Editor, *Rheumatology*
RE: New insights into the epidemiology of gout

Editor,

The recent article by Michael Doherty [1] lists three dietary risk factors for gout: higher intakes of red meat, beer and fructose. Benjamin Franklin's celebrated meaty diet and love for Madeira wine [2] aptly illustrates a historical recognition of meat and alcohol as legitimate risk factors for gout. The addition of fructose to this list by Doherty is completely unwarranted, however, because it lacks adequate justification and proof in real-world diets.

First, all USDA-defined macronutrient categories — added sugars, added fats, flour/cereal, vegetables, fruit, dairy and milk/eggs/nuts — have increased more or less in parallel with total energy intake (+24%) since the introduction of high fructose corn syrup (HFCS) 35 years ago [3]. Because all macronutrients contribute energy to the diet, a focus on fructose is misleading because it cavalierly dismisses other macronutrients and misses the greater issue that we eat too much of *everything*.

Second, Doherty's speculation about fructose differences in sucrose vs. HFCS is completely unnecessary and ignores mainstream consensus on sugars. There is now general agreement that sucrose and HFCS are metabolically equivalent among scientific experts, expert scientific panels like those convened by the Center for Food Safety and Nutrition (University of Maryland) [4], Experimental Biology (FASEB) [5] and ILSI-USDA [6], and professional organizations like the American Medical Association [7] and the American Dietetic Association [8]. Recent human studies by Melanson [9], Angelopoulos [10] and Havel [11] directly comparing HFCS and sucrose for metabolic markers of obesity confirm no substantive differences in serum glucose and insulin, ghrelin and leptin, hunger and satiety, triglycerides and uric acid.

And finally, experimental data used in support of fructose as a dietary risk factor is inappropriately applied from extreme diets that do not resemble real-world human exposures. Rat studies commonly use fructose at 60-66% of energy [see ex., 12]; human studies use fructose at 20-50% of energy [13,14]. The most recent estimate for fructose intake [15] reports the mean whole-population value at 9.1% of energy and the 95th percentile (males and females, 19-22 y) value at 16.1% of energy. Human studies thus test unrealistic fructose levels, while animal studies use highly exaggerated exposures that not only don't remotely resemble human intakes, but may well approach toxic conditions. It is likely that the experimental diet is itself inducing a variant of normal human metabolism not in evidence at typical fructose levels.

At the current state of scientific understanding, it is decidedly premature and unjustified to include fructose on the same list of dietary risk factors for gout as red meat and beer.

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