



# CHARM issue 8

CARE, HEALTH, ARTHRITIC MANAGEMENT

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## EDITOR'S MESSAGE

It is our pleasure to present to you an issue of CHARM on the management of gout. Gout is a common medical condition that is generally considered to be suboptimally managed. Often seen as a one-visit disease to general practitioner during an acute attack, gout may develop into chronic tophaceous arthropathy with high body urate load and is actually a condition that needs multidisciplinary care. Here, we will learn from our rheumatologists about gout and the current management guideline from the American College of Rheumatology. We have invited a biochemist to write on the laboratory diagnostic aspect on gout and pharmacists on the available medical treatment options in Hong Kong. As severe hypersensitivity reactions are observed from time to time with allopurinol use, our rheumatologist is happy to share with you update information regarding a recently identified risk allele HLA-B\*5801 for the adverse effect and its role in current management. Last but not the least, dietary restriction and lifestyle changes as key component in the management of gout will be elaborated by an invited dietician.

Happy reading!

## CLINICAL GUIDELINE FOR GOUT MANAGEMENT

### Dr. Man-choi WAN

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### Introduction

Gout is a disorder of purine metabolism. Gouty attack occurs when the final metabolite of purine, uric acid, crystallizes in the form of monosodium urate and precipitates in joints, tendons and the surrounding tissues triggering a local immune mediated inflammatory reaction. One of the key cytokines in the inflammatory cascade in gout is interleukin  $1\beta$  and this is the primary target in some of the novel treatments of Gout.

### Gout management clinical guidelines

New guidelines for gout management were developed by the American College of Rheumatology (ACR) in 2012, since there have been advances in the understanding of gout from clinical evidence and researches. The ACR 2012 guidelines emphasized several aspects including the importance of effective acute gout treatment; prophylaxis of recurrence of gouty attacks; treat-to-target of serum urate level and risk management in urate lowering drugs in long term gout management; patient education on diet, lifestyle, treatment objectives and management of comorbidities.

# CLINICAL GUIDELINE FOR GOUT MANAGEMENT

The main aspects of ACR 2012 guideline in gout are summarized as follows:

## Acute treatment in gout

Non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids or oral colchicine are appropriate first-line options for treatment of acute gout, and certain combinations can be used for severe or refractory attacks.

1. NSAIDs
  - Start within 24 hours of attack
  - High dose and taper over a few days and stop at least 2 days after attacks subside
  - Indomethacin/Naprosyn /Sulindac approved by FDA though other NSAIDs are also effective
  - Contraindications : gastrointestinal bleeding, chronic kidney disease (CKD)
  - Cautions : elderly, drug interactions (warfarin), history of peptic ulcer
2. Colchicine
  - Start within 36 hours of attack
  - Loading 1 mg, then 0.5 mg 1 hour later followed by 0.5 mg 12 hours later as needed. Can continue colchicine 0.5 mg tid till attack resolves. Avoid dosing 0.5 mg every 1 or 2 hours due to vomiting / diarrhea in 80% of patients
3. Corticosteroids
  - Systemic or intra-articular (need to rule out septic arthritis)
4. IL-1 Inhibitors (off-label use): Anakinra, Riloncept, Canakinumab

## Prevention of gouty attack by urate lowering drugs

1. Reduce production of urate :  
Xanthine Oxidase Inhibitors: Allopurinol and Febuxostat are recommended as the first-line pharmacologic urate-lowering therapy (ULT) in gout.
2. Increase excretion of urate in urine:  
Uricosuric Drugs: Probenecid, Benzbromarone, Sulfapyrazone
3. Break down of urate crystals:  
Uricase: Pegloticase, Rasburicase

## Recommendation on allopurinol in gout management

(Indicated if more than 2 attacks/year or presence of tophus, or urate stone or urate nephropathy)

- Starting dose 100 mg/day or lower in elderly or patients with impaired renal function
- Titrate up every 1 to 4 week to achieve target level: serum urate < 0.36 mmol/l (at least) or 0.3 mmol/l
- Beware of drug interactions: Azathioprine or 6-mercaptopurine and Ampicillin
- Check HLA-B\*5801 in high risk populations before starting allopurinol because HLA-B\*5801 allele has strong association with Allopurinol Hypersensitivity Syndrome (100 -200 times higher risk ) which carries high mortality (20-25%).
- Han Chinese and Thai (6-8%) , Koreans with stage 3 /4 CKD (12%) has higher prevalence of this allele compared to whites in the United States ( <2%) and they are considered high risk groups of Allopurinol Hypersensitivity Syndrome.

## Prophylaxis of recurrent gouty attacks while on ULT

All urate lowering drugs can precipitate gouty attack. Pharmacologic anti-inflammatory prophylaxis is recommended for all gout patients when ULT is initiated, and should be continued if there is any clinical evidence of continuing gout disease activity and/or the serum urate target has not yet been achieved.

- Colchicine 0.5 mg qd or bd or /and low dose NSAIDs daily in 3 to 6 months
- Prednisolone <10 mg /day if colchicine or NSAIDs contraindicated/intolerance
- Stop when target serum urate level achieved and no more gouty attack

# CLINICAL GUIDELINE FOR GOUT MANAGEMENT

## Co-morbidities associated with gout

(Check in every gout patient and treat the co-morbidities as well)

- Chronic kidney disease
- Diabetes Mellitus
- Obesity
- Hyperlipidemia
- Hypertension

## Conclusions

Patient education and good doctor-patient communication is most important in gout management. Patients with gout should understand that perseverance in lifestyle modifications and compliance with urate lowering agents are the cornerstone in long term gout management. Some patients may be disappointed and stop taking the medication if they experience frequent gouty attacks while taking urate lowering agents in the first few months of therapy. They should be well informed about possible flares of gout in the initial phase of gout treatment. Lifestyle modifications including diet and physical fitness can reduce serum urate level by about 10-15% and form a core management of gout. It is essential to advise patients to quit excessive alcohol (all forms) and avoid non-essential drugs which can increase serum urate especially in the elderly. Overall, gout today is better understood and managed through development of guidelines based on researches and clinical evidence.

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# LABORATORY DIAGNOSIS OF GOUTY ARTHRITIS

## Dr. Morris Hok-leung TAI

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Gout is a prevalent disorder of uric acid metabolism. Monosodium urate (MSU) crystals precipitate out of body fluids such as urine or synovial fluid when the salt concentration is greater than the solubility threshold. Factors affecting solubility threshold include concentrations of anions and cations, pH and temperature. In physiological conditions such as body temperature of 37°C and serum sodium concentration of 140 mmol/L, serum urate in excess of 0.40 mmol/L facilitates MSU crystal formation<sup>1</sup>. Deposition of MSU crystals in peripheral synovial joints triggers inflammation and clinical manifestations of gouty arthritis. This well-characterised pathophysiology enables the use of biochemical tests in the investigation of gout. Naturally, clinicians look for presence of MSU crystals or elevation of urate in synovial fluid. As normal synovial fluid is an ultrafiltrate of plasma, plasma urate level is taken as a surrogate marker of urate level in synovial fluid.

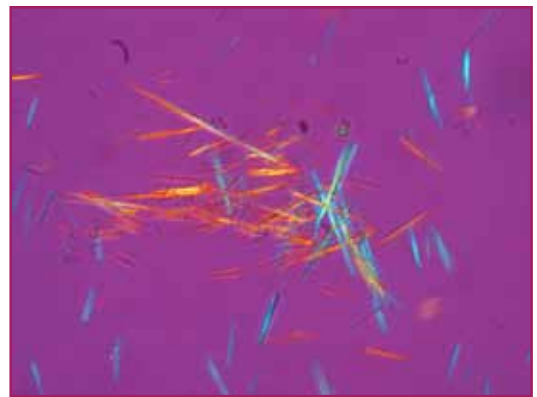
Microscopic examination of joint fluid for MSU crystals provides a simple tool for definitive diagnosis of gout. It has to be emphasized that plain bottle or bottle containing liquid EDTA should be used for synovial fluid collection as other preservatives, especially powdered EDTA, may form crystal which would confuse diagnosis. The sensitivity of this analysis to detect gout ranged from 63% to 78% with specificity ranged from 93% to 100%<sup>2</sup>. Aside from MSU crystals, other crystals like calcium pyrophosphate dihydrate (CPPD), cholesterol, steroids, apatite, other phosphates, oxalate and artifacts can be seen in synovial fluid by phase contrast microscopy<sup>3</sup>. MSU crystals are needle- or rod-shaped and are 1 to 30 micrometre in length. Rarely, other crystalline forms may be seen; spherulites or “beachball-like” MSU crystals have been reported. The identification of MSU crystals can be achieved by examining the fluid sample under polarizing light microscopy. MSU crystal is typically referred as negatively birefringent.

# LABORATORY DIAGNOSIS OF GOUTY ARTHRITIS

Birefringence is the optical property of a material having a refractive index that depends on the polarization and propagation direction of light. MSU crystal is not the only birefringent objects in synovial fluids. CPPD, which is involved in the pathogenesis of pseudogout, is weakly positively birefringent. CPPD crystals are usually rod-shaped, rectangular or rhomboid and can occasionally be needle-shaped. Other birefringent objects include various crystals (e.g. calcium oxalate), fat, starch and fibers. The identification of MSU crystals in joint fluid can be challenging because of the overlapping morphology of various crystals. Because of these potential interferences, the inter-observer reliability is mediocre with kappa value ranges from 0.35-0.63<sup>2</sup>. The experience of the operators as well as training and quality control are important. The use of compensated polarized light allows more definitive microscopic examination of crystals in synovial joint.

Blood is a relatively convenient body sample for examination. Plasma urate level is therefore widely used for assessment of gout, and hyperuricaemia is the most important pre-requisite for gout. Hyperuricaemia is defined by plasma uric acid concentrations greater than 0.42 mmol/L in men or 0.36 mmol/L in women. Some laboratories may define hyperuricaemia as two standard deviations above mean urate level in healthy population. The difference in cutoff will not change the overall diagnostic accuracy as the increase in sensitivity is offset by a decrease in specificity. An alternative approach to the interpretation is to give up a particular cut-off level and consider the degree of hyperuricaemia in relation to the risk of developing gout (i.e. the higher the urate concentration, the greater the risk of gout). For instance, men with plasma uric acid concentrations exceeding 0.54 mmol/L are approximately 150 times more likely to have coexisting gouty arthritis than are men with uric acid less than 0.36 mmol/L<sup>4</sup>. It has to be emphasized that the correlation between plasma urate level and clinical gout is a loose one. Not all hyperuricaemic individuals will suffer from gout and hyperuricaemia is not invariably found in patients with gouty arthritis. Other factors such as local temperature of the tissue may play a role in the development of the condition.

Gout is classified as a primary or secondary clinical condition. Secondary gout is a result of hyperuricaemia attributable to risk factors such as diuretics use, diabetes mellitus, chronic renal failure, hypertriglyceridaemia and metabolic syndrome. Biochemical investigations like blood glucose, renal function tests as well as lipid profile are helpful in the detection of these conditions. In endemic areas of lead poisoning, whole blood lead should also be assessed as it is the cause of uncommon saturnine gout. Cases without secondary causes are coined primary hyperuricaemia and 24-hour urinary urate excretion may be useful test to classify “over-producers” and “under-excretors” for whom different hypouricaemic drugs may be considered. High daily urinary urate output above 6.0 mmol/day suggests “over-producers” or high purine intake. Low-purine diet consumption for five days can help discriminate “over-producers” who has persistently high urinary urate content (>4.5 mmol/day) from “under-excretors” and individuals with previously high purine intake who would have low urinary urate level (<4.0 mmol/day).



Urate crystals, with their long axis seen as horizontal in this view being parallel to that of a red compensator filter. They appear as yellow, and are thereby of negative birefringence.

(Source: <http://en.wikipedia.org/wiki/Birefringence>)

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# ALLOPURINOL HYPERSENSITIVITY AND GENETIC PREDISPOSITION

**Dr. Daniel Kam-hung NG**

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Allopurinol is a major drug used in the treatment of gout. It is generally well tolerated although a minority of people develops hypersensitivity reaction with skin rash. The most common skin reaction (up to 2% of patients) associated with allopurinol is maculopapular exanthema, characterized by mild to moderate rash without fever or internal organ involvement.<sup>1</sup> Less commonly observed are more serious skin reactions designated as allopurinol hypersensitivity (AH). AH encompasses immunologically mediated, delayed reactions characterized by rash and systemic symptoms, notably fever with or without internal organ involvement such as hepatitis. At the less severe end of the AH spectrum, two syndromes with significant overlapping features have been described: DRESS (drug reaction with rash, eosinophilia and systemic symptoms) and DHS (drug induced hypersensitivity syndrome), both characterized by rash and internal organ involvement. The most severe phenotypes of AH includes Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) which are manifestations of severe cutaneous adverse reaction (SCAR). Cases with limited area of epidermal detachment are usually labeled SJS and those with extensive detachment are named TEN (Table 1). These reactions are associated with mortality as high as 27%.<sup>2,3</sup>

**Table 1**

Allopurinol Severe Cutaneous Drug Reaction (SCAR)	Skin detachment (% of body surface area)
Stevens-Johnson syndrome	<10
Overlap Steven-Johnson syndrome/toxic epidermal necrolysis	10-30
Toxic epidermal necrolysis	>30

The mechanisms leading to AH remain unclear. Susceptibility to adverse drug reaction is believed to be genetically determined and human leucocyte antigen (HLA) genes have been implicated in drug-induced hypersensitivity with allopurinol. Hung et al first reported an extremely strong association between the HLA class I allele HLA-B\*58 and allopurinol-associated SCAR in Han Chinese in Taiwan.<sup>4</sup> The HLA-B\*5801 allele was present in all the 51 patients with allopurinol-associated SCAR compared with 15% of the allopurinol-tolerant group and 20% of the general population. A recent local study on 19 patients with allopurinol-induced SCAR reported a sensitivity and specificity of the HLA-B\*5801 allele of 100% and 86.7% respectively for the prediction of SCAR.<sup>5</sup> Similarly, a strong association was also observed in a Thai population. All of the 27 allopurinol-induced SJS/TEN patients carried HLA-B\*5801 whereas only seven (12.96%) of the control patients had this allele.<sup>6</sup> Although HLA-B\*5801 is highly associated with allopurinol-induced SCAR in some populations, it may not linked to other simple or benign cutaneous reactions. A recent retrospective analysis in 448 Korean patients with chronic renal insufficiency showed the presence of HLA-B\*5801 allele in all nine patients with allopurinol-induced SCAR but not in the 7 cases with simple maculopapular rash.<sup>7</sup> Another Australian study revealed that none of the 12 patients including one South-East Asian who had milder allopurinol-induced exanthema carried the HLA-B\*5801 allele.<sup>8</sup> Moreover, weaker associations have been observed in European (55% HLA-B\*5801 positive; n=15) and Japanese populations (36% HLA-B\*5801 positive, n=4).<sup>9,10</sup> Notably, the prevalence of the HLA-B\*5801 is much lower in European/Caucasian populations (1-6% allele carrier rate) compared to Han Chinese in Taiwan (10-15%) and suggests that HLA-B\*5801 is important but not sufficient for allopurinol-induced SCAR. Other cofactors such as renal insufficiency or virus infection have been implicated as risk factors for the development of allopurinol-induced SCAR.

## ALLOPURINOL HYPERSENSITIVITY AND GENETIC PREDISPOSITION

Would this genetic test be helpful in predicting allopurinol-induced SCAR? Although the negative predictive value and sensitivity of HLA-B\*5801 in cases of allopurinol-induced SCAR in South-East Asian patients are both very high, the positive predictive value for developing allopurinol hypersensitivity is very low because of the low incidence of AH and the relatively high prevalence of HLA-B\*5801 among South-East Asian. Thus, its role as a screening test remains limited as a large proportion of patients screened positive for HLA-B\*5801 would be unnecessarily excluded from using allopurinol. The role of potential risk factors, such as other genetic markers, concomitant diuretic use, renal impairment and patch testing needs to be addressed before this allele has high enough positive predictive value to be useful as a predicting tool for allopurinol-induced SCAR.



Allopurinol-induced skin rash

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## CONVENTIONAL AND NEW DRUG THERAPY

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### Introduction

Gout is a common metabolic disorder that is characterised by the formation and deposition of monosodium urate (MSU) crystals. The condition is associated with recurrent episodes of acute joint pain due to deposition of MSU crystals in synovial fluid.<sup>1,2</sup> Hyperuricemia is associated with development of gout and may exist for several years to decades before the first symptoms of gout. Although gout is a well-recognized disease, it appears to be suboptimally managed. There is increasing incidence and prevalence in recent years. The clinical profile of gout has also become increasingly complex as a result of comorbidities, advancing age and chronic tophaceous gouty arthritis refractory to treatment.<sup>3</sup> In this article, we shall look into the current therapeutic approaches and the new therapeutic options in gouty arthritis.

### Current Therapeutic Options for Reducing hyperuricemia in Gout:

Acute gout flares are usually treated by non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids or colchicine aiming to alleviate joint pain and inflammation. When gout flare subsides, the goal of therapy is to prevent recurrence of gout attacks by reducing serum urate (sUr) concentration. Antihyperuricemic maintenance therapy is indicated for recurrent gout attacks (> 2/year) or the presence of gouty tophi. In contrast, asymptomatic hyperuricemia does not require specific treatment.<sup>1</sup> There are two main classes of antihyperuricemic drugs : xanthine oxidase inhibitors (XOIs), e.g. allopurinol, febuxostat; as well as uricosuric drugs , e.g. benzbromarone and probenecid.

## CONVENTIONAL AND NEW DRUG THERAPY

Allopurinol has been the only antihyperuricaemic drug available worldwide for many years. Its effectiveness is limited by the need for dosage adjustment in renal insufficient patients. Failure to achieve optimal lowering of sUr levels occurs a result of subtherapeutic dosing and adverse event (AE) profile that includes gastrointestinal, hepatic, renal, haematological, and skin toxicities that occurs in an approximately 20% of patients taking this drug.<sup>2,3</sup>

Benzbromarone and probenecid have been presented with barriers regarding their availability, but their exact role in treatment strategy is unclear.<sup>2</sup> They are effective in patients with adequate renal function. However, probenecid becomes ineffective if creatinine clearance (CrCL) is  $< 50\text{ml/min}$ . Benzbromarone retains efficacy in patients with stage 3 chronic kidney disease, but it is only available outside the United States (US) on a restricted basis because of its potential hepatotoxic effects.<sup>3</sup> Caution should be taken while using benzbromarone and probenecid for potential risk of urolithiasis in acid urine.<sup>3</sup>

### New therapeutic options in gouty arthritis:

In 2008, the European Medicines Agency (EMA) approved febuxostat, a novel selective XOI. Pegloticase, a polyethylene glycol (PEG) conjugate of a porcine-like uricase enzyme, was approved by the US Food and Drug administration (FDA) in 2010. Lesinurad, a novel uricosuric and other Interleukin-1 inhibitors were also found to be effective in gout treatment.

#### Febuxostat:

Febuxostat is a potent oral XOI. Unlike allopurinol and its active metabolite oxypurinol, febuxostat does not have a purine-like core structure and inhibits only XO, not other enzymes in the purine and pyrimidine metabolic pathways.<sup>3,4</sup> It is primarily metabolized by hepatic oxidation and glucuronidation.<sup>3</sup> Therefore, dose adjustment is not required in patient with  $\text{CrCL} > 30\text{ml/min}$ .<sup>4</sup>

Current data suggests that febuxostat has a better efficacy or tolerability profile than allopurinol. Febuxostat at 80 - 120mg/day is better than 'standard dosage' of allopurinol (300mg/day) in lowering sUr.<sup>1,3,5</sup> The overall reduction in the incidence of gout flares are similar in both febuxostat and allopurinol groups, with slightly higher flare rate in patients taking febuxostat 120mg daily.<sup>5</sup> AE associated with febuxostat includes rash (2%), diarrhoea and elevated hepatic transaminases in a small proportion of patients.<sup>3,5</sup> Clinical experience in everyday practice is still limited with febuxostat and it should not be used with drugs metabolised by XO (e.g. mercaptopurine and azathioprine).<sup>1</sup>

Febuxostat has been approved at doses of 40mg and 80mg daily by FDA in the US in 2009 and at doses up to 120mg daily in Europe.<sup>3</sup> In current clinical practice, the primary use of febuxostat is reserved for patients with allopurinol hypersensitivity, intolerance or treatment failure.

#### Pegloticase:

Pegloticase is a novel pegylated uricase (urate oxidase) enzyme. It was approved for the treatment of patients with conventional therapy refractory gout by the FDA in 2010.<sup>1,2</sup> The active substance is a genetically engineered, recombinant, PEG-conjugated mammalian (porcine-like) uricase enzyme.<sup>2</sup> It metabolizes uric acid into soluble allantoin for excretion by the kidney, with hydrogen peroxide and carbon dioxide as oxidative by-products.<sup>2</sup> PEGylation helps to lengthen the circulating half-life of the active enzyme moiety and to lessen the immunogenicity for long-term use.<sup>2</sup>

## CONVENTIONAL AND NEW DRUG THERAPY

In a six-month placebo-controlled clinical trial, 8mg pegloticase every two weeks induced a lytic decrease of sUr concentrations, leading to dissolution of tophi in 40% of patients at final visit. However, 58% were non-responders to the defined target sUr of 0.36mmol/l (80% were non-responders at months 3 and 6), possibly related to anti-drug antibody formation. In addition, up to one-third of treated patients experienced infusion reactions.<sup>1,2</sup> Acute gout flares are common in the first few months (up to 80% of patients) though frequency reduced with continued therapy in responders.<sup>1,2</sup> Pretreatment with antihistamines and corticosteroids can minimise risk of infusion reaction and anaphylaxis.<sup>1,2</sup> It is worth noting that patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency should be excluded to the use of pegloticase because of the risk of methaemoglobinaemia and haemolytic anaemia.<sup>1,3</sup>

In the part 1 of the 2012 American College of Rheumatology Guidelines for management of gout<sup>6</sup>, it is recommended that pegloticase is appropriate only in cases with severe gout disease burden and refractoriness to, or intolerance of appropriately dosed oral antihyperuricaemic drugs. It is not recommended as a first-line urate-lowering therapy. The appropriate duration of pegloticase therapy is yet to await consensus.<sup>6</sup>

### Therapeutic options for gouty arthritis.

Drug	Route	Action (specified indication)	Daily dose (Standard)	Characteristics
Allopurinol	Oral	Xanthine oxidase inhibitor XOI	100-900mg (300mg)	Dosage adjustment to renal function
Benzbromarone (Not approved in US)	Oral	Urate transporter (low excretor, subject with intolerance or allergy to allopurinol)	50-200mg (100mg)	Poor efficacy in severe renal function impairment
Probenecid	Oral	Urate transporter (Low excretor)	500mg -2000mg: (1000mg) Note: BD dosing	Poor efficacy in moderate to severe renal function impairment
Pegloticase	IV	Urate Oxidase	8mg every 2-4wks	Biologics; Immunogenicity; contraindicated to G6PD deficient patients
Febuxostat	Oral	XOI (particularly in allopurinol intolerance)	40-120mg (80mg)	No dosage adjustment in renal impairment (CrCL > 30ml/min)

### Pipeline drugs:

Apart from oral XOI and uricase agent, a novel strategy is the use of interleukin-1 (IL-1) inhibitors, such as anakinra, rilonacept and canakinumab. These agents have not yet been registered for acute gout therapy, but clinical trials for acute therapy and as prophylaxis for gout are underway.<sup>1</sup>

# CONVENTIONAL AND NEW DRUG THERAPY

## Conclusions:

The ultimate aim of gout management should be targeted to minimise disease burden (gout flares) and to avert long-term effects such as joint damage. Approach to the medical treatment of gout depends on the patient's presentation of the disease. Optimal treatment often requires a combination of pharmacological intervention and lifestyle changes. Primary prevention of gout involves changes in lifestyle, e.g. restricting alcohol intake or low-purine/ weight-reducing diet. Therefore, multidisciplinary approach in gout management is important in order to improve patient education, medication compliance and adherence to dietary changes.

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# GOUT & LOW PURINE DIET

**Ms. Emily YEUNG**

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Gout is a disorder of purine metabolism occurring predominantly in men. Women are more susceptible after menopause. Patients usually have hyperuricemia with deposition of urate crystals in joints. Purine is a substance found in foods of animal origin with exception of egg and dairy products. Uric acid is the end product of purine metabolism. High blood uric acid concentration in patients with gout can result from increase intake of foods high in purine, increase in production of uric acid by the body or under-elimination of uric acid by the kidneys. Excessive deposition of uric acid crystals in the joints causes swelling, redness, pain and inflammation leading to gouty attack.

Dietary management for gout involves formulating dietary plans to improve the above conditions. The goal of dietary management aims to decrease blood and urinary uric acid level and to facilitate efficient uric acid excretion through appropriate choice of food. In addition to restricting food with high purine content, excess amount of ingested protein should be avoided because the rate of purine production in the body is greater while on high protein diet. Uric acid synthesis from glycine is also accelerated when the protein content of the diet is high. Therefore appropriately planned low-purine diet ultimately contributes to decrease gout attacks and maintain general health. Although most patients with gout eventually require long term medical treatment, patients with asymptomatic hyperuricemia should start lowering blood urate levels by changes in their diet or lifestyle.

## Dietary recommendations

- Limit intake of food high in purine. Foods that contain more than 200mg purine per 100g of food are considered high and should be eliminated. Organ meats such as liver, heart, kidney and brains, anchovies, sardines, meat extracts and gravies should be avoided. Excessive intake of foods with medium purine content should also be restricted. Amount of protein in the diet regime should not exceed 1g/ kg ideal body weight per day or does not exceed 90g of meat per meal.

## GOUT & LOW PURINE DIET

- Maintain adequate carbohydrate intake to prevent tissue catabolism and / or ketosis. The American Medical Association recommends people with gout to eat a diet high in complex carbohydrates, low in protein (15% of calories) and no more than 30% of calories to be contributed by fat and from only 10% of animal fats. Patients are advised to take whole grains, vegetable & fruits. Limit intake of meat and seafood to amounts as prescribed. Patients are also recommended to substitute meat with food high in protein but low in purine level such as egg, egg white and milk.
- Fluid intake should be at least 2-3 liters per day (~ 10 cups) to eliminate uric acid via urine and prevent formation of renal calculi.
- Reduce intake of fat and oil to facilitate excretion of uric acid.
- Eliminate or reduce alcoholic intake, especially beer as beer contains a high amount of purine. Excessive amounts of alcohol may inhibit urate clearance. However, wine may not increase the amount of uric acid in blood as much as other types of alcoholic drinks.
- Maintain or achieve a desirable body weight because excess body weight puts stress on the joints. If weight loss is indicated, it should be gradual as severe energy restriction may increase ketone levels which inhibit uric acid excretion.

Foods can be categorized into 3 groups according to purine contents: 'High', 'Moderate' and 'Low' to facilitate adequate food choice and easy menu planning.

### **High (>200 mg/ 100g serving)**

This category of food should be avoided as much as possible.

Anchovies	Scallops	Tongue	Meat extracts
Sardines	Mussels	Kidney	Oxo / Bovril
Mackerel	Dried shrimp	Heart	Gravies
Fish roe	Oyster	Brain	Yakult
Herring	Goose	Liver	Bran & bran products
Tuna	Liver sausage	Yeast	

### **Medium (75-200mg/ 100g serving)**

This category of food can be used according to the diet prescription by dietitian.

Pork	Whitefish	Seaweed	Asparagus
Beef	Eel	Bamboo shoot	Amaranth
Veal	Squid	Kidney Beans	Pakchoi
Lamb	Clam	Lima Beans	Mushrooms
Rabbit	Shellfish	Peas	Chestnuts
Chicken	Crab	Lentils	Lotus seeds
Turkey	Abalone	Tofu	*Nuts
Quail	Lobster & shrimps	Spinach	
Pigeon	Salmon	Cauliflower	
Duck	Tuna fish	Wolfberry leaves	

## GOUT & LOW PURINE DIET

### Low (insignificant amount)

* Cheese of all kinds	Bread	Fruits & Fruit juices	Tea / coffee / cocoa
Eggs	Rice / glutinous rice	Water chestnuts	Sugar / syrups / honey
Milk (low fat)	Noodles / pasta	White fungus	Jam / candies / honey
Ice cream	Sea cucumber	Dried lily	Chocolate
Cereal	Jelly fish	Root vegetables	Carbonated beverages
Oatmeal			

\* High in fat. Should be used with caution if weight control is recommended

### Reference

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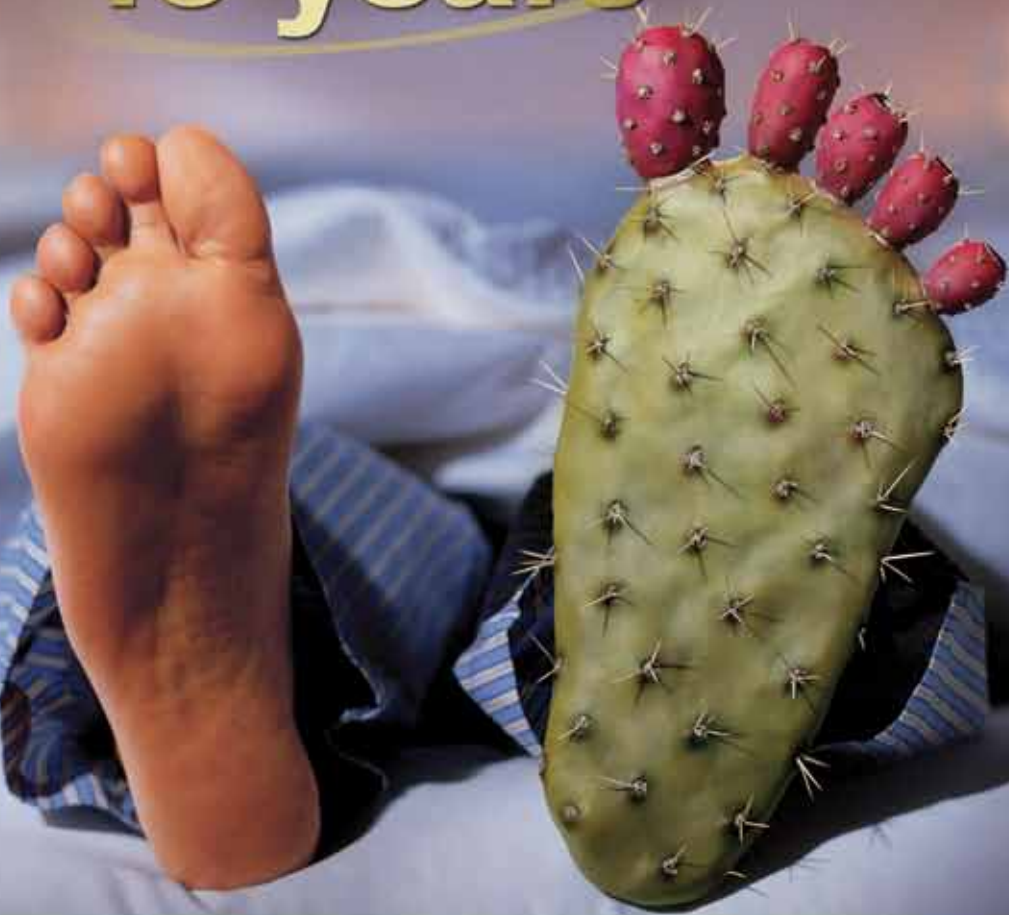
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2. Takano Y et al. *Life Sci* 2005; 76:1835-1847.
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