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Editorial

New therapeutic approach to hyperuricemia and gout in the light of recommendations☆

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The year 2016 may or may not be a pivotal year for gout. The earliest recommendations about the management of gout were issued 10 years ago by the European League Against Rheumatism (EULAR) [1,2] but now exist as a newly revised version that will be published soon. The first recommendations by the American College of Rheumatology were issued only in 2012 [3,4]. In the interval, several national learned societies published recommendations, e.g., the British Society for Rheumatology (BSR) in 2007. The French Society for Rheumatology (SFR) has not developed recommendations about gout, perhaps rightly so. Although inclinations may vary across countries or continents, the only objective differences involve the prevalence of the disease (up to 3.5% in the US, UK, and China versus only 0.9–1.0% in France and Italy) and the drugs available in each country.

The main challenge with recommendations about gout lies, not in their content, but in their implementation. To be effective, recommendations must be disseminated among healthcare professionals, who must then incorporate them into their everyday practice. In other words, healthcare professionals must apply knowledge and practical measures to their management of patients with gout. The development of quality indicators or treatment targets help with the memorization and implementation of recommendations, thereby ultimately improving the quality of care. The objective of this editorial is to summarize the main recommendations and recent revisions and to discuss means of implementing them.

1. Treatment objectives

Gout is characterized by the gradual accumulation in the body of uric acid, which forms crystals of monosodium urate (MSU). Thus, gout is due to an overload of uric acid in the body. MSU microcrystals deposit within and around the joints, entheses, tendons, and ligaments and also, in some cases, the bone and other tissues such as the skin. These clusters of microcrystals, known as tophi, constitute a marker for the severity of this deposition disease.

The serum uric acid level above which crystals form is the saturation point of uric acid, that varies with the temperature, the lowest value being 360 μmoL/L (6.0/mg/dL) [5,6]. This value is therefore the target of uric acid-lowering treatments (ULT). When uric acid levels drop below the saturation point, microcrystals dissolve. The steeper the drop, the shorter the time to dissolution. However, a steep drop is not beneficial as it may result in a gouty attack. Gouty attacks are common early in the treatment and should not be interpreted as indicating a treatment failure. Neither should they be viewed as an adverse effect of ULTs, as they are merely the price of achieving a recovery.

2. European recommendations issued in 2006 and 2014

The EULAR recommendations [1,2] deal with both the diagnosis and the treatment of gout.

2.1. Diagnostic strategies

They are easy to summarize. Podagra is no longer viewed as pathognomonic. In a prospective study, patients seen by primary-care physicians for a first episode of acute arthritis of the first metatarsophalangeal joint were then evaluated by a rheumatologist who performed aspiration of the joint to allow testing for MSU crystals (a procedure described by experts as fairly easy to perform) [7]. Although the primary-care physicians felt that gout was the most likely diagnosis, after a 1-year follow-up only 77% of patients had a definite diagnosis of gout. Thus, the physical assessment by a primary-care physician had high sensitivity (99%) but low specificity (8%).

However, new classification criteria for gout developed by a joint EULAR/ACR task force were reported recently in two very similar articles published in the *Annals of the Rheumatic Diseases* [8] and in *Arthritis & Rheumatology* [9]. They rely heavily on the clinical manifestations of the typical gouty attack, which are described in great detail (Table 1). The criterion for entry into this algorithm is at least one episode of swelling, pain, or tenderness in a peripheral joint or bursa. In patients meeting the entry criterion, the next step

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Table 1
Gout classification criteria issued in 2015 by the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR).

	Categories	Score
Step 1. Entry criterion	At least one episode of swelling, pain, or tenderness in a peripheral joint or bursa	
Step 2. Sufficient criterion (if met, classifies as gout)	Monosodium urate crystals in a symptomatic joint or bursa (i.e., in synovial fluid) or in a tophus	
Step 3. Criteria to be used of sufficient criterion not met		
Clinical		
Pattern of joint/bursa involvement during symptomatic episode(s)	Ankle OR midfoot (as part of monoarticular or oligoarticular episode without involvement of the first metatarsophalangeal joint	1
	Involvement of the first metatarsophalangeal joint (as part of monoarticular or oligoarticular episode)	2
Characteristics of symptomatic episode(s)		
Erythema overlying the affected joint (patient-reported or physician-observed)	One characteristic	1
Can't bear touch or pressure to affected joint	Two characteristics	2
Great difficulty with walking or inability to use affected joint	Three characteristics	3
Time course of episode(s)		
≥ 2 episodes; time to maximal pain < 24 h; resolution in ≤ 14 days	One typical episode	1
Complete resolution between symptomatic episodes	Recurrent typical episodes	2
Clinical evidence of tophus	Present	4
Draining or chalk-like subcutaneous nodule under transparent skin, often with overlying vascularity, at typical locations		
Laboratory		
Serum urate (measured by the uricase method)		
Ideally scored at a time when the patient was not receiving UALD therapy and > 4 weeks from the start of an episode (i.e., during the intercritical period). If practicable, retest under those conditions	< 40 mg/L (< 240 μmoL/L)	−4
	60–80 mg/L (360–480 μmoL/L)	2
	80–100 mg/L (460–600 μmoL/L)	3
The highest value irrespective of timing should be scored	≥ 100 mg/L (≥ 600 μmoL/L)	4
Synovial fluid analysis of a symptomatic joint or bursa (assessed by a trained observer)	MSU negative	−2
Imaging		
Imaging evidence of urate deposition in symptomatic joint or bursa	Present (either modality)	4
Ultrasound evidence of double-contour sign OR dual-energy CT showing urate deposition		
Imaging evidence of gout-related joint damage: conventional radiographs of the hands and/or feet demonstrates at least one erosion	Present	4
A score ≥ 8 points classifies the patient as having gout		
Negative points should be subtracted from the total		
A serum uric acid level between 40 and 60 mg/L is scored as 0		
If polarizing microscopy of synovial fluid from a symptomatic joint or bursa by a trained examiner fails to show monosodium urate (MSU) crystals, subtract 2 points		
If imaging is not available, score this item as 0		
Erosion is defined as a cortical break with a sclerotic margin and overhanging edge. Osteoarthritic changes of the distal interphalangeal joints and a gull-wing appearance are not taken into account		

MSU: monosodium urate; UALD: uric acid-lowering drug; CT: computed tomography.

is assessment of the sufficient criterion, defined as the presence of MSU crystals in a symptomatic joint or bursa or in a tophus. Patients who meet the sufficient criterion are classified as having gout and patients who do not are assessed for a set of clinical, laboratory, and imaging criteria.

An original feature of this classification system is the use of two negative criteria: synovial fluid negative for MSU crystals removes 2 points and an untreated serum uric acid level less than 4 mg/dL removes 4 points. There are no points for a serum uric acid level between 4 and 6 mg/dL. Then as the level rises, 2, 4, or 6 points are added. There are two criteria based on modern imaging modality, namely, ultrasound evidence of a double-contour sign [10] and dual-energy computed tomography showing uric acid deposits. Tophi detected by ultrasonography are not among the criteria. A total score of 8 or more classifies the patient as having gout. A web-based calculator is available at the ACR and EULAR sites and at http://www.goutclassificationcalculator.auckland.ac.nz.

With the clinical criteria alone, sensitivity was 85% and specificity 78%. Adding the laboratory and imaging criteria increased sensitivity to 92% and specificity to 89%. This new classification tool will prove useful for therapeutic trials. It replaces the preliminary criteria issued in 1977.

2.2. Therapeutic strategies

The main therapeutic challenge lies in the presence of comorbidities in most patients with gout [11,12]. These comorbidities may complicate the management of drugs. All the available recommendations support a number of non-pharmacological measures, which are also helpful in the event of diabetes or cardiovascular disease.

2.2.1. Non-pharmacological measures

The changes made in recommendations about non-pharmacological measures are worthy of note. In the 2006 recommendations, these measures consisted of patient information about gout and its treatment, evaluation for comorbidities, weight loss and a decrease in calorie intake, and a restriction in alcohol intake. In 2014, additional recommendations were the modalities of beverages containing high-fructose corn syrup, as