Rheumatology Updates for the Primary Care Provider

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Disclosures

• None
Objectives

1- Review the latest guidelines on the diagnosis and management of rheumatoid arthritis (RA)
2- Review the latest guidelines on the management of gout
3- Review polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) with management update
4- Review the most recent updates in other rheumatic diseases
Objectives

1- Review the latest guidelines on the diagnosis and management of rheumatoid arthritis (RA)

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3- Review polymyalgia rheumatic (PMR) and giant cell arteritis (GCA) with management update

4- Review the most recent updates in other rheumatic diseases
RA: Background

- The most common **autoimmune inflammatory arthritis** in adults (1%)
- Women/men = 2/1
- Joint swelling/tenderness with **destruction** of **synovial joints**
- Significant negative impact on the ability to perform daily activities, and health related quality of life
- Severe disability/Premature mortality
- Smoking is a risk factor
- Strong association with HLA-DRB1 alleles’
- RF and anti–citrullinated protein antibody (ACPA or CCP) can precede the clinical manifestation by many years
RA: Background

• Joint destruction begins **early**
• *Early* therapeutic intervention improves clinical outcomes and reduces the accrual of joint damage and disability
• **Disease-Modifying AntiRheumatic Drugs (DMARDs)**, traditional or biologic agents, have dramatically enhanced the success of RA management

• Minority of patients develop extra-articular features: rheumatoid nodules, lung disease, vasculitis, Sjogren’s syndrome
RA diagnosis

- Primarily clinical diagnosis
- RF and CCP present in 70-75%
- Anti-CCP Ab are more specific and **predict more severe disease**
- **2010 classification criteria**
### 1987 Criteria for the Classification of RA

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning stiffness</td>
<td>Morning stiffness in and around the joints, lasting at least 1 hour before maximal improvement</td>
</tr>
<tr>
<td>Arthritis of 3 or more joint areas</td>
<td>At least 3 joint areas simultaneously have had soft tissue swelling or fluid (not bony overgrowth alone) observed by a physician. The 14 possible areas are right or left PIP, MCP, wrist, elbow, knee, ankle, and MTP joints</td>
</tr>
<tr>
<td>Arthritis of hand joints</td>
<td>At least 1 area swollen (as defined above) in a wrist, MCP, or PIP joint</td>
</tr>
<tr>
<td>Symmetric arthritis</td>
<td>Simultaneous involvement of the same joint areas (as defined in 2) on both sides of the body (bilateral involvement of PIPs, MCPs, or MTPs is acceptable without absolute symmetry)</td>
</tr>
<tr>
<td>Rheumatoid nodules</td>
<td>Subcutaneous nodules, over bony prominences, or extensor surfaces, or in juxtaarticular regions, observed by a physician</td>
</tr>
<tr>
<td>Serum rheumatoid factor</td>
<td>Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in &lt;5% of normal control subjects</td>
</tr>
<tr>
<td>Radiographic changes</td>
<td>Radiographic changes typical of rheumatoid arthritis on posteroanterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints (osteoarthritis changes alone do not qualify)</td>
</tr>
</tbody>
</table>

For classification purposes, a patient shall be said to have rheumatoid arthritis if he/she has satisfied at least 4 of these 7 criteria. **Criteria 1 through 4 must have been present for at least 6 weeks.** Patients with 2 clinical diagnoses are not excluded. Designation as classic, definite, or probable rheumatoid arthritis is **not** to be made.
Facilitate the study of persons at earlier stages of the disease

The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis

<table>
<thead>
<tr>
<th>Target population (Who should be tested?): Patients who</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) have at least 1 joint with definite clinical synovitis (swelling)*&lt;br&gt;2) with the synovitis not better explained by another disease†</td>
<td></td>
</tr>
</tbody>
</table>

Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of 6/10 is needed for classification of a patient as having definite RA)‡

A. Joint involvement§
- 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

B. Serology (at least 1 test result is needed for classification)††
- Negative RF and negative ACPA: 0
- Low-positive RF or low-positive ACPA: 2
- High-positive RF or high-positive ACPA: 3

C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡
- Normal CRP and normal ESR: 0
- Abnormal CRP or abnormal ESR: 1

D. Duration of symptoms§§
- < 6 weeks: 0
- ≥ 6 weeks: 1
RA management

• Most guidelines agree on the following key messages:
  – Early referral to specialist
  – Rapid control of symptoms with NSAIDs or short-term low-dose glucocorticoids
  – DMARDs therapy as soon as possible with early aggressive treatment
  – Advance to biologics or escalate treatment if no response
  – Multidisciplinary approach
  – Constant reassessment
  – Routine monitoring for comorbid conditions, complications, and drug toxicities

• Treat to Target T2T
RA management

Traditional DMARDs
- Methotrexate (Trexall®, Rheumatrex®..)
- Leflunomide (ARAVA®)
- Sulfasalazine (Azulfidine®)
- Hydroxychloroquine (Plaquenil®)

Small molecules (JAK inhibitors)
- Tofacitinib (Xeljanz®)
- Barcitinib (Olumiant®)

Biologic DMARDs
- TNF-alpha inhibitors
  - Adalimimab (Humira®)
  - Certolizumab pegol (Simzia®)
  - Etanercept (Enbrel®)
  - Golimumab (Simponi®)
  - Infliximab (Remicade®)
- Non-TNF-alpha biologics
  - Abatacept (Orencia®)
  - Rituximab (Rituxan®)
  - Tocilizumab (Actemra®)
2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis

JASVINDER A. SINGH,1 KENNETH G. SAAG,1 S. LOUIS BRIDGES JR.,1 ELIE A. AKL,2 RAVEENDHARA R. BANNURU,3 MATTHEW C. SULLIVAN,3 ELIZAVETA VAYSBROT,3 CHRISTINE MCNAUGHTON,4 MIKALA OSANI,3 ROBERT H. SHMERLING,4 JEFFREY R. CURTIS,1 DANIEL E. FURST,5 DEBORAH PARKS,6 ARTHUR KAVANAUGH,7 JAMES O’DELL,8 CHARLES KING,9 AMYE LEONG,10 ERIC L. MATTESON,11 JOHN T. SCHOUSBOE,12 BARBARA DREVLOW,13 SETH GINSBERG,14 JAMES GROBER,13 E. WILLIAM ST.CLAIR,15 ELIZABETH TINDALL,16 AMY S. MILLER,17 AND TIMOTHY MCALINDON3
RA management

• Low-dose glucocorticoid: ≤10 mg/day of prednisone (or equivalent).
• High-dose glucocorticoid: >10 mg/day of prednisone (or equivalent) and up to 60 mg/day with a rapid taper.
• Short-term glucocorticoid: <3 month treatment.
RA management

T2T

- No single measure can serve as a gold standard for patient status in RA
- The joint count is the most specific measure to assess RA, not always available

Table 2. Instruments to measure rheumatoid arthritis disease activity and to define remission*

<table>
<thead>
<tr>
<th>Instrument (reference)</th>
<th>Thresholds of disease activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Activity Scale (PAS) or PASII (range 0–10) (149)</td>
<td>Remission: 0–0.25&lt;br&gt;Low activity: &gt;0.25–3.7&lt;br&gt;Moderate activity: &gt;3.7 to &lt;8.0&lt;br&gt;High activity: ≥8.0</td>
</tr>
<tr>
<td>Routine Assessment of Patient Index Data 3 (RAPID3) (range 0–10) (155)</td>
<td>Remission: 0–1.0&lt;br&gt;Low activity: &gt;1.0–2.0&lt;br&gt;Moderate activity: &gt;2.0–4.0&lt;br&gt;High activity: &gt;4.0–10</td>
</tr>
<tr>
<td>Clinical Disease Activity Index (CDAI) (range 0–76.0) (156)</td>
<td>Remission: ≤2.8&lt;br&gt;Low activity: &gt;2.8–10.0&lt;br&gt;Moderate activity: &gt;10.0–22.0&lt;br&gt;High activity: &gt;22</td>
</tr>
<tr>
<td>Disease Activity Score (DAS) 28 erythrocyte sedimentation rate (ESR) (range 0–94.4) (157)</td>
<td>Remission: &lt;2.6&lt;br&gt;Low activity: ≥2.6 to &lt;3.2&lt;br&gt;Moderate activity: ≥3.2 to ≤5.1&lt;br&gt;High activity: &gt;5.1</td>
</tr>
<tr>
<td>Simplified Disease Activity Index (SDAI) (range 0–86.0) (158)</td>
<td>Remission: ≤3.3&lt;br&gt;Low activity: &gt;3.3 to ≤11.0&lt;br&gt;Moderate activity: &gt;11.0 to ≤26&lt;br&gt;High activity: &gt;26</td>
</tr>
</tbody>
</table>

* These 6 measures were endorsed by the American College of Rheumatology in 2012 (16). Other measures are now available to clinicians, but they were not included in this guideline because it was beyond the scope of this review. Adapted from ref. 16.
RA management

Monitoring DMARDs: CBC, LFTs and Creatinine

Biologics or JAKi: TB screen

TNFi Biologic: Avoid in CHF

Table 3. Recommendations for optimal followup laboratory monitoring intervals for complete blood count, liver transaminase levels, and serum creatinine levels for patients with rheumatoid arthritis receiving disease-modifying antirheumatic drugs

<table>
<thead>
<tr>
<th>Therapeutic agents</th>
<th>&lt;3 months</th>
<th>3-6 months</th>
<th>&gt;6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxychloroquine</td>
<td>None after baseline§</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>2–4 weeks</td>
<td>8–12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>2–4 weeks</td>
<td>8–12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>2–4 weeks</td>
<td>8–12 weeks</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

§ More frequent monitoring is recommended within the first 3 months of therapy or after increasing the dose, and the outer bound of the monitoring interval is recommended beyond 6 months of therapy. Adapted from ref. 6.
† Listed alphabetically.
* The panel indicated that patients with comorbidities, abnormal laboratory results, and/or multiple therapies may require more frequent laboratory testing than what is generally recommended laboratory monitoring for disease-modifying antirheumatic drugs in the table.
§ See ref. 6 for baseline monitoring recommendations.
# RA management

<table>
<thead>
<tr>
<th>Past history of treated or untreated malignancy&lt;sup&gt;4&lt;/sup&gt;</th>
<th></th>
</tr>
</thead>
</table>
| **Previously treated or untreated skin cancer (non-melanoma or melanoma)** | **Use DMARDs over biologics in melanoma (PICO F.1).**  
**Use DMARDs over tofacitinib in melanoma (PICO F.2).**  
**Use DMARDs over biologics in non-melanoma (PICO F.3).**  
**Use DMARDs over tofacitinib in non-melanoma (PICO F.4).** | **Very low (104-106)** |
| **Previously treated lymphoproliferative disorder** | **Use rituximab over TNFi (PICO G.1).** | **Very low (105,107)** |
| **Previously treated lymphoproliferative disorder** | **Use combination DMARD or abatacept or tocilizumab over TNFi (PICO G.2, G.3 and G.4).** | **Very low (105,107)** |
| **Previously treated solid organ malignancy** | **Same recommendations as in patients without this condition (PICO H.1).** | **Very low (105,108)** |

<table>
<thead>
<tr>
<th>Previous Serious Infection(s)&lt;sup&gt;5&lt;/sup&gt;</th>
<th></th>
</tr>
</thead>
</table>
| **Previous Serious infection(s)** | **Use combination DMARD over TNFi (PICO I.1)<sup>5</sup>.**  
**Use abatacept over TNFi (PICO I.2)<sup>6</sup>.** | **Very low (109-116)** |
## RA management

<table>
<thead>
<tr>
<th>Killed vaccines</th>
<th>Recombinant vaccine</th>
<th>Live attenuated vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumococcal&lt;sup&gt;1&lt;/sup&gt; (intramuscular)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Influenza</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatitis B&lt;sup&gt;2&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Human Papilloma</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Herpes Zoster&lt;sup&gt;3&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

### Before initiating therapy

| DMARD monotherapy | ✓ | ✓ | ✓ | ✓ | ✓ |
| Combination DMARDs | ✓ | ✓ | ✓ | ✓ | ✓ |
| TNFi biologics    | ✓ | ✓ | ✓ | ✓ | ✓ |
| Non-TNF biologics | ✓ | ✓ | ✓ | ✓ | ✓ |

### While already taking therapy

| DMARD monotherapy | ✓ | ✓ | ✓ | ✓ | ✓ |
| Combination DMARDs | ✓ | ✓ | ✓ | ✓ | ✓ |
| TNFi biologics    | ✓ | ✓ | ✓ | ✓ | ✓ |
| Non-TNF biologics<sup>4</sup> | ✓ | ✓ | ✓ | ✓ | ✓ |

-<sup>1</sup> Pneumococcal vaccination is recommended before starting biologics.
-<sup>2</sup> Hepatitis B vaccination is recommended before starting biologics.
-<sup>3</sup> Herpes Zoster vaccination is recommended before starting biologics.
-<sup>4</sup> Non-TNF biologics include biologics that target other pathways.
-<sup>5</sup> (PICO J.1)
-<sup>6</sup> (PICO J.4, J.5)
-<sup>7</sup> Not recommended (PICO J.2, J.3)
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Gout background

• Excess body burden of uric acid
• Spectrum of clinical and pathologic features due mostly to tissue deposition of monosodium urate monohydrate crystals (MSU)
• Hyperurecimia = urate > 6.8 or 7.0 mg/dl

• Typically: acute and episodic
• Can be chronic
• Tophi are pathognomonic
Gout background

• Prevalence in the US recently estimated at 3.9% of adults (8.3 million people)

• Comorbidities that promote hyperuricemia:
  • HTN
  • Obesity
  • Metabolic syndrome
  • DM2
  • CKD

• Other factors:
  • dietary trends
  • widespread prescriptions of thiazide and loop diuretics for cardiovascular diseases

• Long term urate lowering to sub-saturation concentrations: improves flares, tophus size and other outcomes 9 (>1year therapy)
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  • Obesity
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  • DM2
  • CKD

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Gout management

2012 American College of Rheumatology Guidelines for Management of Gout. Part 1: Systematic Nonpharmacologic and Pharmacologic Therapeutic Approaches to Hyperuricemia

DINESH KHANNA,1 JOHN D. FITZGERALD,2 PUJA P. KHANNA,1 SANGMEE BAE,2 MANJIT K. SINGH,3 TUHINA NEOGI,4 MICHAEL H. PILLINGER,5 JOAN MERILL,6 SUSAN LEE,7 SHRADDHA PRAKASH,2 MARIAN KALDAS,2 MANEESH GOGIA,2 FERNANDO PEREZ-RUIZ,8 WILL TAYLOR,9 FRÉDÉRIC LIOTÉ,10 HYON CHOI,4 JASVINDER A. SINGH,11 NICOLA DALBETH,12 SANFORD KAPLAN,13 VANDANA NIYYAR,14 DANIELLE JONES,14 STEVEN A. YAROWS,15 BLAKE ROESSLER,1 GAIL KERR,16 CHARLES KING,17 GERALD LEVY,18 DANIEL E. FURST,2 N. LAWRENCE EDWARDS,19 BRIAN MANDELL,20 H. RALPH SCHUMACHER,21 MARK ROBBINS,22 NEIL WENGER,2 AND ROBERT TERKELTAUB7
Gout management - hyperuricemia

Baseline Recommendations for Patients with Diagnosis of Gout

- Patient education, with initiation of diet, lifestyle recommendations See Figure 4
- Consider secondary causes of hyperuricemia ("Co-morbidity Checklist") See Table 2
- Consider elimination of non-essential prescription medications that induce hyperuricemia*
- Clinically evaluate gout disease burden (palpable tophi, frequency and severity of acute and chronic symptoms and signs)

Establish Diagnosis of Gout

# Evidence Grades for Recommendations:
Level A: Supported by multiple RCTs, recent large randomized controlled trials or meta-analyses
Level B: Derived from single random trials, or randomized controlled studies.
Level C: Consensus opinion of experts, case studies, or anecdotal evidence.

*Non-essential prescription medications include: thiazide diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, cholesterol-lowering agents, proton pump inhibitors, and select anti-inflammatory agents.
Gout management - hyperuricemia

Indications for Pharmacologic ULT

- Tophus or tophi by clinical exam or imaging study
- Frequent attacks of acute gouty arthritis (≥2 attacks/yr)
- CKD stage 2 or worse
- Past urolithiasis

If Pharmacologic ULT is indicated

- The minimum serum urate target is <6mg/dL
- Serum urate lowering below 5mg/dL may be needed to improve gout signs and symptoms

Treatment for Serum Urate Target defined for individual patient

- Colchicine 0.6mg QD or BID
- Low dose NSAIDS +/- PMI
- If failure or intolerance to both: low dose prednisone

At least 6 months!
### Gout management - hyperuricemia

**Specific Recommendations:**

**GENERAL HEALTH, DIET, AND LIFESTYLE MEASURES FOR GOUT PATIENTS#:**

<table>
<thead>
<tr>
<th>Avoid</th>
<th>Limit</th>
<th>Encourage &gt;</th>
</tr>
</thead>
</table>
| • Organ meats high in purine content (eg, sweetbreads, liver, kidney) | Serving Sizes of:  
• Beef, Lamb, Pork  
• Seafood with high purine content (eg, sardines, shellfish) | • Low-fat or non-fat dairy products |
| • High fructose corn syrup-sweetened sodas, other beverages, or foods | Servings of naturally sweet fruit juices  
• Table sugar, and sweetened beverages and desserts  
• Table salt, including in sauces and gravies | • Vegetables |
| • Alcohol overuse (defined as more than 2 servings per day for a male and 1 serving per day for a female) in all gout patients  
• Any alcohol use in gout during periods of frequent gout attacks, or advanced gout under poor control | • Alcohol (particularly beer, but also wine and spirits) in all gout patients | |
Gout management: hyperuricemia

• XO inhibitors:
  • Allopurinol
    • Start at 100mg/day (50 for CKD4)
    • Titrate up every 2-5 weeks
    • Can go above 300mg/day, including in CKD
  • HLA-B*5801 in selected patients (Koreans with stage 3 or worse CKD, and Han Chinese and Thai irrespective of renal function)

• Uricosuric therapy
  • Probenecid first choice
  • Not if CrCL<50ml/min
  • Fenofibrate and losartan
  • CI if urolithiasis
  • CI if urinary uric acid elevated
  • Monitor urine uric acid
  • Consider urine alkalinization and increase po fluids

Allopurinol Hypersensitivity Syndrome (AHS):
• Estimated incidence of AHS is 1:1,000 in the US
• Stevens-Johnson syndrome and toxic epidermal necrolysis
• Systemic disease with a clinical constellation of features such as eosinophilia, vasculitis, rash, and major end-organ disease
• Could be very severe with mortality 20-25%
• HCTZ and CKD risk factors
• Highest risk in the first few months
## Gout management - hyperuricemia

**XO inhibitors:**
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  - Titrate up every 2-5 weeks
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**Uricosuric therapy**
- **Probenecid** first choice
- Not if CrCL<50ml/min
- CI if urolithiasis
- CI if urinary uric acid elevated
- Monitor urine uric acid
- Consider urine alkalinization and increase po fluids

- **Febuxostat** (Uloric®40mg and 80mg) if allergic to allopurinol; or failure of allopurinol? **CVD risk? $$$**
- **Lesinurad** (Zurampic®200mg) should only be used in combination with an XOI (approved late 2015)
Table 4. Summary of recommendations for case scenarios of refractory disease in gout (Figure 5), including combination oral ULT and use of pegloticase*

- Attempt upward dose titration of 1 XOI to respective maximum appropriate dose (evidence A).
- Febuxostat can be substituted for allopurinol or vice versa in the event of drug intolerance and adverse events, and such a substitution should be considered after initial failure of upward dose titration of 1 XOI (evidence C).†
- Effective therapeutic options include addition of a uricosuric agent (e.g., probenecid, fenofibrate, or losartan) to an XOI drug (evidence B) or vice versa (evidence C).
- Pegloticase is appropriate for patients with severe gout disease burden and refractoriness to, or intolerance of, conventional and appropriately dosed ULT (evidence A).‡
- Pegloticase therapy is not recommended as first-line ULT agent for any case scenarios.
- LACK OF CONSENSUS: appropriate duration of pegloticase therapy relative to intended and achieved decrease in symptoms and signs of gout, including decrease in tophus size.

* ULT = urate-lowering therapy; XOI = xanthine oxidase inhibitor.
† Important drug label information includes that febuxostat and allopurinol should not be used in combination with each other.
‡ Important drug label information includes that pharmacologic oral ULT agents should be discontinued during the course of pegloticase therapy to avoid masking the loss of a pegloticase serum urate-lowering effect associated with an increased risk of pegloticase infusion reactions.
Gout management - Acute Gout

# Gout management - Acute Gout

### Severity of Acute Gouty Arthritis Attack

<table>
<thead>
<tr>
<th>Intensity of attack based on self-reported pain (0-10 visual analog scale)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Moderate</td>
<td>5-6</td>
</tr>
<tr>
<td>Severe</td>
<td>≥ 7</td>
</tr>
</tbody>
</table>

### Duration of the gouty arthritis attack since onset

<table>
<thead>
<tr>
<th>Duration of the attack</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>&lt; 12 Hours after attack onset</td>
</tr>
<tr>
<td>Well-Established</td>
<td>12 to 36 Hours after attack onset</td>
</tr>
<tr>
<td>Late</td>
<td>&gt; 36 Hours after attack onset</td>
</tr>
</tbody>
</table>

### Extent of acute gouty arthritis attack

Based on number of active joints

- **One or a few small joints**
- **1 or 2 large** joints
  - Defined as: ankle, knee, wrist, elbow, hip, shoulder
- **Polyarticular**
  - 4 or more joints, with arthritis involving more than 1 region
  - Regions defined as: forefoot (metatarsophalangeal joints, toes), midfoot (tarsal) joints, ankle/hindfoot, knee, hip, fingers, wrist, elbow, shoulder, other
  - Acute gout attack involving 3 separate large joints is considered as a form of polyarticular gout for this scheme of management
Gout management- Acute Gout

• General Principles:
  1. An acute gouty arthritis attack should be treated with pharmacologic therapy
  2. Initiated within 24 hours of onset
  3. ULT should be continued
Interactions:
- Clarithromycin
- Erythromycin
- Cyclosporine
- Ketoconazole
- Verapamil
- Disulfiram
Gout management - Acute Gout

**Corticosteroids**

*Extent of joint involvement*

- Option: 1-2 large joints
- Consider intra-articular corticosteroids

**START INITIAL TREATMENT**

**Oral:** Prednisone 0.5 mg/kg per day

- DURATION OF Rx: 5-10 days at full dose then stop [A]
- OR
- for 2-5 days at full dose then taper for 7-10 days then stop [C]

**Methylprednisolone Dose Pack,** then follow-up treatment as indicated [C]

**Intra-articular:** Dose depends on joint size (with or without oral treatment) [B]

**Intramuscular:** Triamcinolone Acetonide 60 mg, then oral prednisone as above* [C]

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* IM Triamcinolone acetonide monotherapy—lack of consensus

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**Evidence Grades for Recommendations:**

- **Level A:** Supported by multiple (i.e., more than one) randomized clinical trials or meta-analyses
- **Level B:** Derived from a single randomized trial, or nonrandomized studies.
- **Level C:** Consensus opinion of experts, case studies, or standard-of-care.
Gout- ACP guidelines 2016*

- Recommend against initiating long-term ULT in most patients after a first gout attack or in patients with fewer than 2 flares/year (ignoring comorbidities)
- Treat to avoid symptoms (NO T2T!)
- Does not advocate either regular serum urate measurements
- ..or dose titration of ULT to reduce the serum urate level to a specific target
- Emphasized the risks of ULT

Discordant American College of Rheumatologists and international rheumatology guidelines for gout management: a consensus statement of the Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN)

Nicola Dalbeth¹, Thomas Bardin², Michael Doherty³, Frédéric Liroté³, Pascal Richette², Kenneth G. Saag⁴, Alexander K. So⁵, Lisa K. Stamp⁶, Hyon K. Choi⁷ and Robert Terkeltaub⁸

supports a treat-to-target approach for gout aimed at lowering serum urate levels to below the saturation threshold.
Objectives

1- Review the latest guidelines on the diagnosis and management of rheumatoid arthritis (RA)
2- Review the latest guidelines on the management of gout
3- Review polymyalgia rheumatic (PMR) and giant cell arteritis (GCA) with management update
4- Review the most recent updates in other rheumatic diseases
PMR/GCA

• Age ≥ 50

• PMR:
  • bilateral upper extremity pain ± pelvic girdle > 2 weeks; AM stiffness > 45 min
  • 16-21% GCA

• GCA:
  • The most common vasculitis of elderly (27/100,000)
  • unilateral or bilateral headache, myalgias, fatigue, fever, weight loss, and sometimes acute vision loss
  • classic cranial (temporal) arteritis/large-vessel vasculitis/single-organ arteritis
  • 40-60% PMR

Buttgereit et al, JAMA. 2016;315(22):2442-2458
PMR
• Clinical presentation
• ESR/CRP elevated >90%
• **Ultrasound:** Subdeltoid bursitis, biceps tenosynovitis, and/or glenohumeral/hip synovitis
• PET
• Response to treatment

GCA
• Clinical presentation/ vision loss 20%
• ESR/CRP elevated > 95%
• Temporal artery biopsy
• Color-duplex ultrasound
• MRI
• PET

Initial laboratory testing not suggestive of another disorder: ANA, RF, SPEP, TFT, UA, CMP, CBC, CK
PMR/GCA-Treatment

Buttgereit et al, JAMA.2016;315(22):2442-2458
PMR/GCA-Treatment

PMR

- Clinically stable at a glucocorticoid dose of 10 mg/d?
  - Yes: Remission
    - Continue medication taper
      - Taper daily oral glucocorticoid dose 1 mg every 4 wk until discontinuation
      - Withdraw methotrexate after glucocorticoid discontinuation on individual basis
    - Treatment-free remission
      - May occur after 1-3 y of therapy; some patients may require treatment for >3 y
  - No: Flare management
    - Increase glucocorticoid to prerelapse dose
    - Taper within 4-8 wk to dose at which the relapse occurred
    - Consider adding methotrexate 7.5-10 mg/wk

GCA

- Clinically stable at a glucocorticoid dose of 20 mg/d?
  - Yes: Remission
    - Continue medication taper
      - Taper daily oral glucocorticoid dose 1-2.5 mg every 2-8 wk until discontinuation
      - Withdraw methotrexate after glucocorticoid discontinuation on individual basis
    - Treatment-free remission
      - May occur after 1-3 y of therapy; some patients may require treatment for >3 y
  - No: Flare management
    - Increase glucocorticoid to prerelapse dose or increase daily dose by 5-10 mg
    - Taper within 4-8 wk to prerelapse dose
    - Repeat induction therapy for ischemic complications
    - Consider adding methotrexate 7.5-15 mg/wk

Buttgereit et al, JAMA.2016;315(22):2442-2458
Trial of Tocilizumab in Giant-Cell Arteritis

Figure 2. Time to First Flare after Clinical Remission of Giant-Cell Arteritis in All Patients.
The Food and Drug Administration (FDA) has granted approval for the use of subcutaneous TCZ to include GCA, making it the first FDA-approved therapy for this disorder.
Objectives

1- Review the latest guidelines on the diagnosis and management of rheumatoid arthritis (RA)
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SLE

• Multi-organ AI disease with **Highly variable clinical course**
• Kidney one of the most targeted organs
• **Anti-DsDNA** associated with renal involvement and a surge **may predict a severe flare**
• ANA >95%; PPV could be as low as 11%
• Infections most common morbidity

• 2-5 fold increased CV morbidity and mortality: Crucial to introduce evidence-based preventative measures
• Statins also improves lupus activity

• FDA approved drugs: ASA (1948), Antimalarial and prednisone (1955).....
• And most recently **Belimumab (anti BlyS) (2011)**
• T2T, **early referral**

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*Pan et al. Lupus 2014
**Willis et al. Clin Exp Rheumatol 2014
Axial Spondyloarthritis

Table 1. Current and Classic Classifications of Spondyloarthritis.*

<table>
<thead>
<tr>
<th>Current classifications</th>
<th>Classic classifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axial spondyloarthritis</td>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>With radiographic sacroiliitis</td>
<td>Reactive arthritis (infection-associated arthritis)</td>
</tr>
<tr>
<td>Without radiographic sacroiliitis</td>
<td>Psoriatic spondyloarthritis</td>
</tr>
<tr>
<td>Sacroiliitis on MRI</td>
<td>Predominantly peripheral</td>
</tr>
<tr>
<td>HLA-B27 positivity plus clinical criteria</td>
<td>Predominantly axial</td>
</tr>
<tr>
<td>Peripheral spondyloarthritis</td>
<td>Enteropathic spondyloarthritis (associated with inflammatory bowel disease)</td>
</tr>
<tr>
<td>With psoriasis</td>
<td>Predominantly peripheral</td>
</tr>
<tr>
<td>With inflammatory bowel disease (Crohn’s disease or ulcerative colitis)</td>
<td>Predominantly axial</td>
</tr>
<tr>
<td>With preceding infection</td>
<td>Juvenile-onset spondyloarthritis (enthesitis-related juvenile idiopathic arthritis)</td>
</tr>
<tr>
<td>Without psoriasis or inflammatory bowel disease or preceding infection</td>
<td>Undifferentiated spondyloarthritis</td>
</tr>
</tbody>
</table>

* Current classifications are adapted from the Assessment of SpondyloArthritis International Society (ASAS) by Rudwaleit et al.\textsuperscript{1,4} MRI denotes magnetic resonance imaging.

Table 2. Characteristics of Inflammatory Back Pain. *

- **Characteristic**
  - Age at onset, <45 yr
  - Duration, >3 mo
  - Insidious onset
  - Morning stiffness >30 min
  - Improvement with exercise
  - No improvement with rest
  - Awakening from pain, especially during second half of night, with improvement on arising
  - Alternating buttock pain

* The presence of two or more of these features should arouse suspicion for inflammatory back pain, and the presence of four or more features can be considered diagnostic. The sensitivity of inflammatory back pain for the diagnosis of axial spondyloarthritis is 70 to 80%. The specificity varies, depending on the population being studied.\textsuperscript{8,9}

\textsuperscript{Taurog et al, NEJM 374;26 June 30, 2016}
Axial Spondyloarthritis

- **NSAIDs** should be the **first line** of treatment for all symptomatic AS
- **TNF-alpha inhibitors**: axial disease
- **DMARDs (MTX, SSZ)**: peripheral disease
- Newest:
  - **Secukinumab** (Cosentyx®): anti-IL17A: FDA approved for AS and psoriatic arthritis in 01/2016
  - **Ustekinumab** (Stelara®): anti-IL12/23: FDA approved for psoriatic arthritis in 2013, studies showing good results for AS

- **HLA-B27**:
  - 90% of AS and 60% of SpA
  - NOT diagnostic
  - Absolute risk of SpA: 2-10%; higher if a first degree relative affected
Thank you!

Questions?