Editorial

Hyperuricemia, Gout, and Lifestyle Factors

Gout, one of the most prevalent inflammatory arthritides, arises from the formation and deposition of monosodium urate (MSU) crystals in and around joints. Hyperuricemia and the saturation of body tissues with urate are essential prerequisites for the development of gout, MSU crystals forming as serum urate (SUA) concentrations rise and exceed the physiological saturation threshold of urate. Recent epidemiological surveys have suggested that the prevalence and incidence of hyperuricemia and gout are rising[1-4]. Frequent suboptimal treatment[5] may also contribute to the prevalence of clinically important, symptomatic gout. Numerous risk factors for the development of hyperuricemia and gout have been described, with the role of dietary and alcohol excess being recognized since ancient times. Historically, epidemics of gout are described in Roman times and in 19th century England that were attributed to a diet excessively rich in purines and alcohol, although the widely recognized association with port is now thought to have been due to lead poisoning that arose from lead contamination of fortified wines[6,7]. More recently, robust prospective epidemiological evidence of the roles played by dietary purines and alcohol in the development of hyperuricemia and gout has emerged. In the Health Professionals Follow-up Study, 47,150 men were followed for 12 years, observing 730 incident cases of gout. The development of gout was associated with alcohol consumption [multivariate relative risk (RR) 1.17 per 10 g increase in daily intake, 95% confidence interval (CI) 1.11–1.22] and intake of meat (RR 1.41, highest vs lowest quintile, 95% CI 1.07–1.86) and seafood (RR 1.51, 95% CI 1.17–1.95)[8,9]. Interestingly, beer conferred greater risk than spirits, whereas consumption of wine and vegetable-purines did not predispose to the development of gout. In a study of 14,809 participants from the Third National Health and Nutrition Examination Survey (NHANES-III), SUA level was found to increase with increasing consumption of meat, seafood, beer, and spirits[10,11]. Similarly, SUA levels were greater with beer than spirits, whereas wine consumption was not associated with hyperuricemia. Further analyses from these studies have suggested that consumption of sugar-sweetened soft drinks and fructose also predispose to hyperuricemia and gout[12,13] and that a number of other dietary factors might protect against their development, for example, vitamin C (see Gao, *et al* in this issue[14]), coffee[15,16], and dairy products[8,11].

In this issue of *The Journal*, Miao and colleagues report the results of an epidemiological survey from China that provides further insights into the effects of dietary factors on the prevalence of hyperuricemia and gout[17]. In this cross-sectional study, 5003 subjects aged between 20 and 80 years across 5 districts underwent a home interview that collected data concerning personal medical history including hyperuricemia and gout, dietary intake within the preceding 7 days, and important comorbidities, and blood samples for measurement of SUA. The prevalences of hyperuricemia and gout in this population were found to be 13.19% and 1.14%, respectively, which are similar to estimates from recent epidemiological studies[18-20]. A previous study undertaken in the same region of China found a higher prevalence of hyperuricemia of 25.3%, yet a lower prevalence of gout of 0.36%[21], providing further evidence that the prevalence of gout may be rising. Higher levels of consumption of meat, fish, seafood, beer, and wine were seen in those with hyperuricemia and gout compared with control subjects. An interesting observation was that the prevalence of hyperuricemia was greater in urban than rural areas. Similarly, both hyperuricemia and gout were more prevalent in the most economically developed city in the region compared with the least developed city. Consumption of meat and seafood but not alcohol was also greater in the city residents compared with countryside residents and in the most economically developed city compared with the least developed. The authors concluded that the prevalence of hyperuricemia and gout is strongly associated with economic development and lifestyle factors.

There are a number of caveats to the study worthy of further discussion. The cross-sectional study design and con-

See Dietary and lifestyle changes associated with high prevalence of hyperuricemia and gout, *page 1859*, and Vitamin C intake and serum uric acid concentration in men, *page 1853*

temporaneous dietary data collection mean that conclusions can only be drawn about the association between current dietary habits and prevalent hyperuricemia and gout. In contrast, the prospective Health Professionals Follow-up Study assessed exposure to alcohol and dietary factors prior to the onset of incident gout, and hence provides more robust evidence of the importance of lifestyle factors as causative factors in the development of gout. This methodological difference is perhaps less critical for hyperuricemia, where SUA levels are more likely to reflect current dietary habits, in contrast to gout, which usually arises after a sustained period of exposure to a risk factor and associated asymptomatic hyperuricemia. Another key difference is the relative size of the study populations, with only 57 subjects having gout compared with 730 in the Health Professionals Follow-up Study. Unexpected findings of the study were that only 2 subjects in the whole population were taking a diuretic, and that all of the subjects with hyperuricemia and/or gout had normal blood urea nitrogen and creatinine, which seems unusual in a study of hyperuricemia and gout.

Despite these caveats, the results of this study pose interesting questions concerning the contribution of lifestyle factors to the epidemiology of hyperuricemia and gout. The observation that urban areas and more economically developed cities had both the highest prevalence of hyperuricemia and gout and the highest levels of consumption of meat and seafood raises the possibility that variations in the prevalence and incidence of gout might be attributable to lifestyle factors. It then follows that the recent increase in the prevalence and incidence of gout might be explained by similar increases in adverse lifestyle habits such as purine-rich diets and excess alcohol consumption[22]. Clinical manifestations of gout show considerable variation, and the reasons why certain patients develop more severe disease are not well understood. It is possible that persistence of adverse lifestyle factors potentiates hyperuricemia and leads to more problematical clinically significant gout. These issues are worthy of further investigation in larger prospective studies.

The natural sequel of the findings of these epidemiological studies is the assumption that modification of adverse dietary habits will be advantageous in the treatment of hyperuricemia and gout. Indeed, recent evidence-based recommendations for the management of gout highlight the importance of a triumvirate of lifestyle modification, which includes weight reduction in addition to modification of intake of dietary purines and alcohol[23,24]. Unfortunately, it appears that advice to modify such risk factors is infrequently offered to patients[5,25]. However, this recommendation is based mainly on extrapolation from epidemiological studies, and there have been relatively few studies of lifestyle modification for the treatment of hyperuricemia and gout. Uncontrolled studies demonstrate reduction in SUA following alcohol restriction and weight reduction in patients with gout[26] and following a low-purine diet in hyperuricemic subjects[27]. In a pilot study in 13 obese men with symptomatic gout, weight loss as a result of restricted carbohydrate intake and increased proportional intake of protein and unsaturated fat reduced both SUA levels and the frequency of acute attacks[28]. While the observation that target urate levels are infrequently reached with urate-lowering therapies in primary care is undoubtedly due, in part, to suboptimal dosing[5], the likelihood remains that the efficacy of urate lowering measures is diminished by persistent unmodified lifestyle factors. There is a need for research studies investigating further the efficacy of lifestyle modification, the influence of adverse life factors on the success of urate-lowering therapy, and how best to implement successful lifestyle modification in patients with hyperuricemia and gout.

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