

# Update on Gout Management

Sadao Jinno, MD, MSc

Rheumatologist QUMG

Assistant professor, UH

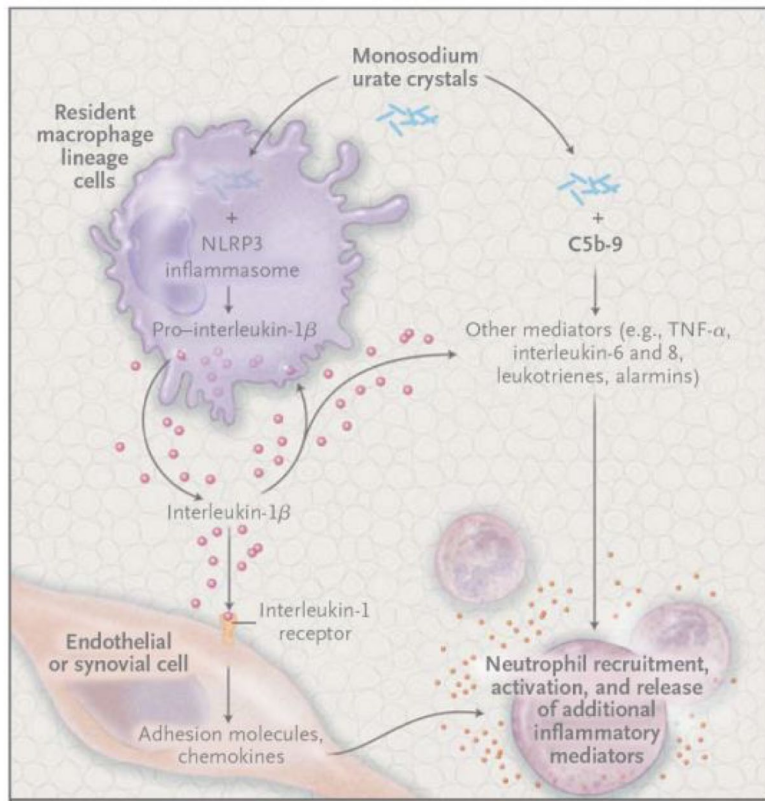
# Gout management

- 1. Indication of ULT**
- 2. Flare Prophylaxis**
- 3. Flare Management**

# Epidemiology

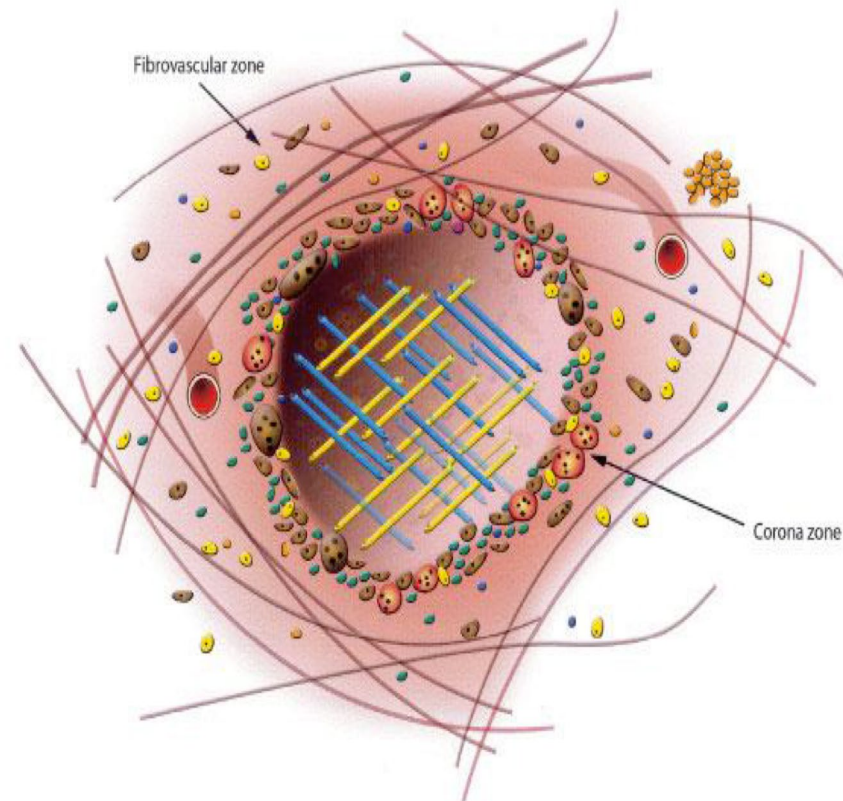
- **Most common inflammatory arthritis:**
- **9 million (4%) in the US**
- **Not only painful but disabling**
- **Comorbidities (CKD and CHF)**

# Pathophysiology



Neogi, *NEJM*, 2011

- T cell
- B cell
- Plasma cell
- Macrophage
- CD68 + MNC
- Mast cell
- Neutrophil
- TRAP + MNC



Dalbeth, et al. *A&R*2010

# Clinical Manifestations

## 1. Flares

Intermittent

Spontaneous resolution 7-10

## 2. Tophi

Longstanding hyperuricemia

chronic inflammation

destructive changes

# Dactylitis and tophus



# Clinical Manifestations

- Pattern of gout flare
  - 1stMTP monoarthritis: 33-40%
  - Lower extremity: 37-50%
  - Upper extremity: 15%
  - Polyarticular:3-9%
- 45-65% did not involve 1stMTP



# X-ray



overhanging edge



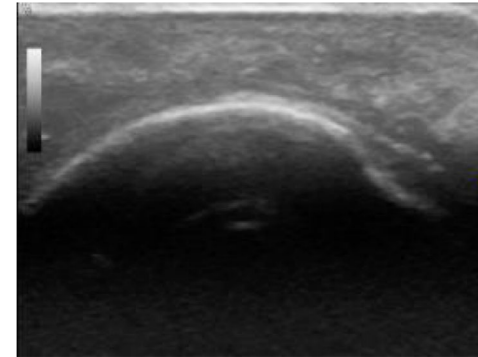
Soft tissue tophi



# Advanced Imaging

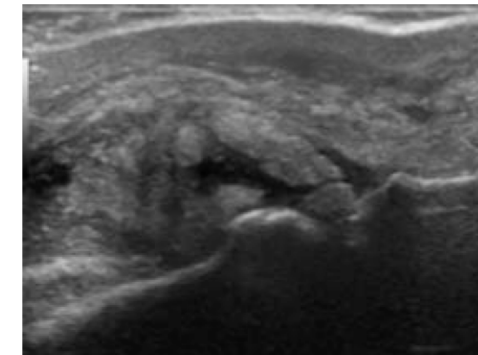
- US Double Contour Sign

–Sn: 0.83. Sp: 0.76



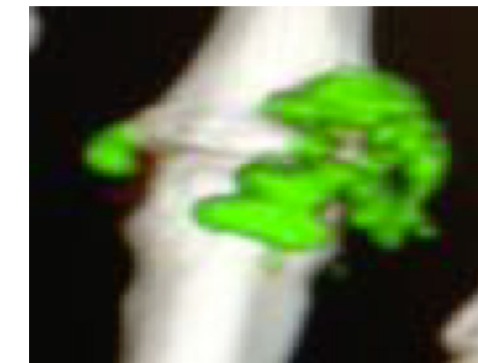
- US Tophus:

–Sn: 0.65 Sp: 0.80



- Dual energy CT:

–Sn: 0.87 Sp: 0.84



# Management guidelines

AMERICAN COLLEGE  
of RHEUMATOLOGY  
*Empowering Rheumatology Professionals*

**Arthritis Care & Research**  
Vol. 72, No. 6, June 2020, pp 744–760  
DOI 10.1002/acr.24180  
© 2020, American College of Rheumatology

## ACR GUIDELINE FOR MANAGEMENT OF GOUT

### 2020 American College of Rheumatology Guideline for the Management of Gout

John D. FitzGerald,<sup>1</sup>  Nicola Dalbeth,<sup>2</sup>  Ted Mikuls,<sup>3</sup>  Romina Brignardello-Petersen,<sup>4</sup> Gordon Guyatt,<sup>4</sup> Aryeh M. Abeles,<sup>5</sup>  Allan C. Gelber,<sup>6</sup>  Leslie R. Harrold,<sup>7</sup> Dinesh Khanna,<sup>8</sup>  Charles King,<sup>9</sup> Gerald Levy,<sup>10</sup> Caryn Libbey,<sup>11</sup> David Mount,<sup>12</sup> Michael H. Pillinger,<sup>5</sup>  Ann Rosenthal,<sup>13</sup> Jasvinder A. Singh,<sup>14</sup>  James Edward Sims,<sup>15</sup> Benjamin J. Smith,<sup>16</sup>  Neil S. Wenger,<sup>17</sup> Sangmee Sharon Bae,<sup>17</sup>  Abhijeet Danve,<sup>18</sup> Puja P. Khanna,<sup>19</sup> Seoyoung C. Kim,<sup>20</sup>  Aleksander Lenert,<sup>21</sup> Samuel Poon,<sup>22</sup> Anila Qasim,<sup>4</sup> Shiv T. Sehra,<sup>23</sup> Tarun Sudhir Kumar Sharma,<sup>24</sup> Michael Toprover,<sup>5</sup> Marat Turgunbaev,<sup>25</sup> Linan Zeng,<sup>4</sup> Mary Ann Zhang,<sup>20</sup>  Amy S. Turner,<sup>25</sup> and Tuhina Neogi<sup>11</sup> 

---

# 2017 ACP guideline



Summary of the American College of Physicians Guideline on Management of Acute and Recurrent Gout

Disease/Condition	Acute or recurrent gout
Target Audience	All clinicians
Target Patient Population	Adults with acute or recurrent gout
Treatments Evaluated	Dietary interventions; other lifestyle measures (smoking cessation, exercise, hydration); dietary supplements and alternative treatments (vitamin C supplementation, traditional Chinese medicine); pharmacologic agents, including anti-inflammatory drugs (NSAIDs, corticosteroids), colchicine, and urate-lowering therapies (xanthine oxidase inhibitors, uricosuric agents); combination drug therapies; or combination drug and dietary or alternative treatments
Outcomes Evaluated	Efficacy, including short-term (pain, joint swelling and tenderness) and long-term (serum urate levels, pain, joint swelling and tenderness) outcomes; activities of daily living; patient global assessment; recurrence; intermediate outcome of serum urate levels; and harms
Benefits	Acute gout treatment (colchicine, NSAIDs, corticosteroids, corticotropin): reduction of pain  Prophylaxis during serum urate-lowering therapy (low-dose colchicine and low-dose NSAIDs): reduced acute gout flares
Harms and Adverse Effects	Colchicine: gastrointestinal adverse effects, such as diarrhea, nausea, cramps, and vomiting  NSAIDs: dyspepsia and potential gastrointestinal perforations, ulcers, and bleeding  Corticosteroids: mood disorders and dysphoria, elevation of blood glucose levels, immune suppression, and fluid retention  Corticotropin: unknown, but probably similar to those of corticosteroids  Serum urate-lowering therapy:  Febuxostat: abdominal pain, diarrhea, and musculoskeletal pain  Allopurinol: rash and reactions (including potentially serious ones)

# Gout management

- Confirm diagnosis (MSU)
- Lifestyle factors
- Lower serum urate
- Prophylaxis->50% don't achieve target urate
- Manage flares
- **~70% experience recurrent flares**

**Inappropriate management is common**

# Lifestyle factors

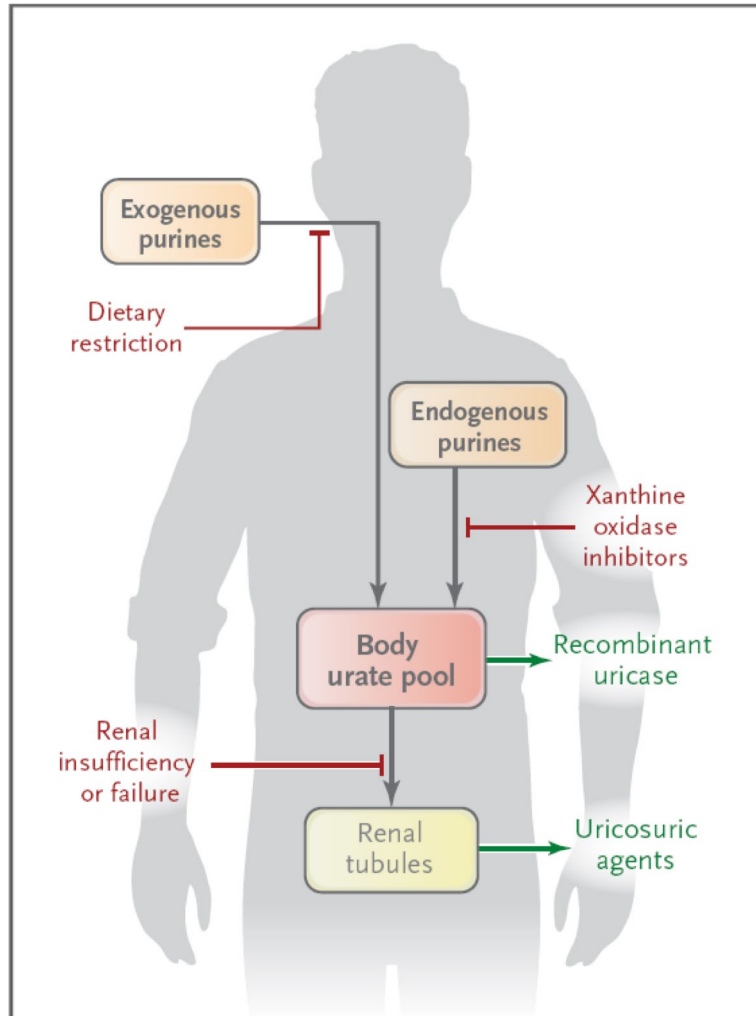
- Caution with patient blaming
- Weight loss (underutilized)
- Strategies to lower uric acid or avoidance of factors that increase uric acid
- Avoidance of triggers
  - Alcohol
  - high purine diet
  - High-fructose corn syrup



# initiation of ULT

- tophaceous gout
- radiographic damage due to gout with erosions
- frequent gout flares  $\geq 2$ /year
  - Not recommended for infrequent flare
- (Conditionally recommended for pts with CKD stage  $\geq 3$ , SU  $>9$ mg/dl, or renal stone)

# FDA-Approved Hyperuricemia Meds



**Allopurinol (1<sup>st</sup> line)**  
Febuxostat  
Pegloticase  
Probenecid  
~~Lesinurad (with XOI)~~

Neogi, *NEJM*, 2011

# Timing of ULT initiation

- OK to start ULT during the gout flare
  - Pros
    - the time efficiency offered by initiating therapy during the flare visit
  - Cons
    - potential extension or worsening of a flare
    - information overload
  - Should be Individualized



# Allopurinol Dosing Principles

- Start at **100 mg/d; 50 mg/d** in CKD  $\geq 4$ 
  - A lower starting dose of any ULT reduces the risk of flare associated with initiation
- Titrate dose every few weeks to SUA target
- **Can titrate to >300 mg/d**
  - **Even with renal impairment (the stop gout trial)**
- >50% will need dose higher than 300 mg/d

# Allopurinol Hypersensitivity Syndrome

- Extremely rare
- Associated with ***starting dose***
- Higher risk in pts with CKD
- HLA-B\*5801 screening
- High risk patients
  - Han Chinese
  - Korean, Thai
  - African American



Ranu H et al., *Ind J Dermatol* 2011

# Febuxostat

- 40mg & 80mg tablets
  - Start 40mg/day
  - DRESS
- CARES RCT (White, et al. NEJM 2018)
  - Increased all-cause and CV mortality
  - Black box warning
- FEATHER RCT (Kimura, et al. AJKD 2018)
  - CV events: 2% FBX vs. 3% PBO
  - Deaths: 1 in each arm
- The STOP Gout trial (O'Dell et al NEJM Evid 2022)
  - CV events **no difference**

# The STOP Gout trial, allopurinol vs febuxostat

- with at least 33% having stage 3 chronic kidney disease
- Among patients with CKD in the trial, the efficacy and safety of allopurinol and febuxostat were similar.
  - % of gout flare at least once
  - 36.5% (allopurinol) vs 43.5% (febuxostat) (non inferior)
- Mod-to-severe CKD have **NOT** been linked to worsening renal function or to reduced survival.
- Cardiovascular events **no difference**

# Probenecid

- 2-3g/d (BID dosing)
- Start at 250mg BID, then titrate up
- Avoid in nephrolithiasis, CrCL<30mL/min
- Needs adequate hydration

# Pegloticase

- IV infusion q2wks x6 mo
- Infusion reactions ~25%; anaphylaxis 5%
- Careful lab monitoring: loss of urate response
- Premedication regimen
- Contraindication: G6PD



# Prophylaxis strongly recommended

Drug	Regimen
Colchicine	0.6mg po daily or bid
NSAIDS	Naproxen 250mg bid
Prednisone	<10mg/day

- **Duration:**
  - 6 months
  - 3 months beyond achieving SUA target
  - 6 months beyond tophus resolution

# ULT Failure?

- Assess adherence to ULT (and prophylaxis), ensure adequate dose titration
- If on XOI, add uricosuric vs. switch to other XOI then add uricosuric
- Oral ULT failure- pegloticase



# Acute Gout Flares

Consideration	Approach
Adequate duration	7-10 days vs 14days
Adequate dosing	High dose, then taper
Urate-lowering therapy	No interruption!!
When to start	Immediately: “medications in pocket”

# Example regimens

Drug	Regimen
NSAIDs	Naproxen: 500mg BID x5-7d, then 250-375mg BID x3-5d or until attack resolves
Colchicine	1.2mg x1, then 0.6mg one hour later and bid dose
Prednisone	40mg/d x3d, then 30mg/d x 3d, 20mg/d x3d, 10mg/d x 3d

**Consider dexamethasone or methylprednisolone in pts with CHF**

Canakinumab: IL-1 antagonist

# Colchicine –Renal Disease

- Avoid if already using for prophylaxis
- Dose reduction; don't repeat <q14d
- Drug interactions
- P-glycoprotein or CYP3A4 inhibitors:  
**contraindicated (fatal)**
  - e.g., clarithromycin, certain antifungals, certain CCBs (verapamil, diltiazem), grapefruit juice
- Caution with cholesterol-lowering meds (neuromyotoxicity)

# Summary

- Gout management has 3 components:
  - **Hyperuricemia**
  - **Flare Prophylaxis**
  - **Flare Management**
- Ongoing flares/tophi: escalate therapy even with CKD

# Thank you!

- Questions: [sajinno@queens.org](mailto:sajinno@queens.org)