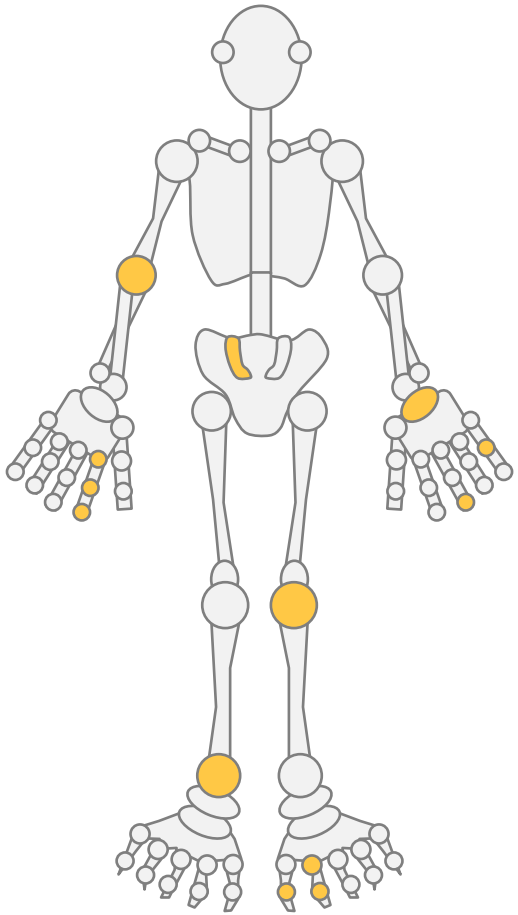
- At least >1 swollen joint, not better explained by another disease
- A score ≥ 6 points for definite RA

Redrawn from: Aletaha D, et al. 2010 Rheumatoid arthritis classification criteria: an ACR/EULAR initiative. Arthritis Rheum. 2010;62(9):2569

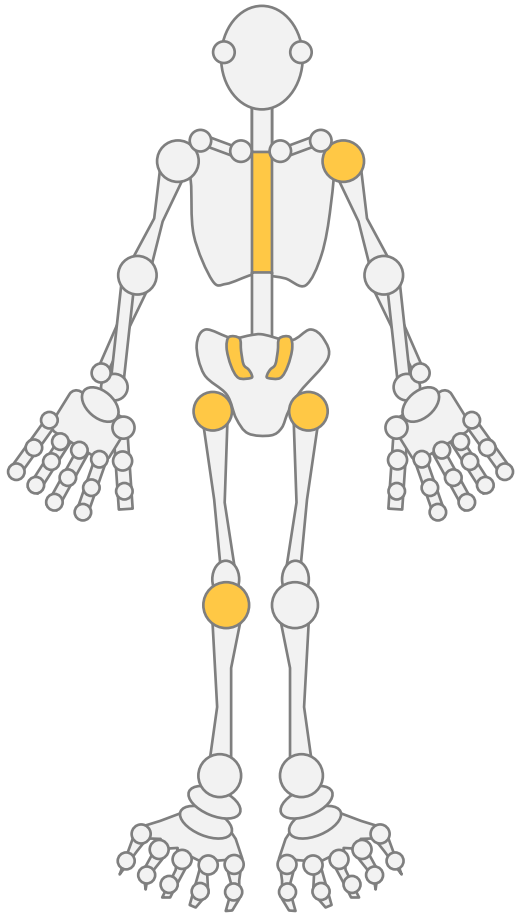
“PATTERN RECOGNITION”



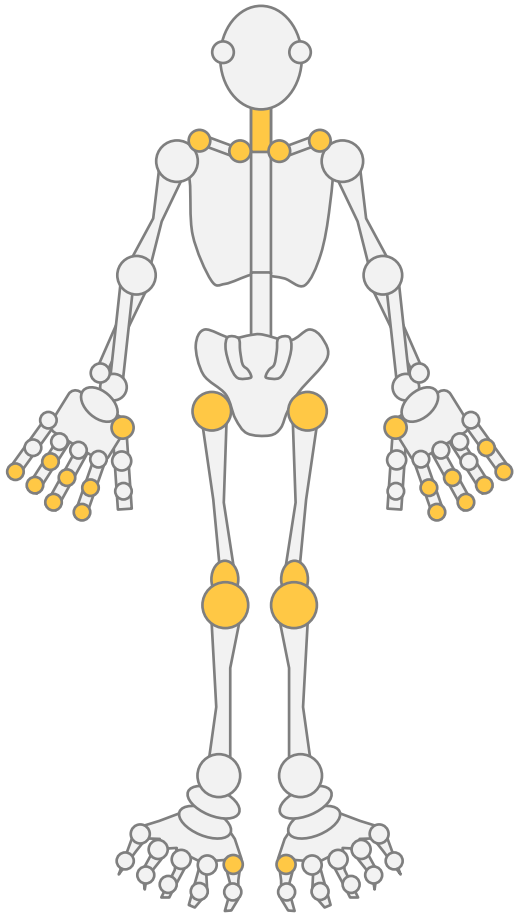
RA



Psoriatic A



Ankylosing S



OA

QUESTION 1

- History : A 48 y/o woman
  - **2 months** of hand pain and swelling
  - 1 hour of morning stiffness
  - Manages a home day care with 7 children attending
  - **Smokes 1 PPD (10 years)**
- Physical Exam
  - Tender and swollen
    - Wrists and Ankles
    - 2nd- 5th metacarpophalangeal (MCP)
    - 2nd-4th proximal interphalangeal (PIP) joints
-

Laboratory testing:

Hemoglobin **11 g/dl** MCV 90 fL

WBC 9.2

Platelet **400**

ESR **50 mm/h** (normal <29)

CRP **25 mg/L** (normal <8)

Rheumatoid factor Negative

ANA Negative

TSH Normal

WHICH OF THE FOLLOWING IS THE MOST APPROPRIATE TEST TO DIAGNOSE THIS PATIENT?

A. Parvovirus IgM and IgG
B. Anti-CCP antibody
C. Lyme Screen
D. Anti-dsDNA antibody

Correct answer: B: **Anti-CCP antibody**

Rationale: This is a case of CCP+ RA

- ✓ Symmetric
- ✓ Small-medium joint inflammatory arthritis
- ✓ Over 6 weeks duration
- ✓ CCP is more specific than RF
  - ✓ More common in smokers

QUESTION 2

- History: A 48 y/o woman with Anti-CCP+ RA diagnosed 6 m ago
  - Ongoing pain & swelling in her hands
  - Morning stiffness 2 hours
  - History of Congestive heart failure, Last flare 6 months ago
- Physical examination
  - Synovitis in both wrists & multiple MCPs
- Medications
  - Furosemide 20 mg qod
  - Lisinopril 5 mg
  - Prednisone 5 mg
  - Methotrexate 25 mg/wk Subcutaneously (max. dose)
  - Hydroxychloroquine 200 mg twice daily (added 3 months ago)
- Laboratory studies
  - CRP of **15** mg/L (normal <8 mg/L)
  - Normal CBC, Liver & Kidney function tests
  - Negative Hepatitis B, C & latent TB tests
  - Urinalysis unremarkable
- Radiographs
  - Peri-articular osteopenia with 2 new erosions at MCP joints

WHICH OF THE FOLLOWING IS THE MOST APPROPRIATE NEXT STEP IN MANAGEMENT?

A. Stop Methotrexate, switch to Leflunomide

B. Add Etanercept

C. Add Abatacept

D. Maintain current treatment regimen for 3 more months

QUESTION 3

History:

- 30 y/o woman
- Rheumatoid arthritis (RA) diagnosed 4 y ago after birth of her first child
- RA has been in remission for last 2 years
- Expresses her desire to expand her family
- Tried unsuccessfully for 9 months

Medications:

- Methotrexate 15 mg/week
- Folic acid 1 mg daily
- Hydroxychloroquine 200 mg twice daily
- Prednisone 5 mg
- Ibuprofen 600 mg at night

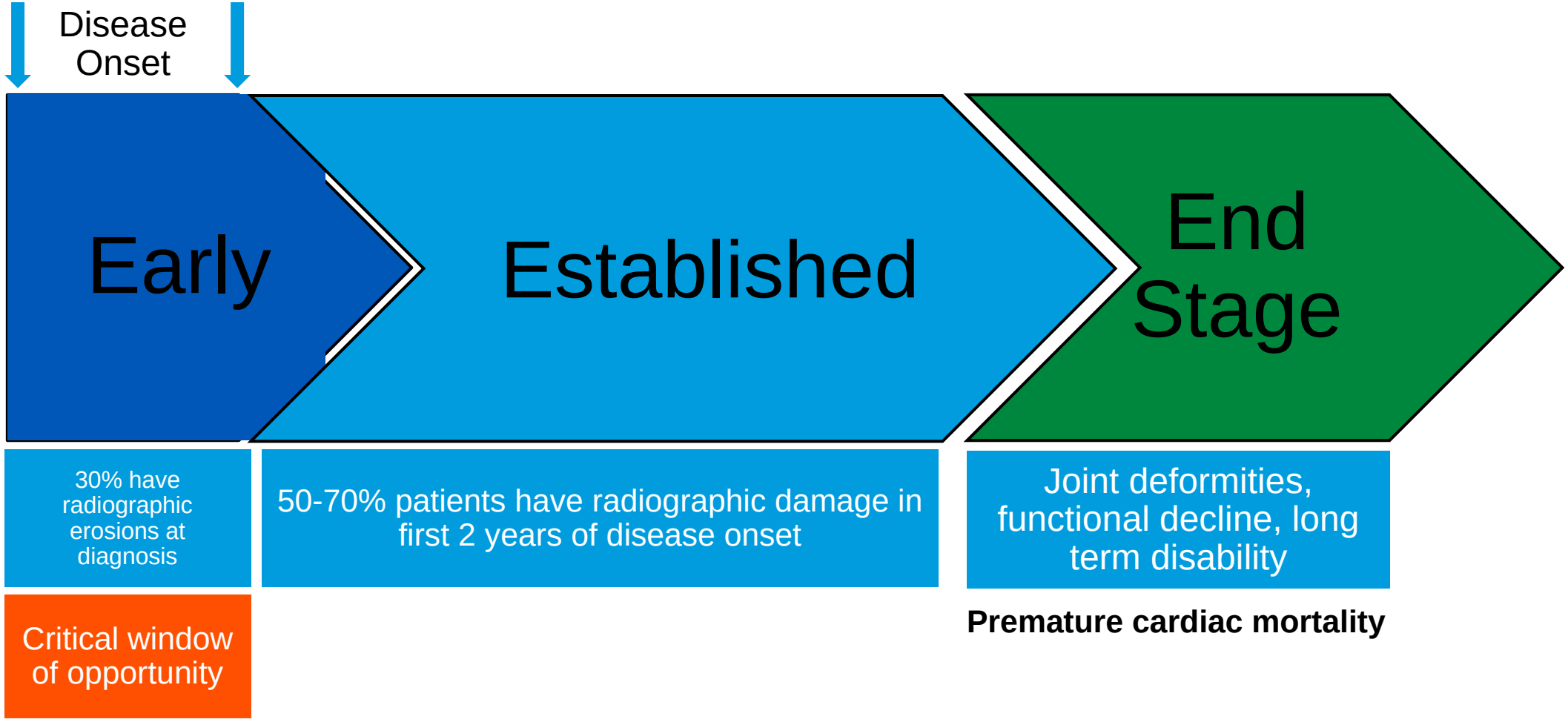
You advise her to discontinue Methotrexate 3 months prior to attempting conception

WHICH OF THE FOLLOWING WILL YOU SUGGEST FOR MANAGING THIS PATIENT'S RA IN EARLY PREGNANCY?

A. Start Leflunomide
B. Discontinue hydroxychloroquine use
C. Discontinue Ibuprofen use
D. Start Certolizumab Pegol

Rheumatoid Arthritis: Treatment

RA – WHEN TO TREAT?



Van der Heijde DM. Br J Rheumatol. 1995:34 9suppl2):74-78

RA TREATMENT

Goals:

- ✓ Treat early (Early initiation of DMARD therapy)
- ✓ Treat to Target (Remission/No or low disease activity)
- ✓ Consider Biologics early if necessary
- ✓ Corticosteroids "bridge" to DMARDs (8-12 weeks)
  - disease modifying (low doses)
  - Intra-articular for symptomatic relief

RA: ASSESS PROGNOSIS – PEARL

Consider features indicating Poor Prognosis

- Seropositive (RF and/or Anti-CCP)
- Radiographic erosions at diagnosis
- Extra-articular disease manifestations
- Functional limitation (HAQ, etc.)
  - 40% have work disability within 10 years of diagnosis.
    - Disability is greatest with delayed treatment

RA: ASSESS DISEASE ACTIVITY

SDAI (Simplified Disease Activity Index)

How to Score the SDAI

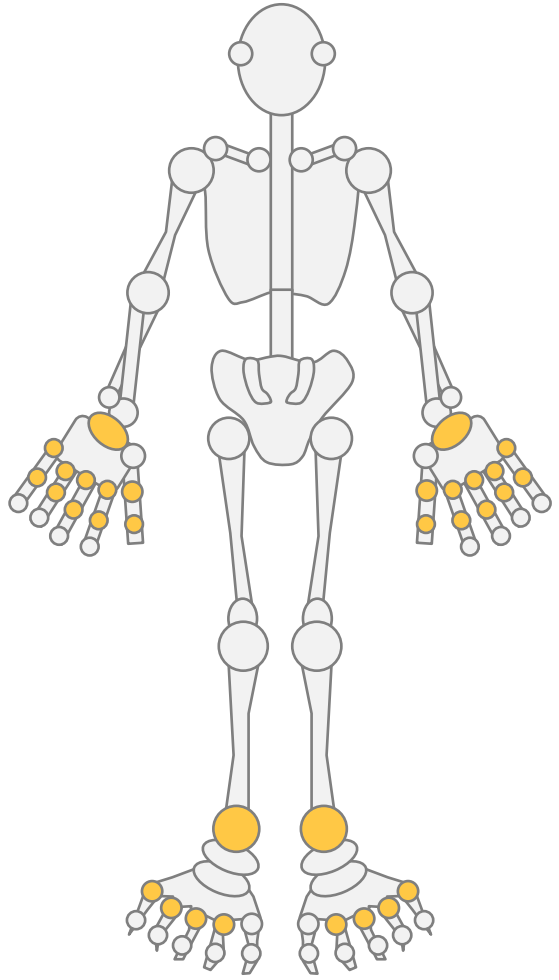
Variable	Range
Tender joint score	(0-28)
Swollen joint score	(0-28)
Patient global score	(0-10)
Provider global score	(0-10)
C-reactive protein (mg/dL)	(0-10)
Add the above values to calculate the SDAI score	**(0-86)**

SDAI Score Interpretation	
0.0-3.3	Remission
3.4-11.0	Low activity
11.1-26.0	Moderate activity
26.1-86.0	High activity

CDAI (Clinical Disease Activity Index)

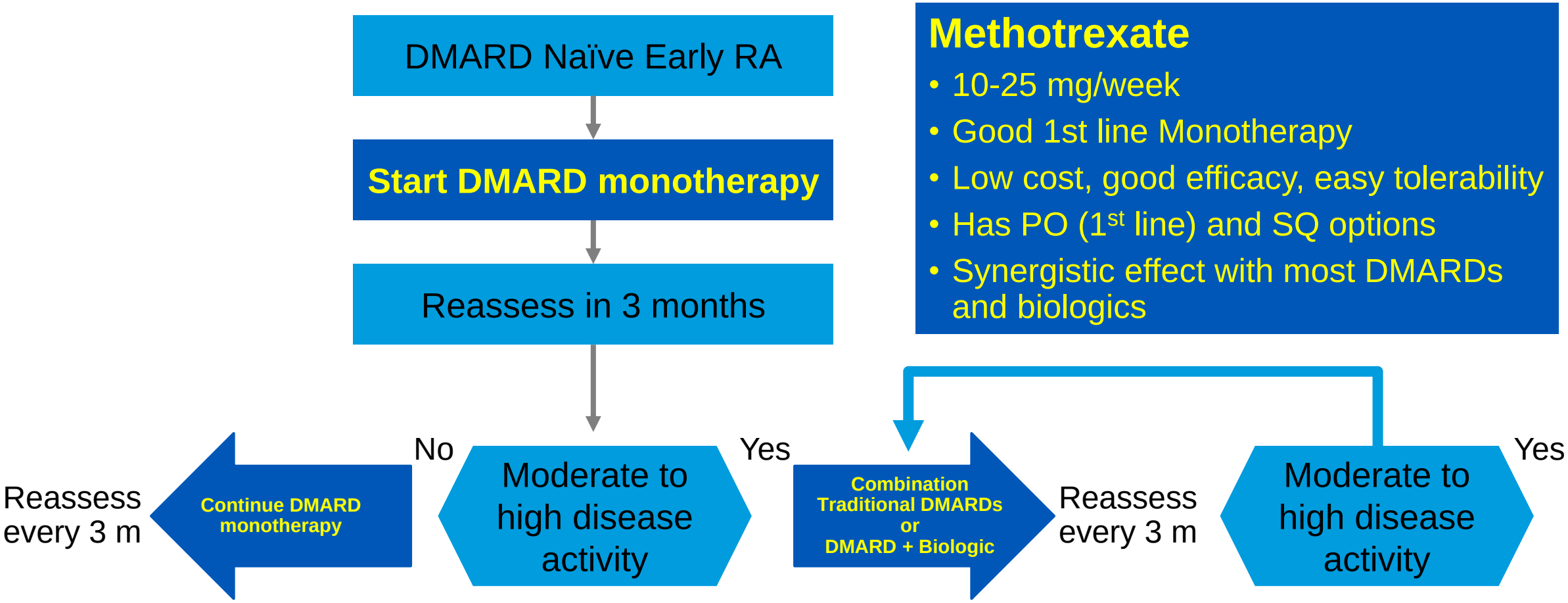
Variable	Range
Tender joint score	(0-28)
Swollen joint score	(0-28)
Patient global score	(0-10)
Provider global score	(0-10)
Add the above values to calculate the CDAI score	**(0-76)**

CDAI Score Interpretation	
0.0-2.8	Remission
2.9-10.0	Low activity
10.1-22.0	Moderate activity
22.1-76.0	High activity



Redrawn from: Salaffi et al. Int. J. Clin. Rheumatol. (2013) 8(3), 347–360

TREATMENT: EARLY RA



Singh JA et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol 2016 Jan;68(1):1-26

RA TREATMENT

csDMARDs:

- Methotrexate 10-25 mg/week
- Hydroxychloroquine 200-400 mg/day
- Sulfasalazine 2-3 g/day
- Leflunomide 10-20 mg/day
- Minocycline 100 mg BID

Biologics:

Anti-Tumor necrosis Factor (TNF):

- Adalimumab (SQ)
- Etanercept (SQ)
- Infliximab (IV)
- Certolizumab pegol (SQ)
- Golimumab (SQ/IV)

Non- TNF:

- Abatacept (IV/SQ)- CTLA-4 Ig fusion protein (T cell costimulation inhibitor)
- Tocilizumab (IV/SQ), Sarilumab (SQ) (Interleukin-6 Antagonist)
- Rituximab (CD 20 B cell depletion)

American College of Rheumatology
Empowering Rheumatology Professionals

Arthritis Care & Research
Vol. 73, No. 7, July 2021, pp 924–939
DOI 10.1002/acr.24596

2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis

Liana Fraenkel,[1] Joan M. Bathon,[2] Bryant R. England,[3] E. William St.Clair,[4] Thurayya Arayssi,[5] Kristine Carandang,[6] Kevin D. Deane,[7] Mark Genovese,[8] Kent Kwas Huston,[9] Gail Kerr,[10] Joel Kremer,[11] Mary C. Nakamura,[12] Linda A. Russell,[13] Jasvinder A. Singh,[14] Benjamin J. Smith,[15] Jeffrey A. Sparks,[16] Shilpa Venkatachalam,[17] Michael E. Weinblatt,[16] Mounir Al-Gibbawi,[18] Joshua F. Baker,[19] Kamil E. Barbour,[20] Jennifer L. Barton,[21] Laura Cappelli,[22] Fatimah Chamseddine,[18] Michael George,[23] Sindhu R. Johnson,[24] Lara Kahale,[18] Basil S. Karam,[18] Assem M. Khamis,[18] Iris Navarro-Millán,[25] Reza Mirza,[26] Pascale Schwab,[21] Namrata Singh,[27] Marat Turgunbaev,[28] Amy S. Turner,[28] Sally Yaacoub,[18] and Elie A. Akl[18]

- DMARD-naive patients with low disease activity
  - HCQ conditionally recommended over other csDMARDs
  - SSZ conditionally recommended over MTX
  - MTX conditionally recommended over LEF
- Addition of a bDMARD or tsDMARD conditionally recommended over triple therapy (i.e., addition of SSZ and HCQ) in patients not at target on maximal dose of MTX
- Switching to a bDMARD or tsDMARD of a different class is conditionally recommended over a bDMARD or tsDMARD of the same class for patients who are not at target

TREATMENT: ESTABLISHED RA

Persistent
Moderate or high
disease activity

MTX/DMARD + different Anti-TNF Biologic
Or
MTX/DMARD + different Non-TNF Biologic
Or
MTX/DMARD +/- JAK Inhibitor

Reassess every 3 months to
maintain low/no disease activity

ts (targeted synthetic) DMARDs

Tofacitinib, Baricitinib, Upatacitinib(PO)

- **Inhibit JAK-STAT pathway**

- Consider in patients with inadequate response to MTX and/or a biologic
- Synergistic effect with most DMARDs and biologics

Pearl

Do Not Combine Biologics

Singh JA et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol 2016 Jan;68(1):1-26

PEARLS ON BIOLOGICS/TSDMARDS

- Biologic to avoid in Congestive Heart Failure/Cardiomyopathy
  - Anti-TNF therapy
- Biologic of choice with history of lymphoproliferative malignancy
  - Rituximab
- Biologic relative contraindicated in COPD
  - Abatacept
- Contraindicated in those with history of arterial/venous thrombosis
  - JAK-Inhibitors (Tofacitinib, Baricitinib, Upatacitinib)
- OK to use/continue MTX in mod-high disease activity RA (conditionally..)
  - Mild/Stable Airway or Parenchymal lung disease, or if incidentally detected on imaging
  - S/C Nodules
  - NASH (if normal LFTs and no evidence of advanced liver fibrosis)

PEARLS ON DRUG MONITORING

- Screen for infections prior to biologic initiation
  - Hepatitis B and C
  - Latent Tuberculosis (Skin test, INF gamma release assays)
- Periodic tests
  - Hydroxychloroquine – eye exams (maculopathy)
  - Methotrexate – CBC, LFT, S. Creatinine
  - Anti-TNF – CBC
  - Tofacitinib, Tocilizumab – Lipid profile, LFT

RA MANAGEMENT IN PREGNANCY

- Often goes into remission; flares post-partum
- Incidence of new RA high in 1st year post-partum

Category X: ***Methotrexate, Leflunomide***

Safe to continue: *HCQ, SSZ, Low dose steroids, Acetaminophen, Anti-TNF (esp. Certolizumab; other anti-TNFs D/C in T3), Azathioprine*

Discontinue at conception: *Abatacept, Rituximab, Tocilizumab, Tofacitinib*

NSAIDS

✓<20 weeks - Impair implantation and increase risk of miscarriage

✓3rd trimester: Premature closure of ductus arteriosus

Sammaritano et. al. Arthritis & Rheumatology Vol. 72, No. 4, April 2020, pp 529–556

RA Management In Men Planning To Father A Child

Strongly recommend continuing	Conditionally recommend continuing	Strongly recommend discontinuing	Conditionally recommend discontinuing	Unable to make a recommendation due to limited data
Azathioprine/ 6-mercaptopurine	Anakinra	Cyclophosphamide *(discontinue 12 weeks prior to attempted conception)*	Thalidomide *(discontinue 4 weeks prior to attempted conception)*	Abatacept
Colchicine	Cyclooxygenase 2 inhibitors			Apremilast
Hydroxychloroquine	Cyclosporine			Baricitinib
Tumor necrosis factor inhibitors (all)	Leflunomide			Belimumab
	Methotrexate			Secukinumab
	Mycophenolate mofetil			Tocilizumab
	Mycophenolic acid			Tofacitinib
	Nonsteroidal anti-inflammatory drugs			Ustekinumab
	Rituximab			
	Sulfasalazine *(semen analysis if delayed conception)*			
	Tacrolimus			

Sulfasalazine – temporary oligozoospermia

Sammaritano et. al. Arthritis & Rheumatology Vol. 72, No. 4, April 2020, pp 529–556

QUESTION 2

- History: A 48 y/o woman with Anti-CCP+ RA diagnosed 6 m ago
  - Ongoing pain & swelling in her hands
  - Morning stiffness 2 hours
  - History of Congestive heart failure, Last flare 6 m ago
- Physical examination
  - Synovitis in both wrists & multiple MCPs
- Medications
  - Furosemide 20 mg qod
  - Lisinopril 5 mg
  - Prednisone 5 mg
  - Methotrexate 25 mg/wk Subcutaneously (max. dose)
  - Hydroxychloroquine 200 mg twice daily (added 3 months ago)
- Laboratory studies
  - CRP of **15** mg/L (normal <8 mg/L)
  - Normal CBC, Liver & Kidney function tests
  - Negative Hepatitis B, C & latent TB tests
  - Urinalysis unremarkable
- Radiographs
  - Peri-articular osteopenia with 2 new erosions at MCP joints

WHICH OF THE FOLLOWING IS THE MOST APPROPRIATE NEXT STEP IN MANAGEMENT?

A. Stop Methotrexate, switch to Leflunomide

B. Add Etanercept

C. Add Abatacept

D. Maintain current treatment regimen for 3 more months

Correct answer: **C**: **Add Abatacept**

Rationale: RA patient has ongoing high disease activity despite methotrexate and hydroxychloroquine for 6 months.

CCP+ is a poor prognostic marker

- ✓ Addition of a biologic is the next best step
- ✓ Anti-TNF contraindicated in CHF

QUESTION 3

History:

- 30 y/o woman
- RA diagnosed 4 y ago after birth of her first child
- RA has been in remission for last 2 years
- Expresses her desire to expand her family
- Tried unsuccessfully for 9 months

Medications:

- Methotrexate 15 mg/week
- Folic acid 1 mg daily
- Hydroxychloroquine 200 mg twice daily
- Prednisone 5 mg
- Ibuprofen 600 mg at night

You advise her to discontinue Methotrexate 3 months prior to attempting conception

WHICH OF THE FOLLOWING WOULD YOU ALSO SUGGEST FOR MANAGING THIS PATIENT'S RA?

A. Start Leflunomide
B. Discontinue hydroxychloroquine use
C. Discontinue Ibuprofen use
D. Start Certolizumab Pegol

Correct answer: **C**:
Discontinue Ibuprofen use

- ✓ NSAIDS should be avoided in 1st trimester to avoid risk of miscarriage
- ✓ Leflunomide is teratogenic

QUESTION 4

History: A 70 y/o woman

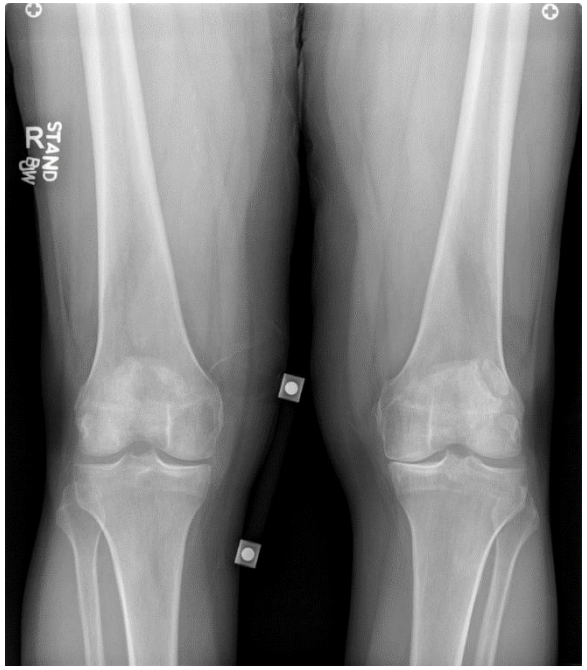
- Recent insidious worsening of left knee pain
- Unable to walk more than 2 blocks
- 30 minutes of morning stiffness and gelling after inactivity
- B/L knee osteoarthritis 10 y ago : poor relief with intra-articular corticosteroid and hyaluronic acid injections

Physical exam:

- BMI is 35
- L knee – varus deformity; small, cool effusion; crepitus; medial joint line tenderness
- Hands – a few tender Heberden's and Bouchard's nodes

Knee x-rays:

- Asymmetric joint space loss, worse in L>R knee with "bone on bone" arthritis
- Osteophytes



WHICH OF THE FOLLOWING IS THE NEXT DIAGNOSTIC TEST FOR THIS PATIENT?

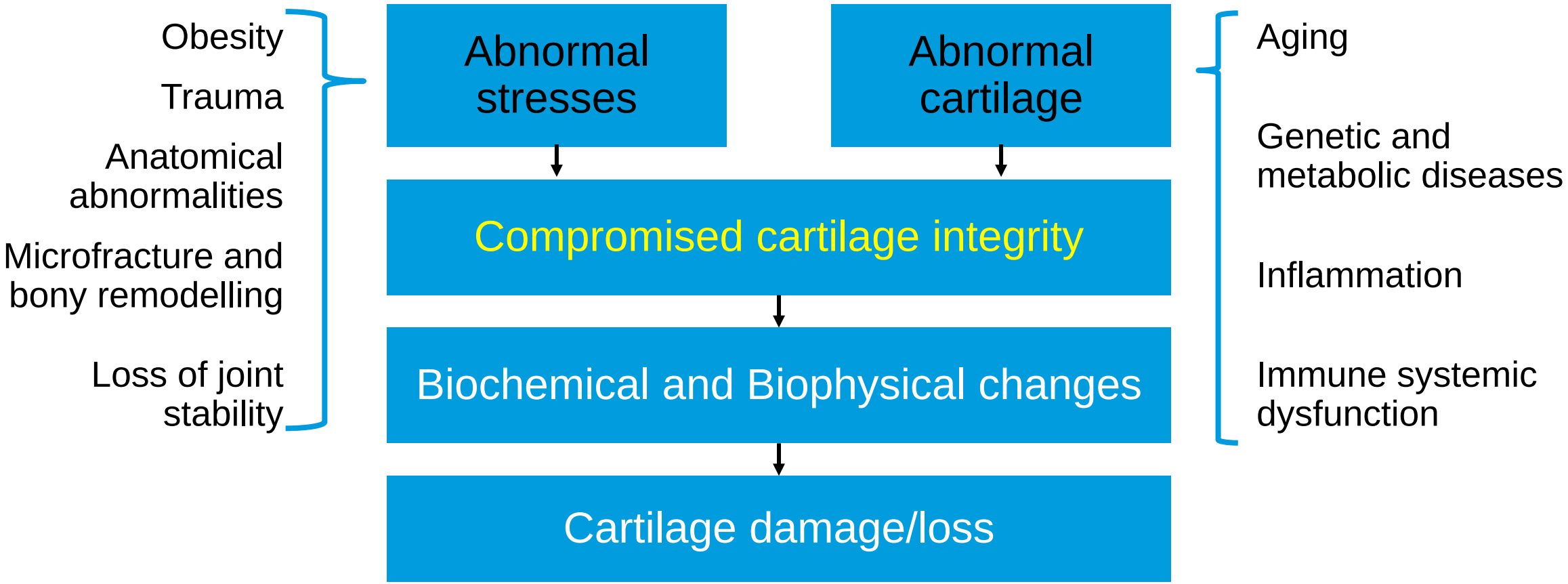
A. Joint aspiration with cell count and crystal analysis
B. MRI of left knee
C. Obtain RF and CCP antibody tests
D. No additional testing

2 DIAGNOSE AND MANAGE SYMPTOMATIC OA

OSTEOARTHRITIS

- Most common type of arthritis: 30 million!
- Most common cause of disability over 65 y
- Prevalence increases with age
  - Radiographic knee OA : 35% adults over 60 y
  - Radiographic hand OA: 60% adults over 60 y
- Risk factors: Age, Female sex, Obesity
- OA in the young
  - Strong genetic predisposition
  - Recreational or occupational injury

OSTEOARTHRITIS: PATHOPHYSIOLOGY



PRIMARY (IDIOPATHIC) OA : DISTRIBUTION

Peripheral Joints

- Hands : DIP, PIP (cf. RA), 1st CMC
- Feet : 1st MTP
- Large weight-bearing joints – hips, knees

Spine (C and L Spine)

- Apophyseal joints
- Intervertebral discs

Secondary Osteoarthritis	
Hemochromatosis	2nd and 3rd MCP joints
CPPD arthropathy	MCPs, wrists, knees, hips, shoulders, atlantoaxial joint
Hyperparathyroidism	Wrists, MCP joints
Acromegaly	knees, shoulders, spine
Ochronosis	spine, hips, knees

Others: Trauma, Congenital abnormality, Neuropathy, Underlying Inflammatory arthritis

OA: CLINICAL FEATURES

- Symptoms:
  - Pain (gradual onset)
    - Worsens with activity/overuse
    - Lessens/relieved by rest
  - Morning stiffness < 30 minutes
  - No systemic symptoms

- Gelling phenomenon: stiffness after a period of rest or inactivity

DIAGNOSIS: PHYSICAL EXAM IS ALL YOU NEED

- Look for signs on exam: bony enlargement
  - Heberden's and Bouchard's nodes
- Restricted joint ROM
- Crepitus (creaking, grinding noise from irregular cartilage) with passive ROM
- Minimal joint swelling, cool effusions
- Periarticular muscle atrophy

No Diagnostic labs

- Check Kidney function if considering NSAIDs
- Labs and synovial fluid evaluation to rule out Secondary etiologies

(CPPD arthropathy, hemochromatosis, hyperparathyroidism)

Heberden’s (DIP) nodes

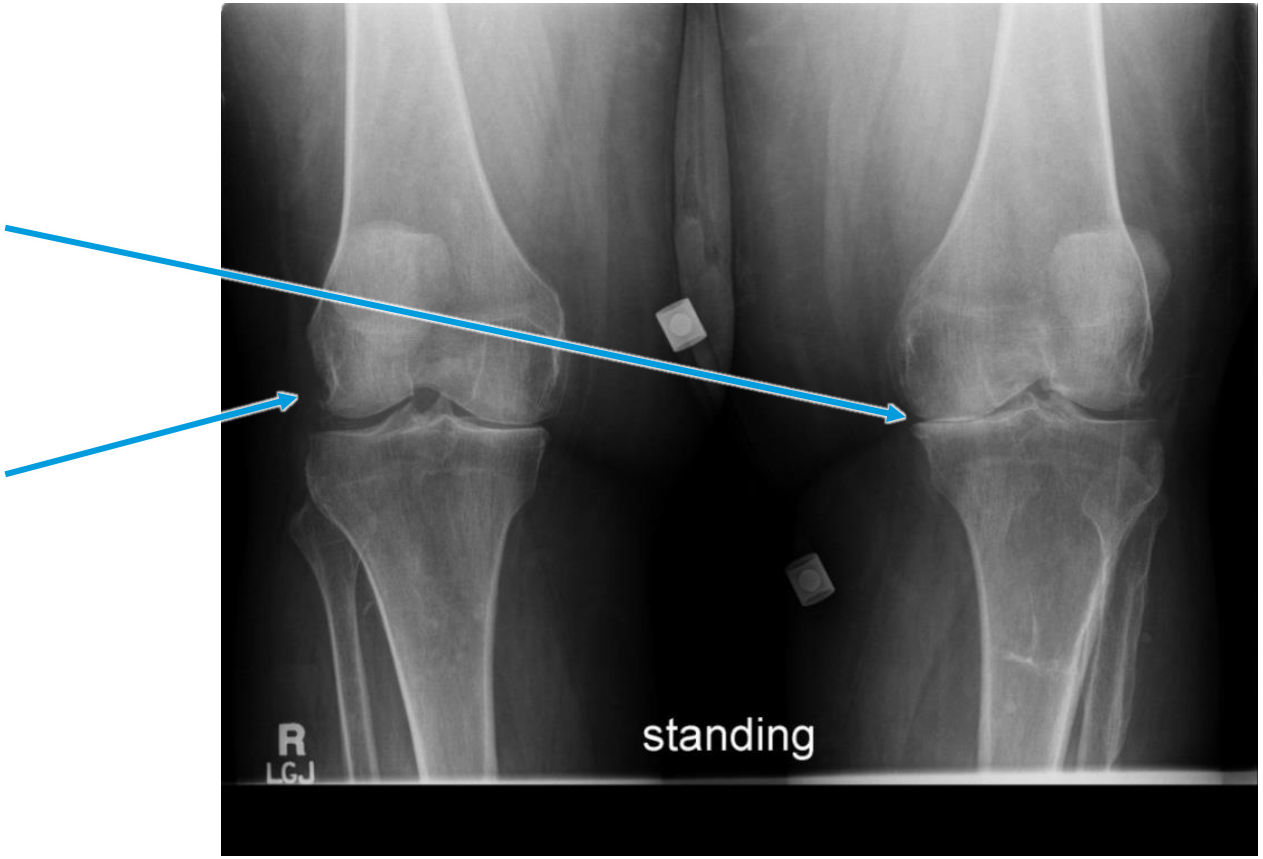
Bouchard’s (PIP) Nodes

Pearl

MCPs spared
– except in Secondary OA (Hemochromatosis, CPPD arthropathy)

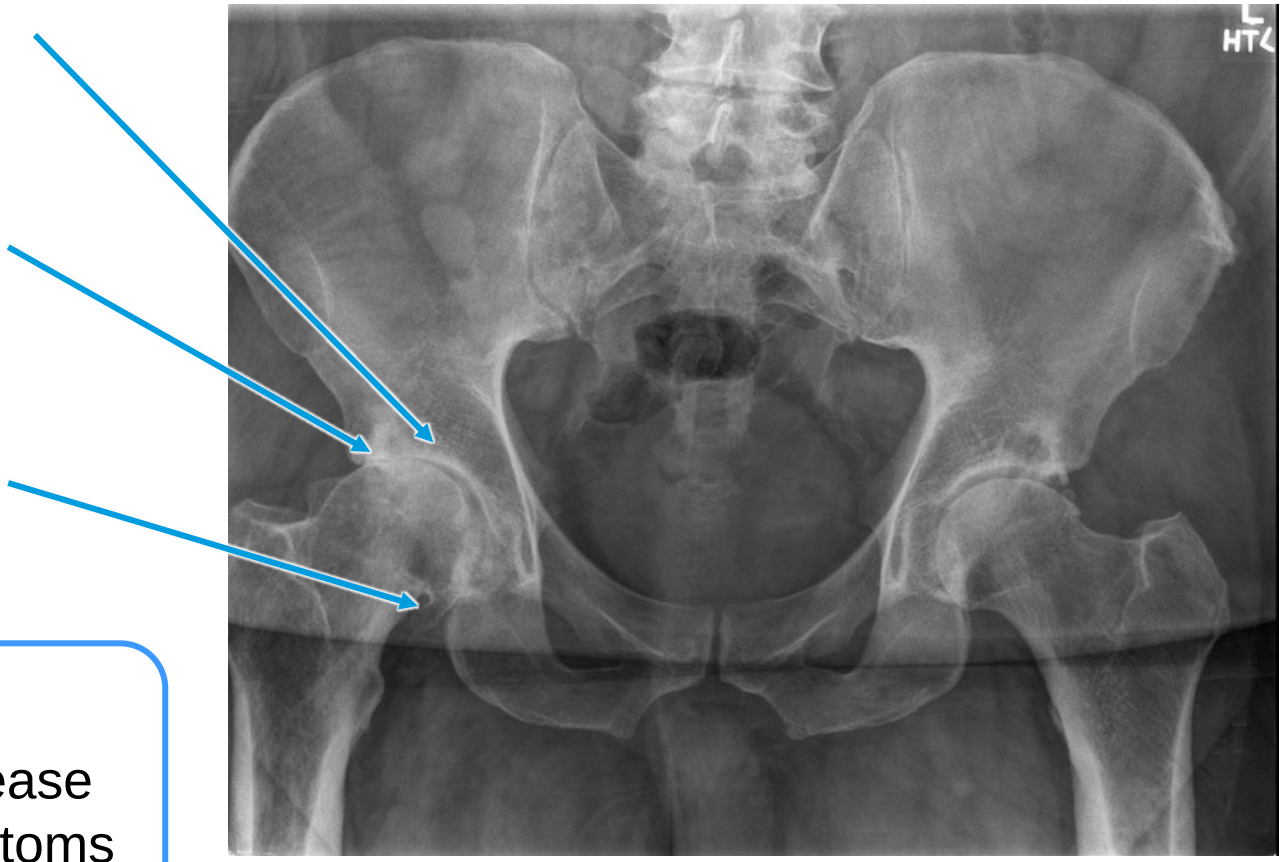
DIAGNOSIS: PLAIN RADIOGRAPHS ONLY

- Asymmetric joint space narrowing (cf. RA)
- Subchondral sclerosis
- Bony cysts formation
- Osteophyte formation



DIAGNOSIS: PLAIN RADIOGRAPHS HIP

- Asymmetric joint space narrowing (cf. RA)
- Subchondral sclerosis
- Bony cysts formation
- Osteophyte formation



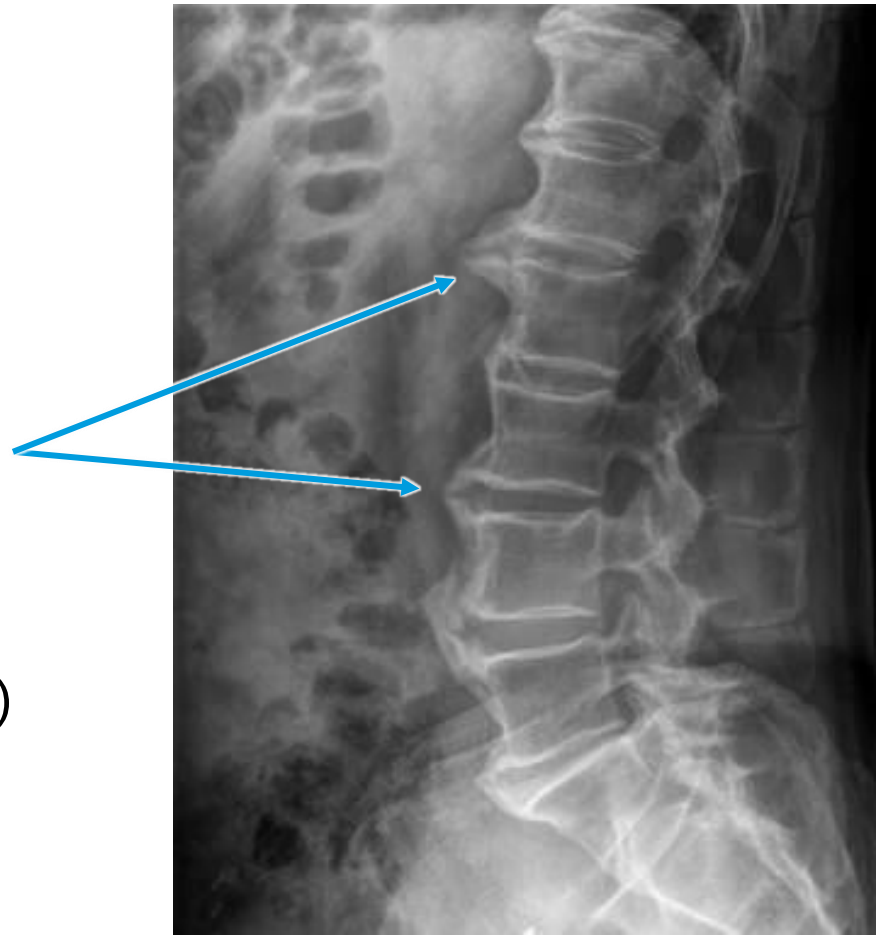
Pearl

Radiographic features
- May be absent in early disease
- May not correlate with symptoms

OA SUBSET: “DISH”

Diffuse idiopathic skeletal hyperostosis

- Calcification of anterior longitudinal ligament
  - Large, flowing osteophytes (4 contiguous vertebral bodies)
- Calcification of tendinous and ligamentous sites
  - Achilles or calcaneal spurs
  - “whiskering” along pelvis
- Metabolic factors, i.e. elevated IGF-1 and GH probably play a role (more common in diabetics)
- More common in men



OA SUBSET: “EROSIVE” OA

- Predominantly women, postmenopausal
- Typically involves DIPs, PIPs, CMCs
- Characterized by “flares” of joint inflammation of DIP, PIP joints manifested by erythema, swelling, pain
- X-rays: **“Gull wing”** deformities at PIPs/DIPs, rarely ankylosis

Image courtesy of Dr Mohammad Taghi Niknejad, Radiopaedia.org, rID: 21250

QUESTION 4

History: A 70 y/o woman

- recent worsening of right knee pain
- unable to walk more than 2 blocks
- 30 minutes of morning stiffness and gelling after inactivity
- B/L knee osteoarthritis 10 y ago: poor relief with intra-articular corticosteroid and hyaluronic acid injections

Physical exam:

- BMI is 35
- R knee – varus deformity; small, cool effusion; crepitus; medial joint line tenderness
- Hands – a few tender Heberden's and Bouchard's nodes

Knee x-rays:

- Asymmetric joint space loss, worse in right knee with "bone on bone" arthritis
- osteophytes

WHICH OF THE FOLLOWING IS THE NEXT DIAGNOSTIC STEP FOR THIS PATIENT?

A. Joint aspiration with cell count and crystal analysis

B. MRI of left knee

C. Obtain RF and CCP antibody tests

D. No additional testing

Correct answer: **D**:
No Additional Testing

Given the typical symptoms and physical examination findings

✓ No additional testing is recommended for OA

QUESTION 5

- She was asked to stop Naproxen after diagnosis of a bleeding peptic ulcer on upper GI endoscopy 4 weeks ago
- She tried acetaminophen up to 3 grams/24 h without relief
- Comorbidities:
  - Chronic kidney disease stage 3
  - Chronic angina
  - Dyslipidemia

WHICH OF THE FOLLOWING IS NEXT BEST STEP IN MANAGING THE PATIENTS PAIN?

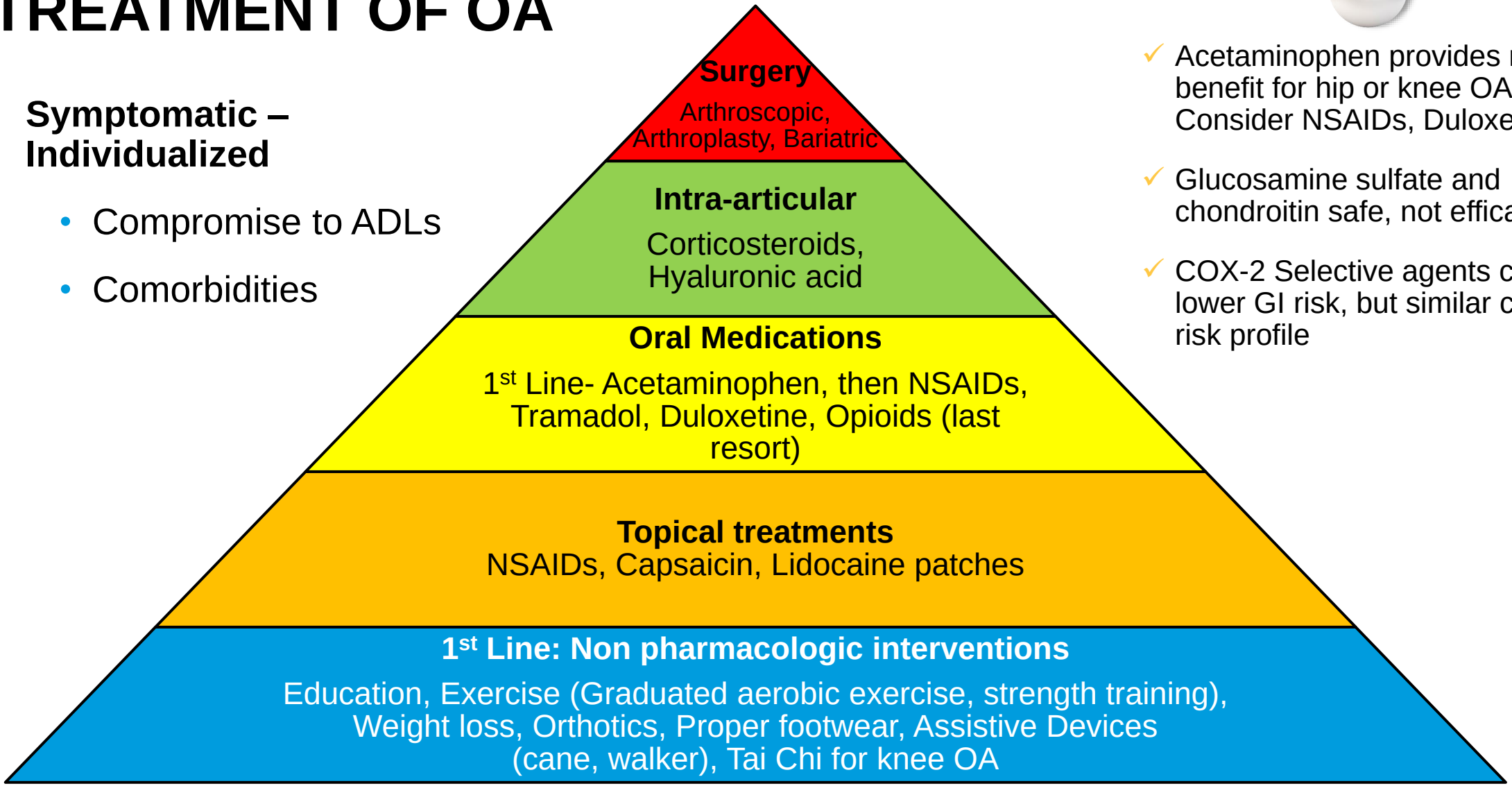
A. Celecoxib
B. Duloxetine
C. Glucosamine sulfate
D. Oxycodone

Osteoarthritis: Treatment

TREATMENT OF OA

Symptomatic – Individualized

- Compromise to ADLs
- Comorbidities



- ✓ Acetaminophen provides no benefit for hip or knee OA → Consider NSAIDs, Duloxetine
- ✓ Glucosamine sulfate and chondroitin safe, not efficacious
- ✓ COX-2 Selective agents carry a lower GI risk, but similar cardiac risk profile

QUESTION 5

- She was asked to stop Naproxen after diagnosis of a bleeding peptic ulcer on upper GI endoscopy 4 weeks ago
- She tried acetaminophen up to 3 grams/24 h without relief
- Comorbidities:
  - Chronic kidney disease stage 3
  - Chronic angina
  - Dyslipidemia

WHICH OF THE FOLLOWING IS NEXT BEST STEP IN MANAGING THE PATIENTS PAIN?

A. Celecoxib

B. Duloxetine

C. Glucosamine sulfate

D. Oxycodone

Correct answer: **B**:

Duloxetine is considered a good option for management of chronic OA pain in patients that have failed Tylenol and cannot take NSAIDS

QUESTION 6

History: 32 y/o woman with 3 y history of RA

- States her rheumatologist “does not take her seriously”
- Generalized musculoskeletal pain and debilitating fatigue for last 2 years
- Constant brain fog, daytime somnolence, impaired short term memory
- Wakes up unrefreshed and gets no exercise as it makes her ‘flare’
- Single mother of 3 and works 40 hours/week at a factory
- Intractable migraines and pelvic pain but extensive subspecialty evaluation has been unrevealing
- Erythema migrans after tick bite treated 5 y ago with Doxycycline x 1 month

- Physical exam: BMI 38; no synovitis or joint effusions; multiple, tender points on her arms, legs, back, and buttocks
- Medications: Methotrexate – no missed doses;
- Prednisone up to 20 mg/day does not help her, transient relief at 40-60 mg
- Laboratory tests:
  - normal CBC, TSH, Cortisol, Vitamin D, CRP.
  - **RF is positive**. CCP negative.
  - **ANA is 1:80, homogenous pattern**

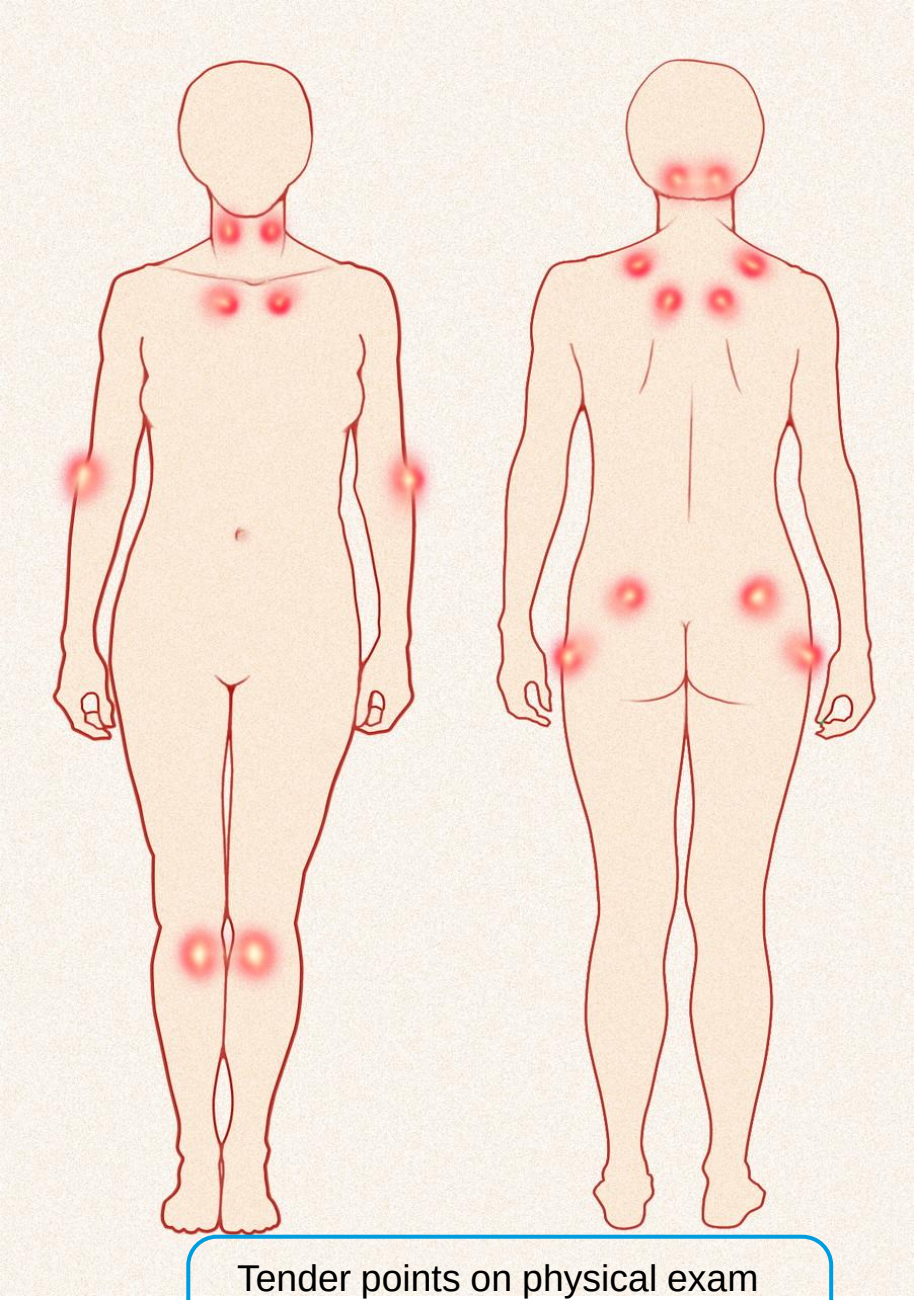
WHICH OF THESE WILL BE MOST BENEFICIAL FOR THIS PATIENT?

A. Add Hydroxychloroquine
B. Add Tramadol
C. Add Milnacipran
D. Add Doxycycline

3 DIAGNOSE AND TREAT FIBROMYALGIA

FIBROMYALGIA

- Chronic condition characterized by widespread, self-sustaining pain (allodynia, hyperalgesia, “central sensitization”)
- Often accompanied by
  - Comorbid fatigue
  - Disrupted, Nonrestorative sleep
  - Cognitive and memory disturbances ‘fibro fog’
  - Psychiatric symptoms (eg, depression, anxiety)
  - Somatic symptoms (eg, headache, paresthesias)
- Usually worse in response to activity, weather changes, menstrual status, injury, other stressors
- Prevalence 2-3%, F:M 3:1



Tender points on physical exam
-subject to physician expertise
-less reported in males

FM DIAGNOSIS

ACR 1990 Criteria

- History of widespread pain for >3m
- 11 of 18 tender points on palpation

New ACR Criteria 2010 – Physical Exam is not a part of this

- Widespread pain index (WPI) ≥ 7 and symptom severity (SS) scale score ≥ 5 (or)
- WPI ≥ 3–6 and SS scale score ≥ 9
  - Symptoms present at a similar level for 3 m
  - Absence of another etiology to explain the pain

Wolfe F, et al. “The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity.” Arthritis Care & Research 2010; 62:600-10

NEW CLINICAL FIBROMYALGIA DIAGNOSTIC CRITERIA – PART 1

To answer the following questions, patients should take into consideration

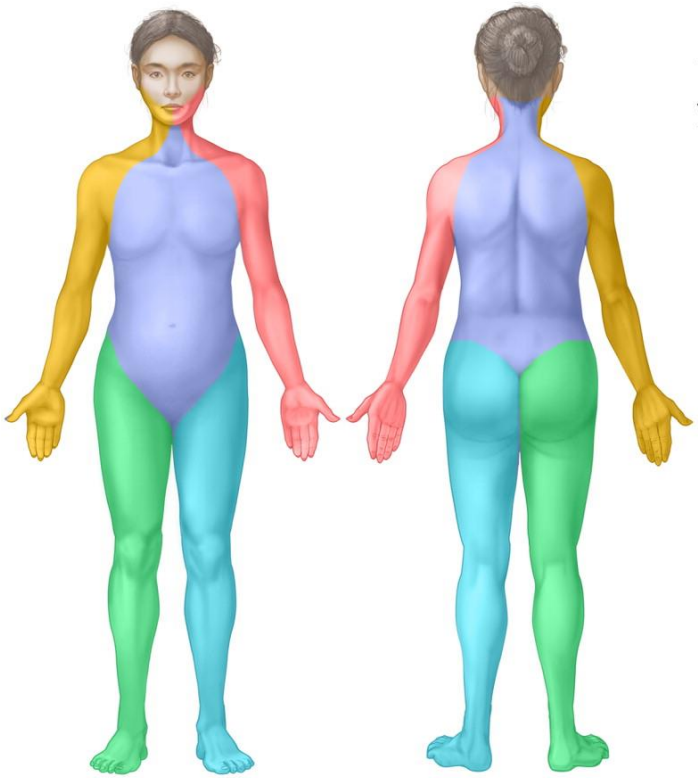
- How you felt the **past week**
- While taking your current therapies and treatments, and
- Exclude your pain or symptoms from other known illnesses such as arthritis, Lupus, Sjogren's, etc.

Check each area you have felt pain in over the past week

☐ Shoulder girdle, left
☐ Shoulder girdle, right
☐ Upper arm, left
☐ Upper arm, right
☐ Lower arm, left
☐ Lower arm, right
☐ Hip (buttock) left
☐ Hip (buttock) right
☐ Upper leg left
☐ Upper leg right
☐ Lower leg left
☐ Lower leg right
☐ Jaw left
☐ Jaw right
☐ Chest
☐ Abdomen
☐ Neck
☐ Upper back
☐ Lower back
☐ Non of these areas

Determining Your Widespread Pain Index (WPI)

The WPI Index score from Part 1 is between 0 and 19



To be diagnosed with Fibromyaglia, you need to be diagnosed with pain coming from for of these five areas:

Region 1- Left jaw, shoulder girdle, upper and lower arm

Region 2- Right jaw, shoulder girdle, upper and lower arm

Region 3- Left hip, buttock, trochanter, upper and lower leg

Region 4- Right hip, buttock, trochanter, upper and lower leg

Region 5- Neck, upper back, chest, abdomen

Count up the number of areas checked and enter your Widespread Pain Index or WPI score score here _____

Symptom Severity Score (SS score) – Part 2a

Indicate your level of symptom severity over the past week using the following scale

Fatigue

- ☐ 0 = No problem
- ☐ 1 = Slight or mild problems; generally mild or intermittent
- ☐ 2 = Moderate; considerable problems; often present and/or at a moderate level
- ☐ 3 = Severe: Pervasive, continuous, life disturbing problems

Waking unrefreshed

- ☐ 0 = No problem
- ☐ 1 = Slight or mild problems; generally mild or intermittent
- ☐ 2 = Moderate; considerable problems; often present and/or at a moderate level
- ☐ 3 = Severe: Pervasive, continuous, life disturbing problems

Cognitive symptoms

- ☐ 0 = No problem
- ☐ 1 = Slight or mild problems; generally mild or intermittent
- ☐ 2 = Moderate; considerable problems; often present and/or at a moderate level
- ☐ 3 = Severe: Pervasive, continuous, life disturbing problems

Tally your score for Part 2a (not the number of checkmarks) and enter it here ____.

Symptom Severity Score (SS score) – Part 2b

Check each of the following OTHER SYMPTOMS that you have experienced over the past week?

- ☐ Muscle pain
- ☐ Irritable bowel syndrome
- ☐ Fatigue/tiredness
- ☐ Thinking or remembering problems
- ☐ Muscle Weakness
- ☐ Headache
- ☐ Pain/cramps in abdomen
- ☐ Numbness/tingling
- ☐ Dizziness
- ☐ Insomnia
- ☐ Depression
- ☐ Constipation
- ☐ Pain in upper abdomen
- ☐ Nausea
- ☐ Nervousness
- ☐ Chest pain
- ☐ Blurred vision
- ☐ Fever
- ☐ Diarrhea
- ☐ Dry mouth
- ☐ Itching
- ☐ Wheezing
- ☐ Raynauld's
- ☐ Hives/welts
- ☐ Ringing in ears
- ☐ Vomiting
- ☐ Heartburn
- ☐ Oral ulcers
- ☐ Loss/change in taste
- ☐ Seizures
- ☐ Dry eyes
- ☐ Shortness of breath
- ☐ Loss of appetite
- ☐ Rash
- ☐ Sun sensitivity
- ☐ Hearing difficulties
- ☐ Easy bruising
- ☐ Hair loss
- ☐ Frequent urination
- ☐ Painful urination
- ☐ Bladder spasms

Count up the number of symptoms checked above **Enter your score for Part 2b here ____.**

*If you tallied:

0 symptoms	Give yourself a score of 0
1 to 10	Give yourself a score of 1
11 to 24	Give yourself a score of 2
25 or more	Give yourself a score of 3

Now add Part 2a AND 2b scores, and enter ___.
This is your Symptom Severity Score (SS score), which can range from 0 to 12.

FM DIAGNOSIS: 2016 UPDATE

- Generalized pain
  - pain in at least 4 of 5 regions
- Symptoms for at least 3 months
- WPI ≥ 7 and SSS score ≥ 5 OR WPI of 4–6 and SSS score ≥ 9
- A diagnosis of fibromyalgia is valid irrespective of other diagnoses

Widespread Pain Index (WPI)

Left upper region (Region 1)	☐		Right upper region (Region 2)
	☐	Jaw*	☐
	☐	Should girdle	☐
	☐	Upper arm	☐
	☐	Lower arm	☐
Left lower region (Region 3)	☐		Right lower region (Region 4)
	☐	Hip (buttock, trochanter)	☐
	☐	Upper leg	☐
	☐	Lower leg	☐
		Axial region (Region 5)	
		Neck	☐
		Upper back	☐
		Lower back	☐
		Chest or breast*	☐
		Abdomen*	☐

Total score (0-19): ___

Symptom Severity Scale (SS) score

	0	1	2	3
Fatigue	☐	☐	☐	☐
Waking unrefreshed	☐	☐	☐	☐
Cognitive symptoms	☐	☐	☐	☐

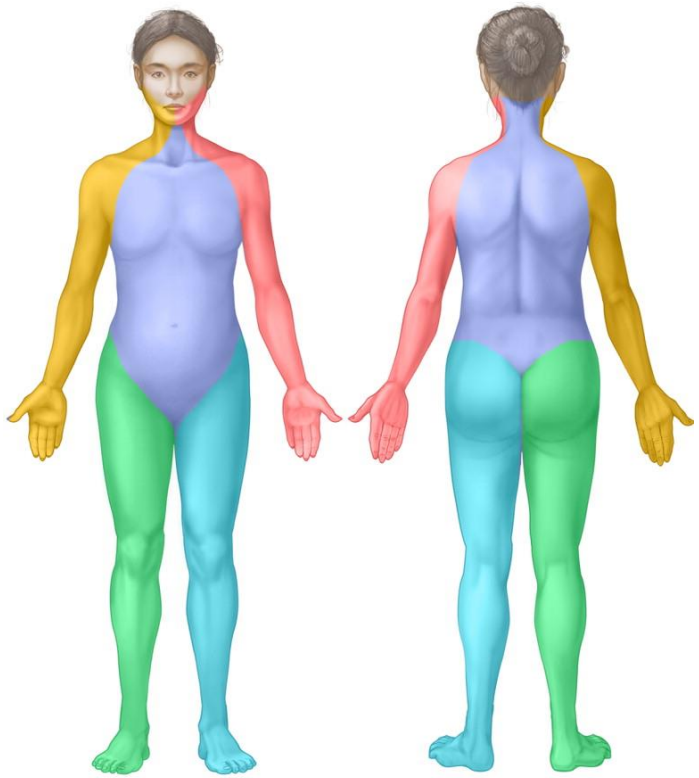
	Present
Headaches	☐
Pain/cramps in lower abdomen	☐
Depression	☐

Total score (0-12): ___

Wolfe et al. Semin Arthritis Rheum. 2016 Dec;46(3):319-329

FMS CRITERIA 2019 – ACTTION-APS PAIN TAXONOMY (AAPT)

- Musculoskeletal pain defined as 6 or more pain sites from a total of 9 possible sites
- Moderate to severe sleep problems OR fatigue
- Musculoskeletal pain plus fatigue or sleep problems must have been present for at least 3 months



- ☐ Head
- ☐ Left arm
- ☐ Right arm
- ☐ Chest
- ☐ Abdomen
- ☐ Upper back and spine
- ☐ Lower back and spine, including buttock
- ☐ Left leg
- ☐ Right leg

Redrawn from: Arnold LM et al. AAPT Diagnostic Criteria for Fibromyalgia. J Pain. 2019 Jun; 20(6):611-628.

TREATMENT

- Challenging
- Multipronged approach
- Rule out mimics
  - Hypothyroidism
  - Depression
  - Vit D deficiency
  - Celiac disease
  - Hypoadrenalism

Strategies for Managing Fibromyalgia	
Initial approach	
Patient education	Educate the patient on fibromyalgia, treatment options, significance of managing any psychiatric comorbidities, and healthy sleep hygiene
Exercise program	Suggest an exercise program that suits the patient's fitness level and interest; if exercise is not possible, refer patient to physiotherapy
Drug monotherapy	Consider duloxetine, pregabalin, or milnacipran
Secondary interventions	
Drug combinations	Consider the patient's tolerance, drug availability, and cost, and the presence of any psychiatric comorbidities; examples of drug combinations include duloxetine and pregabalin, and fluoxetine and amitriptyline
Refer to a psychiatrist	Provides patient with additional treatment modalities, including cognitive behavioral therapy, relaxation, biofeedback, and educational interventions
Consult with or refer to other specialist	Consultation with a rheumatologist and/or a psychiatrist is recommended when patients do not respond to drug monotherapy or combinations or are resistant to multiple treatment approaches
Alternative therapies	Consider trigger point injections, hydrotherapy/ balneotherapy, supplementation, and other interventions as needed

Redrawn from: Consultant. 2016;56(5):402-407

PHARMACOLOGIC TREATMENT OF FM

- Should not be emphasized as the sole solution
  - Patients may not tolerate any of these medications due to side effects

How to choose?

- Pregabalin (inhibits α2δ calcium channel to inhibit glutamate release)
  - Helpful with coexisting sleep disturbance
- Amitriptyline (Tricyclic antidepressant-raises NE level)
  - Can help with disordered sleep
- Duloxetine (SNRI)
  - Effective if depressed mood and/or fatigue
  - Can be constipating
- Milnacipran (SNRI)
  - Beneficial in pts. with cognitive dysfunction, i.e. “fibrofog”

Check for drug interactions & risk of **serotonin syndrome**

QUESTION 6

History: 32 y/o woman with 3 y history of RA

- States her rheumatologist “does not take her seriously”
- Generalized musculoskeletal pain and debilitating fatigue for last 2 years
- Constant brain fog, daytime somnolence, impaired short term memory
- Wakes up unrefreshed and gets no exercise as it makes her ‘flare’
- Single mother of 3 and works 40 hours/week at a factory
- Intractable migraines and pelvic pain but extensive subspecialty evaluation has been unrevealing
- Erythema migrans after tick bite treated 5 y ago with Doxycycline x 1 month

- Physical exam: BMI 38; no synovitis or joint effusions; multiple, tender points on her arms, legs, back, and buttocks
- Medications: Methotrexate – no missed doses;
- Prednisone up to 20 mg/day does not help her, transient relief at 40-60 mg
- Laboratory tests:
  - normal CBC, TSH, Cortisol, Vitamin D, CRP.
  - **RF is positive**. CCP negative.
  - **ANA is 1:80, homogenous pattern**

WHICH OF THESE WILL BE MOST BENEFICIAL FOR THIS PATIENT?

A. Add Hydroxychloroquine

B. Add Tramadol

C. Add Milnacipran

D. Add Doxycycline

Correct answer: **C**:

Add Milnacipran for management of fibromyalgia

Patient does not have SLE or Lyme's disease

BOARD PEARLS

Rheumatoid Arthritis

1. Affects small-medium joints; DIPs spared
2. CCP more specific than RF for diagnosis, BUT both can be Negative
3. Treat to Target – Start DMARD early, add biologic if continued moderate-high disease activity or poor prognostic markers
4. Screen for TB and Hepatitis B/C prior to starting a biologic
5. Do not combine biologics
6. Methotrexate and Leflunomide are Category X drugs
7. Avoid NSAIDs in 1st trimester and >30 weeks gestation

BOARD PEARLS

Osteoarthritis

1. History and physical exam are key to diagnosis
2. 1st line treatment is non-pharmacological
3. Topical NSAIDs, Tylenol, Oral NSAIDS, Tramadol, Duloxetine
4. Intra-articular steroids or hyaluronic acid helpful
5. Glucosamine and Chondroitin are not beneficial

Fibromyalgia

1. Widespread pain and multiple somatic symptoms >3 m
2. Multipronged approach to treatment

REFERENCES FOR ADDITIONAL STUDY

- *Smolen et al. Rheumatoid arthritis. Lancet 2016; 388: 2023–38*
- *Fraenkel et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis.* Arthritis Care & Research Vol. 73, No. 7, July 2021, 924–939.
- *Glyn-Jones et al. Osteoarthritis. Lancet 2015; 386: 376–87*
- *Hauser et al. Review of pharmacological therapies in fibromyalgia syndrome. Arthritis Res Ther. 2014; 16(1): 201.*
- *Arnold LM et al.* AAPT Diagnostic Criteria for Fibromyalgia. J Pain. 2019 Jun; 20(6):611-628.

MAYO CLINIC

THANK YOU

makol.ashima@mayo.edu

@AshimaMakol