# Nursing Considerations in the Diagnosis and Treatment of Gout

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## Questions to be Addressed

- What causes gout?  
- Who develops gout?  
- How is gout diagnosed?  
- How is gout managed?  
- What do nurses need to know?

## Gout: Clinical Features
Humans have conserved mutations in the uricase gene, resulting in inability to convert uric acid to allantoin.

Allantoin is soluble and easy to excrete, while uric acid is less soluble and crystalizes in solution when supersaturated at physiologic concentrations.

Figure from Stamp et al. Intern Med J 2007; 37: 258.

Figure from Choi et al. Ann Intern Med 2005; 143: 499.
Overproduction vs. Underexcretion

- 10% of gout patients

Gout and Inflammation

- Uric acid crystals undergo phagocytosis by synovial macrophages
- Activation of inflammatory cascade
  - Elaboration of inflammatory cytokines
  - Chemokine production
  - Recruitment of inflammatory cells (predominantly neutrophils)
- Mechanisms of spontaneous resolution not well-understood

Epidemiology

- Gout is the most common form of inflammatory arthritis in men > 40 years of age
- Often presents initially in the form of podagra (acute onset of pain, erythema and swelling of the first metatarsophalangeal joint)
- Women usually post-menopausal and more likely to involve the upper extremities.
- The lifetime prevalence of gout in the United States has been estimated at 6.1 million
Prevalence of Gout Increasing

- Due to...
  - Aging population
  - Increasing Obesity
  - Treatment of Cardiovascular Risk Factors
    - Diuretics
  - Improved Longevity with Chronic Kidney Disease / Transplant

Risk Factors

- Hyperuricemia
- Obesity
- Hypertension
- Medications
  - Diuretics, cyclosporine, tacrolimus, low dose aspirin
- Dietary
  - Meat
  - Alcohol
  - Protective (?) Low fat dairy, Coffee

Diagnostic Probability


2 Choi HK et al. Arch Intern Med 2003; 163: 742
4 Choi HK et al. Lancet 2004; 363: 1277
Diagnostic Probability

1. Rapid Pain and Swelling
2. Rapid Pain and Swelling + Erythema
3. Rapid Pain and Swelling + Erythema + Podagra
4. Rapid Pain and Swelling + Erythema + Podagra + Hyperuricemia
5. Rapid Pain and Swelling + Erythema + Podagra + Hyperuricemia + Tophi
6. Rapid Pain and Swelling + Erythema + Podagra + Hyperuricemia + Tophi + X-ray Changes
7. Rapid Pain and Swelling + Erythema + Podagra + Hyperuricemia + Tophi + X-ray Changes + MSU Crystals


Management

Goals of Acute Gout Management
- Reduce pain/swelling/inflammation

Goals of Chronic Gout Management
- Uric acid reduction
- Prevent flares of acute gout

Management

Acute Gout

- Colchicine
- NSAIDs
- Intra-articular corticosteroids*
- Systemic corticosteroids/ACTH
- Analgesics
- Ice
Colchicine

• Use predates systematic trials
• Efficacy greatest when used at the onset of attack
• Common side effect
  – Diarrhea
• Toxicity increased in renal insufficiency and hepatobiliary obstruction
  – Dose reduction essential

Colchicine: Teaching

• Review Dosing
• Review common side effects: nausea, diarrhea, vomiting
• Advise on what to do for rare but serious side effects: fever, severe rash, blood in stool or urine, difficulty breathing, seizures

NSAIDS – Which One?

• Well-established but little studied
  – All NSAIDs likely effective
• Indomethacin traditionally used
  – Risk of GI toxicity
• COX-2 inhibitors appear to be as effective as non-selective NSAIDs
  – Etoricoxib as effective as Indomethacin in a randomized, double-blind clinical trial

Schumacher et al. BMJ 2002; 324: 1488
### NSAID: Teaching

- Take with food
- Dosage increased gradually
- Take even if feeling well
- Drink plenty of water (6-8 glasses/day)

### Corticosteroids

- Intra-articular corticosteroids should be treatment of choice for acute mono / oligoarticular gout
- Refractory to NSAIDs/colchicine
- Contraindications to NSAIDs/colchicine
- May be associated with rebound flares when used without NSAIDs/colchicine\(^1\)

### Gout and Comorbid Conditions

- Often very challenging
- Liver and kidney disease contraindication for both NSAIDs and colchicine
- Corticosteroids often only option
- Focus on urate lowering if indicated and lifestyle changes to reduce future attacks

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\(^1\) Siegel LB et al J Rheumatol 1994; 21: 1325
<table>
<thead>
<tr>
<th>Management Chronic Gout</th>
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<tr>
<td>• Emphasize control of lifestyle factors</td>
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<tr>
<td>• Urate lowering therapy</td>
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<tr>
<td>• Prophylaxis against acute attacks when initiating urate lowering therapy</td>
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<td>• Patients with medical comorbidities</td>
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<tr>
<th>When to use Urate Lowering Therapies</th>
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<tr>
<td>• Dependent on individual patient factors</td>
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<tr>
<td>– 2 or 3 significant attacks per year</td>
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<tr>
<td>– Development of tophi</td>
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<td>– Development of radiographic damage</td>
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<tr>
<th>Urate Lowering Therapies</th>
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<tr>
<td>• Xanthine Oxidase Inhibitor (decreases urate synthesis)</td>
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<tr>
<td>– Allopurinol</td>
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<tr>
<td>– Febuxistat (Uloric®)</td>
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<tr>
<td>• Uricosurics</td>
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<tr>
<td>– Probenecid</td>
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<tr>
<td>– Benzbromarone (not widely available)</td>
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<tr>
<td>– Sulfinpyrazone (not widely available)</td>
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<tr>
<td>• Uricase</td>
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<tr>
<td>– Pegloticase (Krystexxa®)</td>
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<tr>
<td><strong>Allopurinol/Febuxostat</strong></td>
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<td>--------------------------</td>
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<tr>
<td>• Standard urate lowering therapy</td>
</tr>
<tr>
<td>• Can be used in overproducers and under-excretors</td>
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<tr>
<td>• Requires renal dosing for chronic kidney disease</td>
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<td>• Rapid escalation of dose may precipitate acute gout attacks</td>
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<thead>
<tr>
<th><strong>Safety of Allopurinol/Febuxostat</strong></th>
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<tr>
<td>• Uncommon (less than 2%)</td>
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<tr>
<td>– Mild rash, pruritus</td>
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<tr>
<td>• Common Side effects</td>
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<tr>
<td>– Nausea, diarrhea, hepatotoxicity</td>
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<tr>
<td>• Concomitant medications to avoid</td>
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<tr>
<td>– Azathioprine, mercaptopurine</td>
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<tr>
<td>– May potentiate anticoagulant activity of warfarin</td>
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<th><strong>Uricosurics</strong></th>
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<tr>
<td>• Less commonly used</td>
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<tr>
<td>• May precipitate nephrocalcinosis in uric acid over-excretors or patients with a history of renal calculi</td>
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<tr>
<td>• Probenecid</td>
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<tr>
<td>– Molecular target is renal URAT1 exchanger</td>
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<td>– Common clinical utility in patients refractory or intolerant to allopurinol (i.e. allopurinol hypersensitivity)</td>
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<tr>
<td>– Ineffective if used in conjunction with low-dose aspirin</td>
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<td>– Ineffective in chronic kidney disease</td>
</tr>
<tr>
<td>• Benzbromarone/Sulfipyrazone</td>
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<tr>
<td>– Not widely available</td>
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<tr>
<td>• Combining Allopurinol and a uricosuric is an option?</td>
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<td>– Careful monitoring warranted</td>
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Pegloticase (Krystexxa™) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

How does Pegloticase work?

- Pegloticase is a uric acid specific enzyme that helps breakdown uric acid to allantoin.
- Allantoin is more water soluble than uric acid.
- Allantoin is readily excreted which in turn lowers serum uric acid.

Important Safety Information

- WARNING: ANAPHYLAXIS and INFUSION REACTIONS
- See full prescribing information for complete boxed warning.
- Anaphylactic and infusion reactions have been reported during and after administration of KRISTEXXA.
- Anaphylaxis may occur with any infusion, including a first infusion, and generally manifests within 2 hours of the infusion. However, delayed-type hypersensitivity reactions have also been reported.
- KRISTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions.
- Patients should be pre-mediated with antihistamines and corticosteroids.
- Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRISTEXXA.
- Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.

CONTRAINDICATIONS
- Glucose-6-phosphate dehydrogenase (G6PD) Deficiency: Before starting KRISTEXXA, patients at higher risk for G6PD deficiency (e.g., those of African and Mediterranean ancestry) should be screened due to the risk of hemolysis and methemoglobinemia.

### Pegloticase Warnings and Precautions

**• Anaphylaxis: Anaphylaxis occurred in patients treated with KRYSTEXXA. Anaphylaxis may occur with any infusion, including a first infusion, and generally manifests within 2 hours of the infusion. However, delayed-type hypersensitivity reactions have also been reported. KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis. Patients should be pre-medicated with antihistamines and corticosteroids. Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA.**

**• Infusion Reactions: Infusion reactions occurred in patients treated with KRYSTEXXA. KRYSTEXXA should be administered in a healthcare setting and by healthcare providers prepared to manage infusion reactions. Patients should be pre-medicated with antihistamines and corticosteroids. Monitor patients closely for signs and symptoms of infusion reactions. In the event of an infusion reaction, the infusion should be slowed, or stopped and restarted at a slower rate. If a severe infusion reaction occurs, discontinue infusion and institute treatment as needed. The risk of an infusion reaction is higher in patients who have lost therapeutic response.**

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### Pegloticase Dosing

- The dose of pegloticase is 8mg IV every 2 weeks
- No dose adjustment is necessary for gender, age, weight, or renal impairment
- The admixture should only be administered by IV infusion over no less than 120 minutes via gravity feed, syringe-type pump, or infusion pump
- **DO NOT ADMINISTER PEGLOTICASE AS AN IV PUSH OR BOLUS**

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### Pegloticase Adverse Reactions

- **The most common adverse reactions are anaphylaxis, infusion reactions, and gout flares.** The most common adverse reactions occurring in at least 5% of KRYSTEXXA-treated patients are gout flares (77%), nausea (12%), hypertension (11%), nasopharyngitis (7%), constipation (6%), chest pain (4%), anaphylaxis (2%) and vomiting (5%).
Pegloticase is supplied as a clear, colorless, sterile solution for dilution in a single-use glass vial with a latex-free rubber injection stopper to deliver as 8 mg/1 mL for IV infusion.

- Using proper technique, inject 1 ml of pegloticase (8 mg/1 mL vial) into a 250-mL bag of 0.9% Sodium Chloride Injection, USP or 0.45% Sodium Chloride Injection.
- Gently invert the infusion bag containing the diluted pegloticase solution a number of times to ensure thorough mixing. Do not shake the bag.
- Mixed solution is stable for 4 hours at 2º to 8ºC (36º to 46ºF) and at room temperature (20º to 25ºC, 68º to 77ºF).
- However, it is recommended that diluted solutions be stored under refrigeration, not frozen, protected from light, and used within 4 hours of dilution.

Discard any unused portion remaining in the vial.

- Do not mix or dilute pegloticase with other drugs.
- Before administration, allow the diluted solution of KRYSTEXXA™ (pegloticase) to reach room temperature.
- KRYSTEXXA in a vial or in an IV infusion fluid should never be subjected to artificial heating (e.g., hot water or microwave).

- Pegloticase should be administered by trained medical professionals experienced in the administration of medicines with known risks of anaphylaxis and infusion reactions.
- Patients should receive pre-infusion medications (antihistamines and corticosteroids) to minimize the risk of anaphylaxis and infusion reactions.
Monitoring

• Monitor patients closely for signs and symptoms of infusion reactions
  – In the event of a reaction, the infusion should be slowed, or stopped and restarted at a slower rate
  – If a severe reaction occurs, discontinue infusion and institute treatment as needed
• Since an infusion reaction can occur after completion of an infusion, consider observation of patients for approximately 1 hour post-infusion

Infusion reactions and anaphylaxis

• Infusion reactions occurred at any time during a course of treatment with approximately 3% occurring with the first infusion, and approximately 91% occurred during the time of infusion.
• Manifestations of these reactions included urticaria (frequency of 10.6%), dyspnea (frequency of 7.1%), chest discomfort (frequency of 9.5%), chest pain (frequency of 9.5%), erythema (frequency of 9.5%), and pruritus (frequency of 9.5%). These manifestations overlap with the symptoms of anaphylaxis, but in a given patient did not occur together to satisfy the clinical criteria for diagnosing anaphylaxis.
• Diagnostic criteria of anaphylaxis were skin or mucosal tissue involvement, and, either airway compromise, and/or reduced blood pressure with or without associated symptoms, and a temporal relationship to KRYSTEXXA or placebo injection with no other identifiable cause.

Reference: 1. KRYSTEXXA Prescribing Information.
Storage

- Protect from light. Do not shake or freeze
- After dilution of KRYSTEXXA™ (pegolitacase) 8 mg in 250 mL of normal or half-normal saline, infusion is carried out in ambient light without necessity for covering of the infusion bag or intravenous tubing. Protection from light specifically refers to requirements for such protection under storage conditions for KRYSTEXXA, either for the vial or for diluted solutions not used immediately.
- KRYSTEXXA diluted in infusion bags is stable for 4 hours at 2°C to 8°C (36°F to 46°F) and at room temperature (20°C to 25°C, 68°F to 77°F). If not used immediately, it is recommended that diluted solution be stored under refrigeration, not frozen, protected from light, and used within 4 hours of dilution.
- Do not use beyond the expiration date.

Non-pharmacologic Management

- Ice to area
- Increase fluid intake
- Decrease diuretics
- Diet adjustments- avoidance of high purine food and beverage

Dietary Management

- Foods very high in purines include:
  - hearts
  - herring
  - mussels
  - yeast
  - smelt
  - sardines
  - sweetbreads
**Dietary Management**

- Foods moderately high in purines include:
  - anchovies
  - mutton
  - bacon
  - salmon
  - kidneys
  - trout
  - haddock
  - scallops
  - grouse
  - veal
  - liver
  - turkey
  - partridge
  - goose
  - pheasant

**Alcohol Consumption**

- Avoid Beer
  - As few as two to four beers a week increased the risk of gout by 25%.
  - Two beers a day were more than 200% as likely to develop gout as non-beer drinkers.
  - One liquor/wine drink a month increases risk, but the chance of gout jumps 60% with >2 drinks/day.

**Conclusions**

- Gout is common
- Prevalence is increasing
- Diagnosis can be made with great certainty in most patients
- Management differs for acute vs. chronic gout
- Lifestyle modification a must for management
- With current therapies, compliance with chronic therapy is poor
- Newer agents may make more effective chronic gout therapy possible for patients with medical comorbidities

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THANK YOU