Expanding Primary Care Capacity to Provide Rheumatic Disease Care in Underserved Areas

Richard W. Martin, MD MA
Professor of Medicine, Rheumatology
MSU, College of Human Medicine
Grand Rapids, MI
www.mi-arthritis.com
Lost Rheumatologist FTE

Dr. Irene S Kazmers, MD (Petosky) 2021
Rheum Centers of WM (Muskegon and GR) 2022
UM-West/MetroHealth (Grand Rapids) 2022
Dr. Jonathan Rene MD (Saginaw) 2022
Dr. Carlos Diola, MD (Midland, MI) 2022
Dr. Kimberly Thomsen, MD (Marquette, MI) 2023
Context Rheumatology Manpower Shortage
Objectives

Reflect on the differences between patients who develop multisystem rheumatic diseases compared to those with unexplained symptoms.

Summarize a community needs assessment of patients taking low and moderate risk medications that may need prescription and monitoring to Primary Care providers.

Identifying 3 common disease states and 6 classes of medications that we will be targeting.

Provide background to help primary care providers prescribe and monitor medications not typically within their current practice.
A challenging patient

Imagine that you are in Friday afternoon clinic and your last patient presents

with a list of concerning symptoms that span multiple organ systems
• Constitutional
• Pulmonary
• Cardiac
• Gastrointestinal
• Neurologic
• Musculoskeletal
• Skin / hair
• Metabolic

How do you even begin to try to approach this patient?
Unexplained Symptoms

- Any age
- Insidious to subacute onset symptom (s)
- Multiple (>3 men, > 5 women)
- Organ systems: MSK, GI, nervous, or ill-defined typical in severe + very severe.
  - Atypical chest pain, palpitations, hyperventilation
  - Tinnitus, dizziness, headache
  - Chronic fatigue
  - Irritable bowel
  - Pelvic pain, PMS, interstitial cystitis
  - Neck, TMJ, back or FMS pain

Multisystem Rheumatic Disease

- Any age – most common 15 - 50
- Subacute to acute onset symptom (s)
- One or multiple symptoms adding over time
- Progressive unaffected by with stress
- Co-exist depression / GAD similar to population
- Constellation of constitutional symptoms with
  - Inflammatory arthritis
  - Raynaud’s phenomenon
  - Photosensitive rashes
  - Cytopenia
  - Sicca symptoms
  - Interstitial lung disease
  - Dysphagia

References:
Unexplained symptoms – Psychological characteristics

Worsens with stress

Co-existing depression / GAD 20-99%

Personality structure abnormality

• Worried well (80%)
• Moderate (15%)
• Severe (5%) - ‘Personality disorder’
• Very severe (<1%) - ‘Personality disorder +/- psychosis’

Organ systems: MSK, GI, nervous, or ill-defined typical in severe + very severe.

References:
An Exercise in Clinical Reasoning

Every problem that has at least 6 possible etiologic differentials to consider:

1. Developmental – Degenerative – Traumatic
2. Infectious
3. Immunologic - inflammatory
4. Endocrine – Metabolic
5. Neoplastic
6. Vascular – Thrombotic

- **Probabilistic consideration** of diagnostic options
- Lab and ancillary testing should be based on a specific diagnostic theory
- Recognize unexplained symptoms are prominent in the population and that individual with 3 or more unexplained symptoms have an increased prevalence of generalized anxiety, depression and personality disorder.
- Symptom management with observation and support is often less expensive than extensive or repeated testing.
A Typology of the Rheumatic Diseases

**Typology or Framework** - a system of groupings defined by attributes that are mutually exclusive and collectively exhaustive.

**Attribute** – a verifiable chunk knowledge i.e., a characteristic historical clue or a physical finding

**Concept** - something formed by mentally combining all its defined attributes
Histology of Connective Tissue

Cellular Components
• Fibroblasts
• Macrophage
• Plasma cells
• PMN, lymphocytes
• Adipose cells

Structural Proteins
• Collagen
• Reticulin fibers
• Elastic fibers

Reference: Histology: A Text and Atlas: With Correlated Cell and Molecular Biology, 8e, 2020
<table>
<thead>
<tr>
<th>Genetic Diseases vs. Diffuse Connective Tissue Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Genetic diseases structural proteins</strong></td>
</tr>
<tr>
<td><strong>Benign Hypermobility</strong></td>
</tr>
<tr>
<td>• Mutation Unknown</td>
</tr>
<tr>
<td>• Joint laxity</td>
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<tr>
<td>• No organ abn</td>
</tr>
<tr>
<td><strong>Ehlers Danlos Syndrome Classic</strong></td>
</tr>
<tr>
<td>• Mutation COL5A1 or 2</td>
</tr>
<tr>
<td>• Hypermobility, pes planus, dislocations.</td>
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<tr>
<td>• Valve, aortic root or vascular dissection</td>
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<tr>
<td><strong>Marfan’s Syndrome</strong></td>
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<tr>
<td>• Mutation Fibrillin1</td>
</tr>
<tr>
<td>• Tall stature</td>
</tr>
<tr>
<td>• Arachnodactyly</td>
</tr>
<tr>
<td>• Pectus excavatum</td>
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<tr>
<td>• Aortic aneurism</td>
</tr>
<tr>
<td>• Myopia</td>
</tr>
<tr>
<td>• Arched palate</td>
</tr>
<tr>
<td><strong>Osteogenesis Imperfecta</strong></td>
</tr>
<tr>
<td>• Mutation Type 1 Collagen</td>
</tr>
<tr>
<td>• Short stature</td>
</tr>
<tr>
<td>• Fracture</td>
</tr>
<tr>
<td>• Blue sclerae</td>
</tr>
</tbody>
</table>

**Vascular Inflammatory**

- Undifferentiated Connective Tissue Disease
- Mixed Connective Tissue Disease
- Diffuse Connective Tissue Disease
Case: middle-aged runner with a cough

HPI  55 yo female Boston marathon qualifier develops a cough.

Family history: Aneurism father and sister.

PE 68 inches, weight 115 lbs

Skin: The skin was unremarkable.

HEENT: faces and external eye and ears normal.

Chest, Lungs, Heart = normal

Joints: Beighton score = 6

1. Flexion of waist with palms on the floor (with the knees fully extended) (0 of 1)
2. Hyperextension of elbow >10 degrees (2 of 2)*
3. Hyperextensibility of the knee >10 degrees (0 of 2)
4. Passive apposition of the thumb to the flexor aspect of the forearm (2 of 2)*
5. Passive dorsiflexion of the fifth finger >90 degrees with forearm flat ( 2 of 2)*

Labs: Normal

CXR  Pulmonary nodule otherwise normal.

Chest CT  Ascending aortic aneurism of 4.3 cm.

See YouTube for demo videos
What is a diffuse connective tissue disease?

5 major connective tissue diseases in typical typology

- Systemic lupus erythematosus
- Systemic sclerosis / Scleroderma
- Polymyositis
- Dermatomyositis
- Rheumatoid arthritis
What is an undifferentiated connective tissue disease (CTD)?

645 patients presenting with manifestations suggestive, but not diagnostic, of specific CTD were followed for five years.

- Raynaud’s phenomenon
- Arthritis or arthralgia
- Pleuritis or pericarditis
- Dry eye and dry mouth symptoms
- Photosensitivity or rash
- Central nervous symptoms or peripheral
  - Final diagnosis based on clinical manifestations suggestive of a connective tissue disease
  + at least one autoantibody (dsDNA, Smith, RNP, SSA, SSB, Scl-70, centromere, Jo1 PM-Scl)

- Clinical Course over 5 years
  - 35% developed a defined CTD
  - 65% remained in an undifferentiated state
  - 12% fully remitted

Raynaud’s Phenomenon

**Defining characteristics**
- Provoked by cold or vibration
- Sequential Tricolor Digital Color changes
  - Blanching finger 2-5 tip > 1 or toes.
  - Duration ~ 5-20 minutes
  - Numbness, pain, sensitivity to touch
- Dependent on skin surface temperature
- More common in woman and low BMI

**Primary vs. Secondary**
- Age of onset 15-30 yr; < 1% > 60 yr
- Female
- Occupational vibration or frostbite
- Periungal capillary loop dilation
- Puffy fingers, telangiectasia
- Centromere or SCL70 antibodies

**Historical Clues of RP**
- Are your fingers unusually sensitive to cold?
- Do your fingers change color when they are exposed to cold temperatures?
- Do your fingers turn white, blue, or both?
Scleroderma: Raynaud’s & Early features

- Puffy Fingers
- Skin Induration or thickening
- Telangiectasia
- Dysphagia or Delayed Gastric Emptying

For more information see: ACR Scleroderma Classification Criteria
Interstitial Lung Disease, PAH, and HTN Renal Crisis

Asymptomatic
Dry cough
Mild PFT abnormalities
- FEV1/FVC – nl or ↑
- FVC ↓
- DLCO ↓

Chest X-ray = normal

HRCT
- Subtle ground glass attenuation
- Reticular opacities

Pulmonary arterial hypertension
Scleroderma: Applying the ACR Criterion

For more information see: ACR Scleroderma Classification Criteria
Sicca symptoms: Sjogren’s Syndrome

Exocrinopathy
- Lacrimal glands
- Minor salivary glands
- Parotid glands
- Pancreatitis

Co-existing Immune disease
- Small vessel vasculitis
- Interstitial lung disease
- Pulmonary hypertension
- Primary Biliary Cirrhosis
- Celiac disease

Serologic markers
- ANA +
- SSA and SSB
- RF +
- Polyclonal gammopathy

2016 ACR Sjogren’s Classification Criterion
sum of 5 items (each scoring 1):
- anti-SSA/Ro antibody positivity
- Schirmer’s test result of 5 mm/5 minutes
- focal lymphocytic sialadenitis on minor salivary gland biopsy
- abnormal ocular staining
- unstimulated salivary flow rate of 0.1 ml/minute

For more information see: 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjogren’s Syndrome. ARTHRITIS & RHEUMATOLOGY Vol. 69, No. 1, January 2017, pp 35–45.
Inflammatory Myopathy: Muscle weakness and dysphagia

- Proximal muscle weakness
- Pharyngeal phase dysphagia
- Extensor rashes: Gottron’s plaques
- CPK > 1000
- Serologic markers Jo-1, other

- EMG = ↓ amplitude, short duration action potentials.
- MRI with myoedema
- Muscle biopsy
Pathology: osteoarthritis & inflammatory arthritis

Osteoarthritis

Inflammatory Arthritis
Pathogenesis of Osteoarthritis: Degeneration & Inflammation
Clinical Findings of
Inflammatory Arthritis & Osteoarthritis

Inflammatory Arthritis

Osteoarthritis
Osteoarthritis

Degeneration of cartilage causing joint space narrowing and remodeling of subchondral bone
Common Medications Prescribed for Osteoarthritis

<table>
<thead>
<tr>
<th>Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)</th>
<th>Non-NSAID Pain Relievers</th>
<th>Corticosteroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin (Ecotrin)</td>
<td>Acetaminophen</td>
<td>Prednisone</td>
</tr>
<tr>
<td>Ibuprofen (Motrin)</td>
<td>Topical Diclofenac gel (Voltaren)</td>
<td>Methylprednisolone (Medrol)</td>
</tr>
<tr>
<td>Naproxen (Aleve)</td>
<td>Tramadol (Ultram)</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td>Diclofenac (Voltaren)</td>
<td>— an opioid</td>
<td></td>
</tr>
<tr>
<td>Meloxicam (Mobic)</td>
<td>Duloxetine (Cymbalta)</td>
<td></td>
</tr>
<tr>
<td>Celecoxib (Celebrex)</td>
<td>Gabapentin (Neurontin)</td>
<td></td>
</tr>
<tr>
<td>Nabumetone (Relafen)</td>
<td>— an anti-seizure</td>
<td></td>
</tr>
<tr>
<td>Indomethacin (Indocin)</td>
<td></td>
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</tbody>
</table>

Learning Resources


Sharon L. Kolasinski,1 Tuhina Neogi,2 Marc C. Hochberg,3 Carol Oatis,4 Gordon Guyatt,5 Joel Block,6

UptoDate:
- Overview of the management of osteoarthritis
- UptoDate Pathway: Knee Osteoarthritis
6 common types

- Rheumatoid Arthritis
- Psoriatic Arthritis
- Reactive Arthritis
- Systemic Lupus Erythematosus
- Gout
- Polymyalgia Rheumatica
1. At least one swollen joint > 6 weeks
   • Typically, 3 or more joints
   • ‘Small joint, symmetric synovitis’
   • Classic deformities: Swan neck, boutonniere

2. Elevated blood markers of inflammation i.e., ESR or CRP

3. Biomarkers
   • rheumatoid factor (RF) ~ 70%
   • cyclic citrullinated peptide (CCP) ~ 75%

4. Erosive joint damage on x-ray
Rheumatoid Arthritis
Development of Joint Deformities

Erosive changes of the anchors of the supportive ligaments cause malalignment leading to classic deformities

- Palmar subluxation of MCPs
- Ulnar deviation
- Boutonnière deformity
- Swan Neck deformity
Rheumatoid Arthritis: Extra-articular manifestations

- Rheumatoid nodules
- Entrapment neuropathy i.e. carpal tunnel syndrome
- Pericarditis
- Pleural effusion
- “Rheumatoid Lung” – UIP/Interstitial Pulmonary Fibrosis
  - Prevalence ILD: 7.7%, median survival 2.6 years after dx of ILD
- Odontoid erosion
  - can lead to instability of C1/2 and cervical cord compression
- Peripheral Ulcerative Keratitis
  - can lead to corneal melt – ocular perforation.
Diagnosis of Gout: Clinical Features

- Patient with CRI, CHF, HTN, post-menopause, acute leukemia, lead toxicity.
  - Triggered by dehydration, diuretics, joint trauma
  - Presents with a single acutely swollen joint (great toe = ‘podagra’)
    - Max inflammation in 1 day
  - Redness over joint
  - MTP and tarsus most common
  - +/- tophi
  - Serum uric acid > 7.0
  - MSU in joint during attack
  - Synovial fluid culture = negative
Diagnosis of Gout: Crystal Identification

Arthrocentesis  Synovial Fluid Analysis  Identify Crystals on Polarizing Microscopy

Diagnosis of Gout: Crystal Identification

Plain X-ray – Chondrocalcinosis - CPPD

Dual Energy CT – Uric Acid Tophus
HLA B27 Associated Spondyloarthritis

Epidemiology

• Young: Onset teens to 40 yo.

• Sex: AS = Male: Female. SpA Male > Female

Etiology

• Genetics: HLA B27 = 23% risk, non-HLA genes = 4.3% risk.

• Environment: Mucosal infection i.e. urethritis and bowel infection interact with HLA – B27 to predispose to initiating SpA.

Clinical Features (“P E A R”)

• Psoriatic arthritis
• Enteric Arthritis / IBD Associated
• Ankylosing Spondylitis
• Reactive Arthritis (including HIV associated)
• Undifferentiated Spondyloarthritis (SpA)
Psoriasis: Clinical Findings

Skin characteristics

- Erythema
- Scale
- Induration

% Body Surface Area: 1 patient palm = 1% BSA

Nail characteristics

Onycholysis  Nail Pitting  Oil Drop discoloration  Extensor Surface Rash
Applying GRAPPA Treat to Target Principles

Clinicians must be able to recognize and quantify: Dactylitis

References:
2. American College of Rheumatology Slide Collection.
Applying PsA Treat to Target Principles

Clinicians must be able to recognize and quantify: Enthesitis

Leeds Enthesis Index\(^4\)
(score 0-6)
- Achilles tendon insertions
- Lateral Epicondyles
- Medial femoral condyles

References:
2. American College of Rheumatology Slide Collection.
Applying GRAPPA Treat to Target Principles

Clinicians must be able to recognize: Axial Psoriatic Arthritis

Modified Schober Test:
A distance <20 cm is abnormal

References:
Applying GRAPPA Treat to Target Principles

Clinicians must be able to recognize: Axial Psoriatic Arthritis

- Early Spondylitis & narrowed SI joints
- Squaring of vertebrae & calcification of anterior longitudinal ligament
- Advanced Spondylitis with fused SI joints

Polymyalgia Rheumatica +/- Giant Cell Arteritis

<table>
<thead>
<tr>
<th>Classification Scheme</th>
<th>Criterion</th>
</tr>
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<tbody>
<tr>
<td>Chuang</td>
<td>50 yo with bilateral aching/ stiffness &lt; 1 month in 2 regions</td>
</tr>
<tr>
<td></td>
<td>• Neck, shoulders/upper arms, hips/thighs</td>
</tr>
<tr>
<td></td>
<td>• ESR &gt;40</td>
</tr>
<tr>
<td></td>
<td>• Exclude other causes</td>
</tr>
<tr>
<td>Healey</td>
<td>50 yo with persistent pain in 2 regions</td>
</tr>
<tr>
<td></td>
<td>• Neck, shoulders, pelvic girdle</td>
</tr>
<tr>
<td></td>
<td>• AM stiffness &gt; 1 hour</td>
</tr>
<tr>
<td></td>
<td>• ESR &gt;40</td>
</tr>
<tr>
<td></td>
<td>• Rapid response to prednisone 15-20 mg/day</td>
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<tr>
<td></td>
<td>• Exclude other causes</td>
</tr>
<tr>
<td>Bird</td>
<td>65 yo with bilateral shoulder pain and stiffness</td>
</tr>
<tr>
<td></td>
<td>• Onset within 2 weeks</td>
</tr>
<tr>
<td></td>
<td>• Initial ESR increased, AM stiff &gt;60 min</td>
</tr>
<tr>
<td></td>
<td>• Exclude depression or weight loss other causes.</td>
</tr>
</tbody>
</table>

HLA DR4 associated variant of RA

Clinical diagnosis:
- 3 proposed schemes
  - 10 % PMR develop GCA

Treatment
- prednisone, typically 18-24 months.
- Kevzara (anti IL-6 Mab)
Fibromyalgia – 1990 Classification

In 1990, it was all about trigger points

**Criteria**
1. History of Widespread Pain
   - Must include:
   - Left sided pain
   - Right sided pain
   - Pain above the waist
   - Pain below the waist
   - Axial skeletal pain
2. 11 of 18 Tender Points

**Tender Point Sites (Bilateral)**
1. Occiput
2. Low Cervical
3. Trapezius
4. Supraspinatus
5. Second Rib
6. Lateral Epicondyle
7. Gluteal
8. Greater Trochanter
9. Knee

Giant Cell Arteritis

Presenting symptoms

Ischemic branches of the external carotid
- Temporal headache
- Scalp tenderness – nodularity of TA
- Ischemic optic neuropathy (amaurosis fugax)
- Jaw claudication
- Upper extremity vascular claudication

Diagnosis

Clinical - Polymyalgia rheumatica (50%), occlusive symptoms,
+/- in some elderly: fever, weight loss, failure to thrive.

↑ESR

Temporal Artery biopsy
- Granulomatous infiltrate of adventitia.
- Disruption of the internal elastic membrane.

Treatment
- Prednisone 40 to 60 mg qd
- +/- tocilizumab (anti IL6) SQ x 2-3 years.
Problem: Community loses its rheumatologist
Response: Primary Care Needs Assessment

> 1500 Medications Identified Needing Monitoring and Prescription Transition

Classified into 4 groups

- Primary Care Management (no added training)
- Primary Care Management (added training support)
- Rheumatology Specialty Management
- Primary Care Evaluate and Triage
3 Main Disease States Identified

1. Osteoarthritis
2. Inflammatory Arthritis
   - Rheumatoid Arthritis
   - Psoriatic Arthritis
   - Systemic Lupus Erythematosus
   - Gout
3. Sjogren’s Syndrome
Rheumatic Disease Medications

**Nonsteroidal Anti-inflammatory Drugs (NSAIDS)**
- Aspirin (Ecotrin)
- Ibuprofen (Motrin)
- Naproxen (Aleve)
- Diclofenac (Voltaren)
- Meloxicam (Mobic)
- Celecoxib (Celebrex)
- Nabumetone (Relafen)
- Indomethacin (Indocin)

**Non-NSAID Pain Relievers**
- Acetaminophen
- Topical Diclofenac gel (Voltaren)
- Tramadol (Ulteran)
- an opioid
- Diclofenac sodium (Cymbalta)
- an antidepressant
- Gabapentin (Neurontin)
- an anti-seizure

**Corticosteroids**
- Prednisone
- Methylprednisolone (Medrol)
- Dexamethasone

**Gout**
- Allopurinol
- Febuxostat
- Colchicine

**Sjogren’s Syndrome**
- Pilocarpine (Salagen)
- Cevimeline (Evoxac)

### Safety Monitoring Standards for Common RA Medications

*Table 4. Recommendations on baseline evaluation for starting, resuming, or significant dose increase of a therapy in patients with rheumatoid arthritis receiving nonbiologic and biologic disease-modifying antirheumatic drugs*°

<table>
<thead>
<tr>
<th>Therapeutic agents</th>
<th>CBC</th>
<th>Liver transaminases</th>
<th>Creatinine</th>
<th>Hepatitis B &amp; C testing†</th>
<th>Ophthalmologic examination†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxychloroquine</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>Leflunomide</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Methotrexate</td>
<td>X</td>
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<tr>
<td>Sulfasalazine</td>
<td>X</td>
<td>X</td>
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<td></td>
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<tr>
<td>All biologic agents</td>
<td>X</td>
<td>X</td>
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</tbody>
</table>

### Learning Resources
- UptoDate General principles and overview of management of RA in adults
Monitoring Synthetic DMARDs: Hydroxychloroquine

**Drug class:** Antimalarial drug

**Use:**
- Rheumatoid Arthritis: inflammatory arthritis.
- SLE: ↓ flairs, arthritis, skin manifestations
- Sjogren’s: fatigue (off label).
- Varied ‘orphan’ inflammatory skin conditions.

**Adverse Events:**
- Dyspepsia
- Retinal fibrosis
- Hemolytic anemia in G-6-P deficient individuals
- Prolonged QT interval related arrhythmia

**Dose:** the lessor of 400 mg/day or ≤ 5 mg/kg

**Monitoring:**
- Baseline
  - G6PD: glucose-6-phosphate enzyme
  - Eye exam: dilated +/- OCT or visual field
- Yearly: dilated eye exam
- Q 5 years: OCT or visual field
- Limit use to < 10 years

**Screen for Retinal Fibrosis**

![Images of dilated eye exams and OCT scans](attachment:image.png)
Monitoring Hydroxychloquine (HCQ)

Case 1:
48 yo woman with SLE managed with hydroxychloroquine 400 mg/day presents for med renewal. Weight 60 kg, Creatinine 0.8.

1. What is the maximum safe dose of hydroxychloroquine for this patient?
   a. 200 mg/day
   b. 200 mg alternating with 400 mg/day
   c. 400 mg/day
   d. 600 mg/day

2. Select the correct HCQ safety monitoring order.
   a. CBC, CMP every 6 months
   b. CBC, CMP every 3 months
   c. Hepatic profile every 3 months
   d. Yearly ophthalmologic exam.

3. Select the most common laboratory abnormalities associated with hydroxychloroquine.
   a. Leukopenia
   b. ↑ ALT
   c. ↓ Calcium
   d. None

4. Who is the appropriate professional to do retinal safety exams?
   a. Ophthalmologist
   b. Neuro-ophthalmologist
   c. Optometrist
   d. All of above

Answers: 1 = b, 2 = d, 3 = e, 4 = d.
A Primer of Methotrexate Use in RA

MTX is a structural analogue of folic acid that inhibits dihydrofolate reductase. This impairs purine & pyrimidine synthesis needed for DNA replication in overactive inflammatory cells.

Contra-indications
- Pregnancy
- Liver disease i.e. hepatitis B or C, cirrhosis (multiple etiology)
- Severe cytopenia
- Chronic kidney disease with GFR < 30 ml/min.

Dosing 2.5 mg tablets or 25 mg/1cc sq injectable solution.
  Take 15 to 20 mg once a week as a single dose + folic acid 1 mg/day.

Monitoring
- Pre-screen for hepatitis B and C
- CBC, AST, ALT, albumen (if > 50 yo creatinine) q 2 months x 3. If normal, then q 3 months.
- If any LFT abnormality in > 50% of monitoring labs reduce dose,
- If persists, stop MTX or biopsy liver.
- Q 3-6 months clinical evaluation for intolerance, infection or pneumo-toxicity.

Assess disease activity at baseline and at least twice-yearly w/ articular index, PRO questionnaires. “Treat to Target” to low or moderate disease activity.
Sulfasalazine
- Contra-indications: Sulfa-allergy
- Dose: two 500 mg tab BID (range 2-3000 mg/d)
- AE: headache, ↑LFT, anemia, photosensitivity, ILD
- Monitoring: CBC, CMP q 3 months.

Leflunomide
- Contra-indications: childbearing potential
- Dose: 10 or 20 mg/day.
- AE: diarrhea, ↑LFT, anemia, ↑ BP, rash,
- Monitoring: CBC, CMP q 3 months.

5. Select the best medication safety monitoring order.
   a. CBC, CMP every 6 months
   b. CBC, CMP every 3 months
   c. Hepatic profile every 3 months
   d. CBC, CMP every 1 month
   e. Yearly ophthalmologic exam.

6. Select the two most common lab abnormalities seen monitoring sulfasalazine therapy.
   a. Anemia
   b. Leukopenia
   c. ↑ alkaline phosphatase
   d. ↑ ALT
   e. ↓ Calcium

Answers: 5 = b, 6 = a,d,
Monitoring Synthetic DMARDs: SSA, MTX & Leflunomide

What do I do if the monitoring studies are abnormal?

- **Drop of Hb/HCT > 10 %** ask patient re symptoms or signs of gi / gu bleeding or other change of health.

- **Elevated AST or ALT**
  - If >2.5x normal hold DMARD and reassess in 2-4 weeks.
  - If < 2.5x normal observe. Consider alcohol, statin use and fatty liver.
  - For MTX if 50% of transaminase or albumen abn in a year either stop MTX or liver biopsy.
  - For SSA and MTX recommendations not fixed.

- **Elevated Alkaline phosphatase** – typically no a sign of DMARD toxicity.
- **Leucopenia** with ANC < 1000 stop DMARD
- **Thrombocytopenia** < 100,000 evaluate & increase surveillance, < 40,000 stop DMARD
- **Creatinine > 2.5 or ↑CKD**: MTX = stop; LEF or SSA = observe & stop if ↓ blood cts.

Other problems? Uncertain re best course? Seek out help – colleague, pharmacist, rheumatologist, ID.
What is the best action re DMARD therapy if the patient has an infection?

- If has a **minor URI/sinusitis** no change in medication is needed.
- Evaluate **chronic cough** for pneumonia or drug induced pneumonitis/fibrosis.
- If has infection **requiring antibiotic**, hold DMARD until complete treatment course.
- If patient has acute **herpes zoster**, hold DMARD until vesicles crusted ~ 10 days.
- If patient has **recurrent** pulmonary, vaginal, urinary or skin infection consult with rheumatologist.
- For **COVID** hold DMARD until symptoms resolve.
Case 3:
58 yo male smoker with RA managed with methotrexate 20 mg/week presents with a 3-month history of increasing cough and dyspnea on exertion.

7. Which is the least likely explanation for his symptoms?
   a. Chronic bronchitis
   b. Infectious pneumonia
   c. Pulmonary embolism
   d. Drug induced pulmonary fibrosis

8. How would you manage this patient?
   a. Stop methotrexate and review DMARD options.
   b. Continue methotrexate and observe clinical course.
   c. Hold methotrexate and check CXR + pulmonary function tests.
   d. Check urinary histoplasma antigens.

Answers: 7 = b, 8 = c, 9 = a, 10 = b.

Case 4:
32 yo woman with psoriatic arthritis managed with methotrexate.

9. Which of the following labs is most c/w methotrexate toxicity?
   a. ALT = NL, AST ↑ 2x, albumen ↓, Tbili = NL.
   b. ALT = NL, Alk phosp ↑ 5x, albumen = normal.
   c. ALT = NL, AST = NL, Alk phos = NL, Tbil = ↑ 1.5x
   d. ALT = ↑ 3x, AST ↑ 6x, Alk phos = ↑ 2x, Tbil = NL.

10. How would you manage this patient?
   a. Stop methotrexate and review DMARD options.
   b. Continue methotrexate and repeat labs in 2-3 months.
   c. Hold methotrexate then check CXR and pulmonary function tests.
   d. Check for urinary histoplasma antigens.

Answers: 7 = b, 8 = c, 9 = a, 10 = b.
Hyperuricemia results from increased production or reduced excretion of uric acid.

1. Uric acid is filtered, actively reabsorbed and secreted by the kidney.

Catabolism and Renal Handling of Purines

2. **Increased production**
   - Usually genetic
   - Diet typically not critical

3. **Reduced excretion**
   - Post-menopausal women
   - All diuretics
   - ↓ GFR d/t CKD or CHF

Management focuses primarily on xanthine oxidase inhibitors.
Management of Gout

ACR Guidelines: Management of ↑ Urate & Gout
Monitoring of XO inhibitors
Acute gout management

Learning Resources

2020 American College of Rheumatology Guideline for the Management of Gout

John D. FitzGerald, Nicola Dalbeth, Ted Mikuls, Romina Brisnardello-Petersen, Gordon Guvatt

UptoDate:
• Overview of the management of gout
• UptoDate Pathway: Gout: Initial management of adults with a gout flare
ACR Guidelines for the Management of Gout

• When possible, confirm acute gout via arthrocentesis and synovial fluid analysis for crystals.
• Initiate ULT for all patients with tophaceous gout or frequent gout attacks.
• Allopurinol as the preferred first-line ULT, including for those with CKD stage >3
• Start allopurinol (≤100 mg/day or febuxostat (≤ 40 mg/day in CKD).
• Titrate ULT to a urate target of < 6.0 mg/dl.
• Switching HCTZ to an alternative or using losartan preferentially as an antihypertensive.
• When initiating ULT use anti-inflammatory prophylaxis for at least 3–6 months.
• Treat gout flares with colchicine, NSAIDS, or glucocorticoids (PO or intraarticular).

ULT = urate lowering drug; HCTZ = hydrochlorothiazide; NSAID = Nonsteroidal ant inflammatory drug
Management of Gout

Allopurinol is the preferred XO inhibitor.
Typical dose is 100 to 300 mg/day.

Febuxostat
- Advantage: lowers uric acid more + hepatic excretion may be safer in CKD.
- Disadvantage: higher rate of CV death compared to those treated with allopurinol, so only used if allopurinol fails or contra-indicated.

Goal of Therapy:
- Reduce the frequency of gout attacks,
- Reduce the bulk of tophi and
- Reduce nephrolithiasis.

Monitoring Drug Toxicity: Because of the risk of myelosuppression and hepatotoxicity these medications do require ongoing monitoring with CBC, CMP and uric acid at least q 6 months.

XO = Xanthene Oxidase Inhibitor; CV = cardiovascular; CKD – chronic kidney disease.
Management of Gout

Acute gout can be managed with colchicine, NSAIDS, or glucocorticoids (PO or IA).

- **NSAIDS**: If there are no renal or CV related contra-indications, ibuprofen, naproxen or celecoxib could be used as monotherapy or in conjunction with colchicine.
- **Colchicine**: At the start of acute swelling caused by gout, take colchicine: 1st dose of two .6 mg tablets and a 2nd dose one hour later of one .6 mg tablet.
- **Corticosteroids**: prednisone: ie. 40 mg/day tapered over 14 days or intra-articular injection of 6 mg betamethasone.
Sjogren’s Syndrome: Treatment

Interventions:
- Prevention of dryness
- Saliva replacement and topical stimulants
- Sialagogues
  - Pilocarpine (Salagen) – 5 mg QID ac.
  - Cevimeline (Evoxac) – 30 mg TID ac.
- Disease modifying drug – none available.

Sialagogues
- Adverse Events: diarrhea, nausea, flushing, sweating, tachycardia.
- Interactions: No formal studies. Caution B-blocker.
- Monitoring: No labs required.

Learning Resources
- UptoDate: Treatment of dry mouth and other non-ocular sicca symptoms in Sjögren's syndrome.
- Sjogren’s Foundation: www.sjogrens.org
- Prescribing Information: Dailymed.nlm.nih.gov
3 Main Disease States Identified

Osteoarthritis
Inflammatory Arthritis
• Rheumatoid Arthritis
• Systemic Lupus Erythematosus
• Psoriatic Arthritis
• Gout

Sjogren’s Syndrome