Dr. Paul Doghramji is attending physician at the Pottstown Memorial Medical Center and medical director of Health Services at Ursinus College in Collegeville, PA. He is also senior staff member of Collegeville Family Practice in Collegeville, having recently transferred his practice from Brookside Family Practice & Pediatrics in Pottstown, PA, both subsidiaries of Pottstown Medical Specialists, Inc.

Dr. Doghramji earned his medical degree from Jefferson Medical College and completed a residency in family practice at Chestnut Hill Hospital in Philadelphia, PA.

Dr. Doghramji is a member of various professional societies, including the American Academy of Physicians and the Pennsylvania Academy of Family Physicians. He holds a fellowship in the American Academy of Physicians, has several journal and internet publications, has co-authored one textbook, *Clinical Management of Insomnia*, and lectures on various topics in family practice, particularly sleep disorders and insomnia.

During the past 5 years, Dr. Doghramji has taught extensively in a wide range of gout educational initiatives. In 2015 alone, over 4000 primary care practitioners were educated during these live gout programs.

**Dr. Doghramji, there seems to be more focus on gout in primary care over the past few years. Is there a particular reason?**

Dr. Doghramji: There is much more focus on gout, not only through the development of new medications and dosages, but also new information. Gout is now twice as prevalent as it was 30 years ago for a number of reasons. But most importantly, gout is associated with increased rates of atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), and hypertension (HTN). In the last few years, there has been a new understanding of the disease, as well as new medications to enhance that understanding and focus on patient treatment. We have a host of anti-inflammatories to treat painful gout flares, as well as many medications to reduce uric acid. A sad fact is that gout has been poorly managed, and gout goals in primary care have not been achieved.

**Gout has been described as a ‘rich man’s disease’ and perhaps summarily dismissed or not on the ‘seriousness’ radar. Yet, doesn’t gout cause tremendous pain?**

Dr. Doghramji: The ‘rich man’s disease’ moniker became popular as the wealthy were heavier, possibly lived longer, and they also passed on hereditary gout amongst themselves. Today more people are ‘rich’, with heavier people living longer and genetically passing gout to their offspring. Patient feedback on the pain of gout is noteworthy - descriptions of pain that is intolerable - to the point that “even a sheet touching the gouty toe” is tough and many patients lose sleep. In fact, one patient stated that even a draft on the big toe caused pain.
Why is gout prevalence increasing? What can primary care providers do to insure proper treatment?

Dr. Doghramji: Probably a key reason there is more gout is that people in general are getting heavier. In addition, they are living longer and have more chances to develop HTN, CKD, and accumulate more uric acid. Coupled with that, many are getting more illnesses and medications that raise uric acid. So, there is a confluence of factors that leads to gout. Important to us as practitioners, are the steps we need to take in our practices:

1. **Know enough about gout** - one of the advantages we have is a lot of excellent research done recently that has led to a greater understanding of the disease process.
2. **Understand the role of chronic kidney disease (CKD)** - the kidneys excrete uric acid, so CKD patients are predisposed to hyperuricemia. Complicating the situation is that a number of agents used in the management of gout have contraindications in CKD. It is important to establish monitoring in your practice for any potential therapeutic choice issues.
3. **Pass on necessary information to patients** - as a critical part of reaching gout goals, patients need to understand their disease. There are significant patient knowledge gaps in gout, such as not understanding disease progression, how ‘flares’ result in chronic joint damage, the concept of urate lowering therapy (ULT) to avoid complications and disability, treatment options and duration of therapy, as well as gout ‘goals’. A major factor leading to treatment failure is the patient ‘stopping’ their urate-lowering medication because the medication has caused a flare-up, and not understanding the relationship between ULT and gout flares.
4. **Insert shared decision making into your practice** - this is an excellent way to get a patient involved in their gout goal achievement. Using a shared decision aid which will bring them up-to-speed on gout and treatments, some models provide a ‘plan’ that captures the patient’s thoughts, concerns, and values, so the shared decision making discussion takes their preferences into consideration and together we can develop a plan to achieve set goals. Although it takes a bit of system consideration and change, shared decision making is well worth the time, resources and effort. We utilize a gout specific tool - PEPtools: Gout (www.peptools.com). An important aspect of the tool is to inform the patient and his/her concerns and choices are captured in a plan. That helps in our discussion.
5. **Establish regular follow up for gout, including twice a year lab tests and follow up visits** - it is important to assure that everything around gout is carefully managed.

How does gout affect patients over the longer-term?

Dr. Doghramji: Gout is associated with significant morbidity, work-related disability which affects not only the patient’s health status but their work and opportunity, loss of productivity, significant increase in healthcare costs, and all cause hospital admissions. We have tried over time to estimate costs connected with many of these issues. It is very difficult, but some recent studies suggest very high numbers associated with productivity loss, healthcare costs, comparative costs of gout/non-gout patients and the significantly higher economic burden of gout. This is why gout needs attention in the practice - placing it ‘on the practice radar’.
**How has the increase in gout changed your practice?**

Dr. Doghramji: In our practices, we needed to take a number of proactive steps to address gout appropriately. First, we had to get gout ‘on our radar’. This means making it a part of the overall patient review process. You should:

- Know how gout presents and be able to make a clinical diagnoses followed by appropriate work-up
- Know the goals of therapy, including treatment of acute attacks, as well as when to begin ULT
- Initiate flare prophylaxis when ULT is used
- Focus on uric acid level goals when initiating uric acid lowering therapy - uric acid should be ≤6 mg/dL, or in the presence of tophi ≤5 mg/dL
- Consider the targets that must be met to keep gout under control and also know about ULT pharmacologic therapies and emerging combinations to get to UA goals. We now are better armed to get our patients to goal.
- Very important to goal achievement is to educate the patient and utilize a shared decision making approach

**What causes gout specifically?**

Dr. Doghramji: Gout is caused by accumulation of uric acid in the joints. When the crystals accumulate in the joints, they are encapsulated in proteinaceous conglomerates that accumulate to cause microtophi. At some point, when the uric acid load is too high and sometimes initiated by minor trauma, encapsulated uric acid is released and bare crystals cause rapidly progressive, severe inflammatory cascade. In between attacks, the accumulating uric acid also causes premature erosion and destruction of cartilage surfaces, premature osteoarthritis (OA).

Uric acid, overproduction or, as is in most cases, reduced clearance, causes the elevation of serum uric acid (SUA) level beyond its saturation point. Thus, uric acid crystalized everywhere in the body, but most harmful in the kidneys, joints, and inflammation of coronary arteries, increasing the rates of ASCVD. In reduced clearance, the kidneys are unable to reduce uric acid to appropriate levels. Purines which come from the breakdown of nucleic acids are enzymatically reduced to hypoxanthine and then xanthine with the enzyme, xanthine oxidase. The end product of this process in humans and great apes is uric acid. In all other animals, uric acid is further degraded to allantoin via uricase. Allantoin is much more water soluble.

**Where does gout strike?**

Dr. Doghramji: It can affect any diarthrodial joint and even some soft tissue. Because uric acid crystalized in lower concentrations at lower temperatures peripheral joints, whose temperature can be 10 degrees lower than core body temperature, more commonly get gout attacks. Podagra, gout attack of the big toe, is the initial presentation in half of those who get gout. But patients present with an acute arthritis of the any peripheral joint like wrists, ankles or knees. In patients with very high uric acid levels for many years, uric acid can accumulate in soft tissue, like under the skin in the form of soft, painless nodules, tophi. These patients with tophaceous
gout can see these nodules as being disfiguring and distorting when they occur at joints, eventually leading to disabilities and discomfort.

**Who gets gout?**

Dr. Doghramji: Certain groups of individuals are at higher risk of getting gout:
- Men (except women after menopause, as estrogen is urocosuric)
- Older people
- Some specific ethnic and race groups (e.g. Pacific Islanders)
- Obese individuals
- Consuming a diet rich in meat, seafood, organ meat and beer
- Consuming high fructose in foods like juices and soft drinks
- Patients with hypertension
- Chronic kidney disease
- Those who have had organ transplantation
- Patients taking certain medications like thiazides or loop diuretics
- Patients with metabolic syndrome
- Those who have a family history of gout

**Why is treating gout so important?**

Dr. Doghramji: The obvious is that gout attacks are very painful, often causing one to lose time from work and from family and social activities. They often last several days if treated, but can go on for weeks if not treated. But other than these attacks, and also their association with premature OA, gout is now associated with ASCVD, CKD and HTN. Finally, gout, especially poorly treated gout, contributes to rising medical costs and healthcare utilization. Less than half of patients reach uric acid goals. This indicates there is not an awareness of gout guidelines and the appropriate gout UA goals. Urate lowering therapy usually extends over a lifetime.

Also, prescribing gout medications in patients with chronic kidney disease is particularly important as many patients with gout have high rates of kidney disease.

**How do you treat gout?**

Dr. Doghramji: There are two parts of gout treatment: managing the acute gout attack and then reducing uric acid to prevent gout attacks. Gout is not just a problem with an inflamed toe. Even though we may provide some relief through administration of colchicine or steroids or NSAIDS, which should be given as soon as possible and at the maximum dose, we also need to focus on uric acid levels. With the pain gone, it is easy to put off taking additional action until the next acute attack. But, it is important to check the uric acid levels and prescribe medication if the SUA cannot be reduced to target with lifestyle changes and other non-medicinal means. If one misses this part of the treatment equation, the patient will certainly continue to sustain joint damage and an increased frequency of acute attacks, and be at higher risk of ASCVD, HTN and CKD.
For those who can’t tolerate NSAID’s oral low-dose colchicine regimen (two tablets at onset of the attack, then one tablet after one hour in those with normal renal function) may be used, especially in patients who are able to take orals medication but have contraindications to NSAID therapy, moderate or more severe chronic kidney disease, active peptic ulcer disease, or a history of NSAID intolerance. Colchicine is contraindicated in patients with advanced renal or hepatic impairment because the liver and kidney are involved in colchicine metabolism.

Glucocorticoids may be used in patients who cannot use either colchicine or NSAIDS and who have no contraindication to steroids.

*Why do patients stop taking their gout medications?*

Dr. Doghramji: Patients don’t adhere to gout medication mainly because of misinformation or lack of information. One common problem is that patients often get more flares during the first 3-6 months of ULT. And if they don’t know that this is normal, an indication that uric acid is leaving their body, they will mistakenly think that ULT is causing more problems causing them to stop the medication. The patient needs to be instructed to continue the medication even if a flare occurs. Now, this is where flare prophylaxis comes in. Long-term therapy reduces joint destruction, and this is an area that patients don’t understand. All gout is tophaceous.

*So much has been stated about achieving gout goals. The ideal UA level should be 6 mg/dL?*

Dr. Doghramji: It depends. The goal is 6 if there are no tophi. In the presence of tophi, however, that goal should be more aggressive. In that case, we recommend 5 mg/dL so the SUA can be low enough to help melt away the tophi. Interestingly, one treatment for severe, recalcitrant gout is using intravenous peglated uricase (pegloticase). This lowers SUA to less than one and has a dramatic effect in reducing tophus size.

*What are the therapeutic options for reducing uric acid?*

Dr. Doghramji: Up until a few years ago, there were very limited options for reducing serum uric acid. Allopurinol, a xanthine oxidase inhibitor (XOI), has been around the longest and perhaps has been most misunderstood. The drug is relatively well tolerated, inexpensive and commonly used. One begins with doses as low as 100 mg daily (50 mg in CKD stage 3 or worse) and titrating up every 2-4 weeks. Titration seems to be difficult for many providers and substandard doses don’t produce the appropriate reduction in SUA to target. Liver tests, blood counts and renal function should be monitored while on therapy. Toxicities include rash, hepatotoxicity, bone marrow suppression and severe hypersensitivity reactions.

A newer agent, febuxostat (Uloric in the US), a nonpurine selective inhibitor of xanthine oxidase, was introduced in 2009, the first in a long, long time. The drug is administered orally and metabolized mainly in the liver vs. allopurinol which is excreted primarily by the kidneys. Given that, febuxostat can be used in patients with mild to moderate renal impairment with no dosage adjustment. The starting dosage is 40 mg for 2 weeks, and if the SUA does not normalize after 2 weeks, increase the dosage to 80 mg daily. The most common side effects are rash, elevated liver function tests (LFTs) and arthralgia.
Lesinurad (Zurampic) is the first selective uric acid reabsorption inhibitor (SURI) and was recently approved by the FDA and marketed. This drug is only appropriate for patients not achieving SUA goals while on maximum dose of allopurinol or febuxostat and must be co-administered with one of those xanthine oxidase inhibitors. Renal function should be assessed before initiating therapy as it cannot be used for CrC <45. Kidney functions should be checked periodically after that. In clinical studies, Lesinurad plus febuxostat or allopurinol reduced serum uric acid levels statistically significantly better than placebo. Starting dose of Lesinurad is one 200 mg tablet daily in combination with either Febuxostat or Allopurinol. There is no requirement for dose adjustment for mild to moderate renal impairment, mild or moderate hepatic impairment, or for those patients 65 and older. There is a risk of acute renal failure that is more common when used without an XOI. Common side effects include headache, flu symptoms, increased blood creatinine, GERD, kidney related side effects and kidney stone.

**So, Dr. Doghramji, what advice can you give for managing the gout patient long-term?**

Dr. Doghramji: As I stated previously, achieving the uric acid goal of less than 6 mg/dL (or 5) is key, especially over the long term. The aim of long-term treatment of gout is to reduce SUA levels to <6 mg/dL, which is below the saturation point of monosodium urate (MSU) (6.8 mg/dL) to inhibit formation of new crystals and to promote dissolution of existing crystals. Gout treatment should improve disease outcomes. There are several new urate-lowering drugs available, yet achievement of serum urate targets is infrequent. With treatment and patient adherence, gout is a curable disease.

**Are lifestyle choices important to the gout patient as well?**

Dr. Doghramji: There are lifestyle changes that gout patients can make that can also assist with reaching gout goals. First, the patient needs to exercise regularly, and the formula is easy to remember. “Exercise with moderate intensity for 30 minutes per day. Ask them to strive for that goal as many days as possible. Along with that, patients need to maintain a healthy body weight. This is something you need to discuss with patients - how to achieve the proper weight. This is an area which many times is not addressed during patient visits. There are many plans and resources to help with that. Also, advise your patients to stay hydrated with 64 oz of water per day or more if the patient is exercising. The hydration should not include alcoholic or sugar beverages, however.

**How would you summarize the best practice approach to treating gout?**

Dr. Doghramji: There are four key things that a primary care provider needs to focus on:

1. Know gout and make sure that it is on what I term “the practice radar”
2. Know that treating an acute attack is NEVER enough
3. Know that getting SUA to <6 mg/dL (<5 mg/dL where tophi are present) is the GOAL
4. Know that >25% of patients will need ‘combination meds’ to achieve goal

**Dr. Doghramji, thanks for your time and practice advice.**