RHEUMATOID ARTHRITIS
Peek' n Peak - 2016

General characteristics of RA

- Epidemiology
- Clinical manifestations
- Radiographic changes
- Treatment

A 50 year-old obese white female comes to your office with a chief complaint of morning stiffness for at least one hour every day for the past year. She can no longer button her blouses and is having difficulty using a computer of work because of bilateral wrist and hand pain. She cannot walk long distances because both feet also become sore. Upon further questioning she tells you her joints get warm, red, swollen and that the knuckles of her hands appear to be getting bigger. Your exam reveals hoarseness, the beginnings of swan-neck and boutonniere deformities. Her Achilles tendon has a nodule and the subtalar joints are tender. What treatment is the best choice for this patient?

A. Loose weight and take acetaminophen 3 grams a day and return in 3 months.

B. Loose weight, take acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs) and return in 3 months for follow-up.

C. Discuss the benefits and secondary effects of disease modifying anti-rheumatic drugs (DMARDs), and start them as soon as preliminary testing is accomplished.

D.Do aerobic exercise at least once a day when the joints are inflamed.

E. Start a biologic-response modifier such as adalimumab, infliximab or etanercept without preliminary testing.

RA

- Most common inflammatory arthritis
- Severity and incidence: decreasing
- Blend of environmental and genetic factors
- Monozygotic twins: concordance rate: 30-50%, fraternal twin: 2-5%, general: 1%
- Female:male 2-4:1
- Pregnancy: flare, inc RF titers weeks or months after delivery
- Multiparity may be a risk > 3 children

RA – Rheumatoid Factor

- RF often precedes the onset by many years
- “Seronegative”
- +RF: more severe clinical disease and complications
- 75-90% RF+
- Antibodies: citrullinated peptides: anti-CCP- precedes 5 years
- 14-3-3 eta

RA – Clinical Symptoms

- 55-65%: insidious onset (weeks-months)
- Pain: systemic, articular, diffuse musculoskeletal
- Puffy hands: MCP, PIP, MTP, wrists
- Symmetric (initially can be unilateral)
- Fatigue, malaise, fever (unusual)
- Morning stiffness: 30-45 minutes
- Muscle atrophy: weakness – doors, stairs, work
- Depression, anxiety
- Weight loss

RA – Clinical Complications Cervical Spine

- Atlantoaxial joint: prone to Subluxation in several directions
- Lateral radiographs- neck in flexion: reveal > 3 mm of separation between the odontoid peg and the axial arch
- CT, MRI
- Progression of peripheral joint erosions parallels cervical spine disease
- Cervical collar, operative stabilization

RA – Clinical Complications

- Temporomandibular Joint: 55% at some time
- Cricoarytenoid Joints: vary the pitch and tone of the voice, hoarseness in up to 30%, inspiratory stridor
- Ossicles of the Ear: decrease in hearing
- Sternoclavicular: pain lying on side

RA – Clinical Complications Wrist & Hand

- Ulnar deviation of MCPs and fingers
- Dorsal swelling on the wrist
- Synovial protrusion cyst: volar side of wrist
- Wrist: loss of joint space, ankylosis
- Decreased grip strength
- Swan neck deformity
- Boutonniere deformity
- Resorptive arthropathy
- DeQuervain's tenosynovitis: Finkelstein's test

RA - Clinical Complications Pulmonary Disease

- Pleural disease: 20% rheumatoid effusion: glucose= 10-50 mg/dl
- Interstitial fibrosis
- Nodular lung disease
- Caplan's syndrome: pneumoconiosis and RA
- Bronchiolitis
- Arteritis, with pulmonary hypertension: > 30
- Small airways disease: 50%
- Reactivation of TB by anti-TNF alpha biologic agents

RA – Clinical Complications Ankle and Foot

- Ankle: rare in mild or oligoarticular RA
- Pronation deformities & eversion of foot
- Achilles tendon: nodules, spontaneous rupture
- Pain walking on uneven ground: subtalar joint
- "rocker bottom" deformity: lateral subluxation midfoot
- Downward sublux of MTP heads: "cock-up"
- Hallux valgus: "stacking of 2nd & 3rd toe on 1st toe

Unusual Pattern of Disease
Adult-Onset Still's Disease

Major Criteria

- 1. Temperature of > 39 C for > 1 wk: quotidian
- 2. Leukocytosis > 10,000/mm3
- 3. Typical rash: evanescent salmon or pink macules
- 4. Arthralgias > 2 wks
- Minor Criteria
- 1. Sore throat
- 2. Lymph node enlargement
- 3. Splenomegaly
- 4. Liver dysfunction (high AST/ALT)
- 5. Negative ANA, RF

FELTY'S SYNDROME

- Triad: chronic arthritis, splenomegaly and granulocytopenia
- Prevalence - unknown: 3% of RA
- 2/3 women
- 5^{th} – 7^{th} decade who have had RA for 10 yrs or >
- Articular disease is usually severe
- ESR elevated, RF+, ANA (62-80%)
- Spleen size variable: 4x, hepatomegaly 25%
- Weight loss may be striking
- Brown pigmentation over extremities
- Treatment: MTX
- Prognosis: death rate similar to matched RA

2010 ACR/EULAR Classification Criteria for RA

JOINT DISTRIBUTION (0-5)	
1 large joint	0
2-10 large joints	1
1-3 small joints (large joints not counted)	2
4-10 small joints (large joints not counted)	3
>10 joints (at least one small joint)	5
SEROLOGY (0-3)	
Negative RF AND negative ACPA	0
Low positive RF OR low positive ACPA	2
High positive RF OR high positive ACPA	3
SYMPTOM DURATION (0-1)	
<6 weeks	0
≥6 weeks	1
ACUTE PHASE REACTANTS (0-1)	
Normal CRP AND normal ESR	0
Abnormal CRP OR abnormal ESR	1

≥6 = definite RA

What if the score is <6?

Patient might fulfill the criteria…

→ **Prospectively** over time (cumulatively)

→ **Retrospectively** if data on all four domains have been adequately recorded in the past

American College of Rheumatology — Education · Treatment · Research

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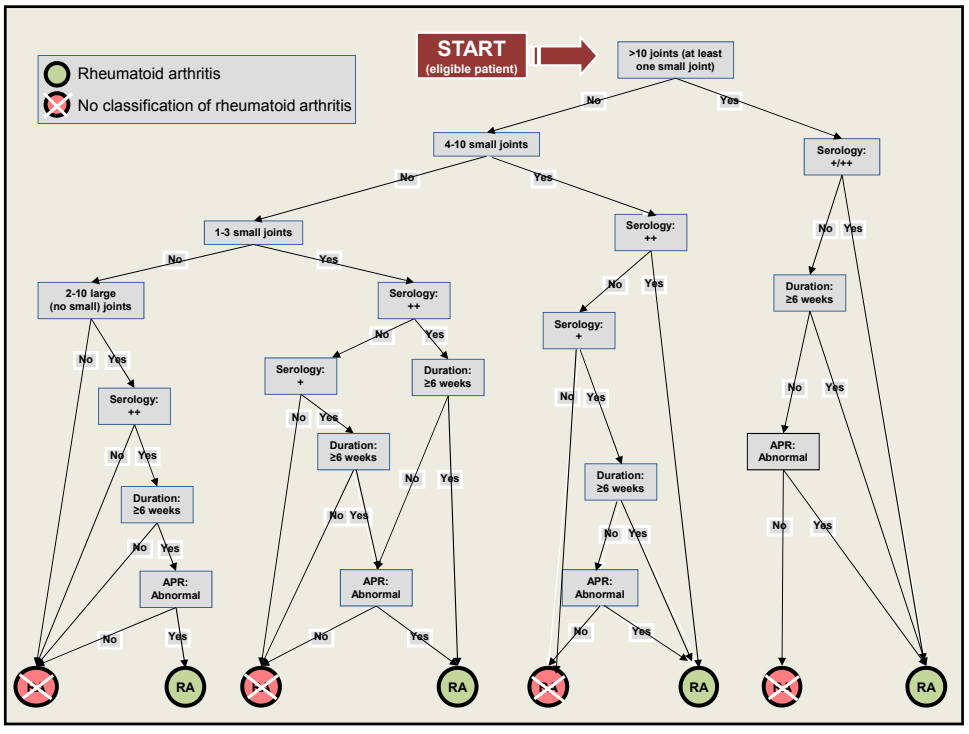

RA - Treatment

- Educate patient and family
- Loose weight
- Exercise – careful when flaring
- Baseline Xrays: hands, feet, CXR
- DXA scan
- Check Vitamin D3 level
- Check vaccine status
- PPD or Quantiferon-Gold
- Check Hepatitis B & C status

RA – Treatment

- Acetaminophen
- NSAIDs
- Glucocorticoids
- OT & PT
- DMARDs
- Biologics
- Immunosuppressives
- Surgery
- Alternative medicine

Table 1. Overview comparison of topics and medications included in the 2008 and 2012 American College of Rheumatology rheumatoid arthritis recommendations*

Topic area considered	2008	2012
Indications for starting or resuming DMARDs and biologic agents	√	√
DMARDs included†	1. Hydroxychloroquine 2. Leflunomide 3. Methotrexate 4. Minocycline 5. Sulfasalazine And, when appropriate, combination DMARD therapy with 2 or 3 DMARDs†	1. Hydroxychloroquine 2. Leflunomide 3. Methotrexate 4. Minocycline 5. Sulfasalazine And, when appropriate, combination DMARD therapy with 2 or 3 DMARDs‡
Biologic agents included§	Non-TNF 1. Abatacept 2. Rituximab Anti-TNF 3. Adalimumab 4. Etanercept 5. Infliximab	Non-TNF 1. Abatacept 2. Rituximab 3. Tocilizumab Anti-TNF 4. Adalimumab 5. Etanercept 6. Infliximab 7. Certolizumab pegol 8. Golimumab
Role of cost and patient preference in decision making for biologic agents	√	See 2008 recommendations¶
Switching between therapies	Considered, but not addressed in detail	√
Monitoring of side effects of DMARDs and biologic agents	√	See 2008 recommendations¶
TB screening for patients starting/ receiving biologic agents	√	√
Use of biologic agents in high-risk patients (those with hepatitis, congestive heart failure, and malignancy)	√	√
Vaccinations in patients starting/ receiving DMARDs or biologic agents	Pneumococcal, influenza, and hepatitis vaccines	Pneumococcal, influenza, hepatitis, human papillomavirus, and herpes zoster vaccines

* DMARDs = disease-modifying antirheumatic drugs; non-TNF = non–tumor necrosis factor; TB = tuberculosis.
† Cyclosporine, azathioprine, and gold were included in the literature search, but due to the lack of new data and/or infrequent use, they were not included in scenarios and the recommendations.
‡ Triple therapy with methotrexate + hydroxychloroquine + sulfasalazine.
§ Anakinra was included in the literature search, but due to the lack of new data and/or infrequent use, it was not included in the recommendations.
¶ No significant new data related to these topics.

RA - DMARDs

- Hydroxychloroquine sulfate: Plaquenil
- Methotrexate
- Sulfasalazine: Azulfidine
- Leflunomide: Arava

RA – Anticytokine Therapies
Anti-TNFs

- Infliximab – Remicade
- Etanercept – Enbrel
- Adalimumab – Humira
- Certolizumab pegol - Cimzia
- Golimumab – Simponi, Simponi Aria

RA – Anticytokine Therapies
Interleukin Inhibitors

- IL-1 inhibition – Anakinra: Kineret
- IL-6 inhibition – Tocilizumab: Actemra

RA – Cell-Targeted Biologics

- T-cell Co-stimulator blocker – Abatacept: Orencia
- B-cell inhibition – Rituximab: Rituxan
- Non-receptor kinases: Jak –Tofacitinib: Xeljanz

RA – Immunosuppressive drugs

- Azathioprine -Purine analogue cytotoxics
- Cyclophosphamide- Alkylating cytotoxics
- Cyclosporine- Calcineurin inhibitors
- Mycophenolate mofetil- Purine synthesis inhibitor

RA Alternative Treatments

- Nutrition: no processed foods, whole foods
- Exercise: aerobic, pool, Yoga, Tai-Chi
- Bodywork: PT, massage, TENS
- Mind-Body Therapy: Meditation, Biofeedback, Hypnotherapy, Relaxation training, Cognitive-behavioral
- Emotional Awareness
- Acupuncture
- Homeopathy
- Supplements

RA – Alernative - Supplements

- Conjugated linoleic acid: evening primrose oil, borage oil 2.5 g/D
- Vit E: mixed tocopherols
- Vit C 250 mg BID
- Omega-3 fatty acids: cold-water fish, flaxseed meal/oil, olive oil
- Magnesium
- Vit D
- Selenium100-400 mcg/D
- Ginger 1 g BID – max 4 g
- Tumeric: spice or 0.5-1g BID/TID