# Gout Progression is Driven by Hyperuricemia, Which can Lead to Deposition of MSU Crystals in Joints and Tissues[1]

**Uric acid overproduction[2]** → **Uric acid underexcretion[2]**

## Hyperuricemia[3,4]

**Uric acid super-saturation is the key factor for MSU crystal formation**

### Uric acid super-saturation[4]

Uric acid levels exceed the solubility limit of 6.8 mg/dL (hyperuricemia)

### Nucleation[4]

Uric acid molecules start to cluster together, acting as centers of crystallization

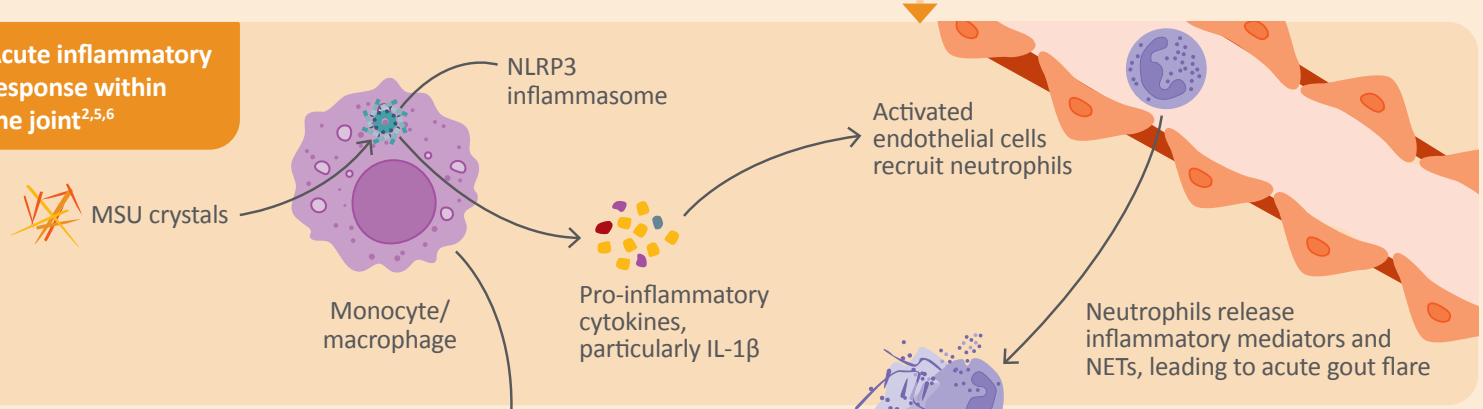
### MSU crystal growth[4]

Continued sUA super-saturation leads to crystal growth

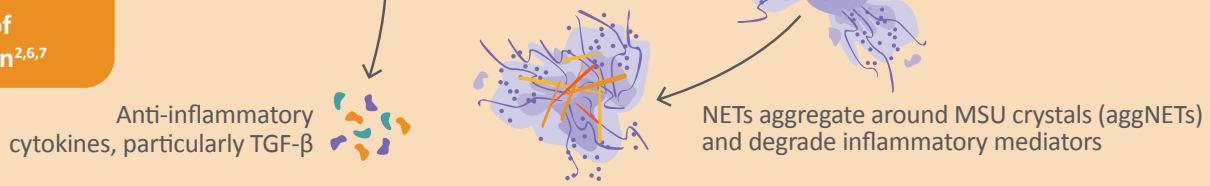
## MSU crystal deposition and growth[3,4]

## Acute gout flare[5,6]

### 1 Acute inflammatory response within the joint[2,5,6]




### 2 Resolution of inflammation[2,6,7]




**Gout flares are caused by an acute inflammatory response to MSU crystal deposition:[2,5,8]**

- Rapid onset
- Painful, swollen, red, and hot joint

**NLRP3 inflammasome activation is a key mechanism driving acute gout flares[2]**

**Flares generally resolve within 7–10 days and are interspersed by asymptomatic periods[8]**

**See back page for more on tophaceous gout**


**References**

1. Girardet JL, Miner JN. *Annu Rep Med Chem* 2014;49:151–164.
2. Dalbeth N, et al. *Lancet* 2021;397:1843–1855.
3. Kuo CF, et al. *Ann Rheum Dis* 2015;74:369–374.
4. Chhana A, et al. *BMC Musculoskelet Disord* 2015;16:296.
5. Busso N, So A. *Arthritis Res Ther* 2010;12:206.
6. Li C, et al. *J Inflamm Res* 2024;17:1735–1763.
7. Yagnik DR, et al. *Arthritis Rheumatol* 2004;50:2273–2280.
8. Dalbeth N, et al. *Nat Rev Dis Primers* 2019;5:69.


**Abbreviations**

aggNET, aggregated neutrophil extracellular trap; IL-1β, interleukin-1 beta; MSU, monosodium urate; NET, neutrophil extracellular trap; NLRP3, NLR family pyrin domain containing 3; sUA, serum uric acid; TGF-β, transforming growth factor beta.

**Disclaimers**

For US healthcare providers only. Do not copy or distribute.


©2026 Sobi, Inc.
All rights reserved.
NP-47168 02/2026

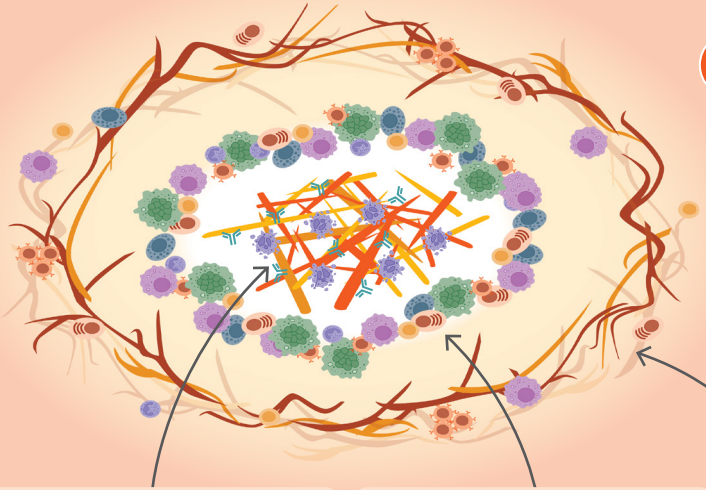
# Tophi Can Form by Foreign-Body Reaction of Immune Cells to MSU Crystals and Cause Joint Destruction[1]

Continued from reverse side

## Tophaceous gout[1]

### Tophi are granuloma-like structures consisting of three zones[2]

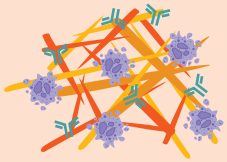
Expression of both pro- and anti-inflammatory cytokines suggests a cycle of chronic inflammation, attempted resolution, and tissue remodeling[3]



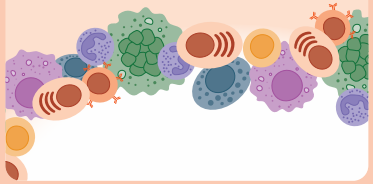
**Tophi may be formed by NET aggregation[4]**

**Tophi can occur without manifestations of acute inflammation, such as pain and swelling, but lead to joint destruction over time[4]**

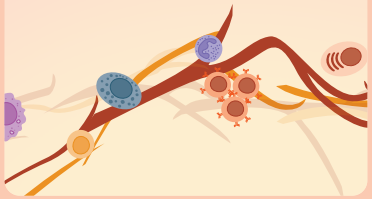
The crystalline zone is acellular and contains MSU crystals, antibodies, and monocyte-derived debris[2]



The corona zone contains mono- and multi-nucleated macrophages and high numbers of plasma cells[3]

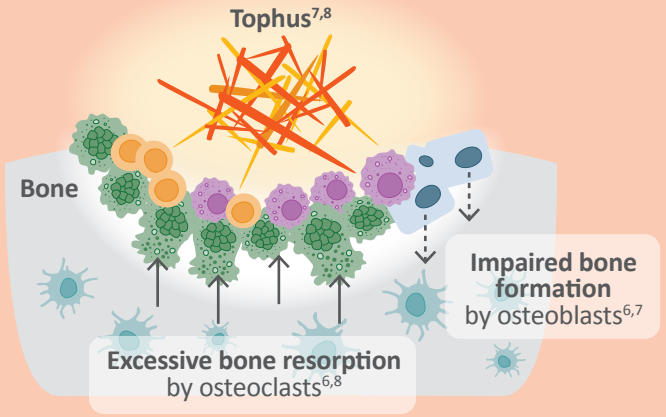


The fibrovascular zone consists of connective tissue with scattered immune cells[5]



### Tophus-induced joint damage may be related to imbalanced bone turnover[6–8]

The tophus microenvironment may promote excessive osteoclast formation and reduce osteoblast differentiation[6–8]




### Key

- Macrophage/monocyte
- Monocyte-derived debris
- Activated osteoclast
- Osteoclast
- T cell
- B cell
- Plasma cell
- Mast cell
- Neutrophil
- Osteocyte
- Osteoblast
- Antibody

**References**

1. Dalbeth N, et al. *Lancet* 2021;397:1843–1855.
2. Towiwat P, et al. *BMC Musculoskelet Disord* 2019;20:140.
3. Dalbeth N, et al. *Arthritis Rheum* 2010;62:1549–1556.
4. Desai J, et al. *Trends Mol Med* 2017;23:756–768.
5. Narang RK, Dalbeth N. *Semin Nephrol* 2020;40:550–563.
6. Chhana A, et al. *Ann Rheum Dis* 2011;1684–1691.
7. Naot D, et al. *Arthritis Res Ther* 2022;24:212.
8. Lee S-J, et al. *Arthritis Res Ther* 2011;13:R164.

**Abbreviations**

MSU, monosodium urate; NET, neutrophil extracellular trap.

**Disclaimers**

For US healthcare providers only. Do not copy or distribute.

©2026 Sobi, Inc.
All rights reserved.
NP-47168 02/2026