Editors’ Note: Dr. Mauskop reviews the literature on the use of butterbur extract for migraine prophylaxis and concludes that it has the potential for serious toxicity. Authors Holland et al. disagree with Dr. Mauskop’s interpretation. Dr. Sethi, in response to Drs. Stone and Edwards’ “Trick or treat? Showing patients with functional (psychogenic) motor symptoms their physical signs,” airs the difficulty, which most neurologists can relate to, of discussing a psychogenic diagnosis with a patient. Dr. Tfelt-Hansen calls attention to an error in the classification of evidence in the American Academy of Neurology guideline on episodic migraine prevention by Silberstein et al. The authors concur and an erratum appears in this issue.

Megan Alcauskas, MD, and Robert C. Griggs, MD


Alexander Mauskop, New York: Holland et al. consider Petasites (butterbur) to have “established efficacy” for the prophylactic treatment of episodic migraines. The first of 2 studies of butterbur involved 60 patients and 100 mg of butterbur. Review of that study’s data concluded that “The original protocol and analysis had a number of major shortcomings.” The second study, in which this author participated, involved 245 patients and showed that a daily dose of 100 mg of butterbur extract was ineffective, while 150 mg was effective. However, the main concern is not efficacy, but safety. The butterbur extract used in these clinical trials has since been reformulated and is no longer available in Germany, where it is manufactured. Unlike the United States, Germany regulates herbal products and requires them to undergo teratogenicity and carcinogenicity studies. The original butterbur extract did pass those tests, but the manufacturer did not repeat them for the new formulation. Butterbur contains pyrrolizidine alkaloids, which are hepatotoxic and carcinogenic. In view of the lack of regulation of herbal products in the United States and because of the potential for serious toxicity, none of the butterbur extracts—including the one manufactured in Germany—can be safely recommended to our migraine patients.

Author Response: Starr Holland, Savannah, GA; Stephen D. Silberstein, Philadelphia; Frederick Freitag, Dallas; David W. Dodick, Scottsdale, AZ; Charles Argoff, Albany, NY: We appreciate Dr. Mauskop’s concerns regarding the safety of Petasites (butterbur) extract that was reviewed in the American Academy of Neurology guideline for complementary preventive migraine treatments in adults. Dr. Mauskop is correct that the formulation Petadolex, which was the formulation of Petasites subjected to controlled clinical trials examined for the guideline, underwent reformulation and that the current formulation is not registered in Germany. However, the formulation that was used in the clinical trials reviewed for the guideline was the replacement formulated in 1988 (Reiter Rittinghausen, MD, CEO, Weber and Weber GmbH and Co., personal communication). The new formulation was evaluated for pyrrolizidine alkaloids and none were found, as was recently confirmed by Avula et al. This study demonstrated that the Petadolex formulation of butterbur extract was among only 7 of 21 formulations that contained the active petasins in the amounts stated in the label. In addition, from a safety perspective, these same authors found no detectable toxic pyrrolizidine alkaloids in the Petadolex samples. This reinforces the efficacy and safety of the recommendation for the butterbur extract. Indeed, as Dr. Mauskop suggests, there are continued concerns regarding the use of natural products and the lack of consistent, regulatory review of these products that are openly marketed in the United States.

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Author Response: Jon Stone, Edinburgh; Mark Edwards, London:
In our article, we suggested that being transparent with patients may, among other things, help in persuading them of the diagnosis, and the potential reversibility of their symptoms. While this may be true, my personal experience of patients with nonepileptic events has varied. Many patients feel vindicated when shown the nonepileptic event captured on video-EEG. Their complaints finally stand justified in the eyes of their doctor and loved ones. That said, patients rarely if ever completely stop having their typical events after this. In a few patients, the event frequency may exacerbate and new events with previously unreported clinical semiology may be reported. These patients are frequently lost to follow-up only to seek medical care in another institution under another physician where invariably diagnostic workup is repeated. This also adds to health care costs to society as a whole. Explicitly telling patients that their events are psychogenic in origin has its own challenges. The discussion is invariably rough for the physician—sometimes heated—and the psychogenic explanation is not readily accepted by most patients. I tell my patients that there is no organic basis to the symptomatology and advise that underlying psychogenic factors need to be aggressively addressed rather than say that the events are real, not imagined, or “all in the mind.”

Editor’s Note: A correction appears in this issue, on page xx.

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*Neurology* 2013;80;868-869
DOI 10.1212/WNL.0b013e318287d94b

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