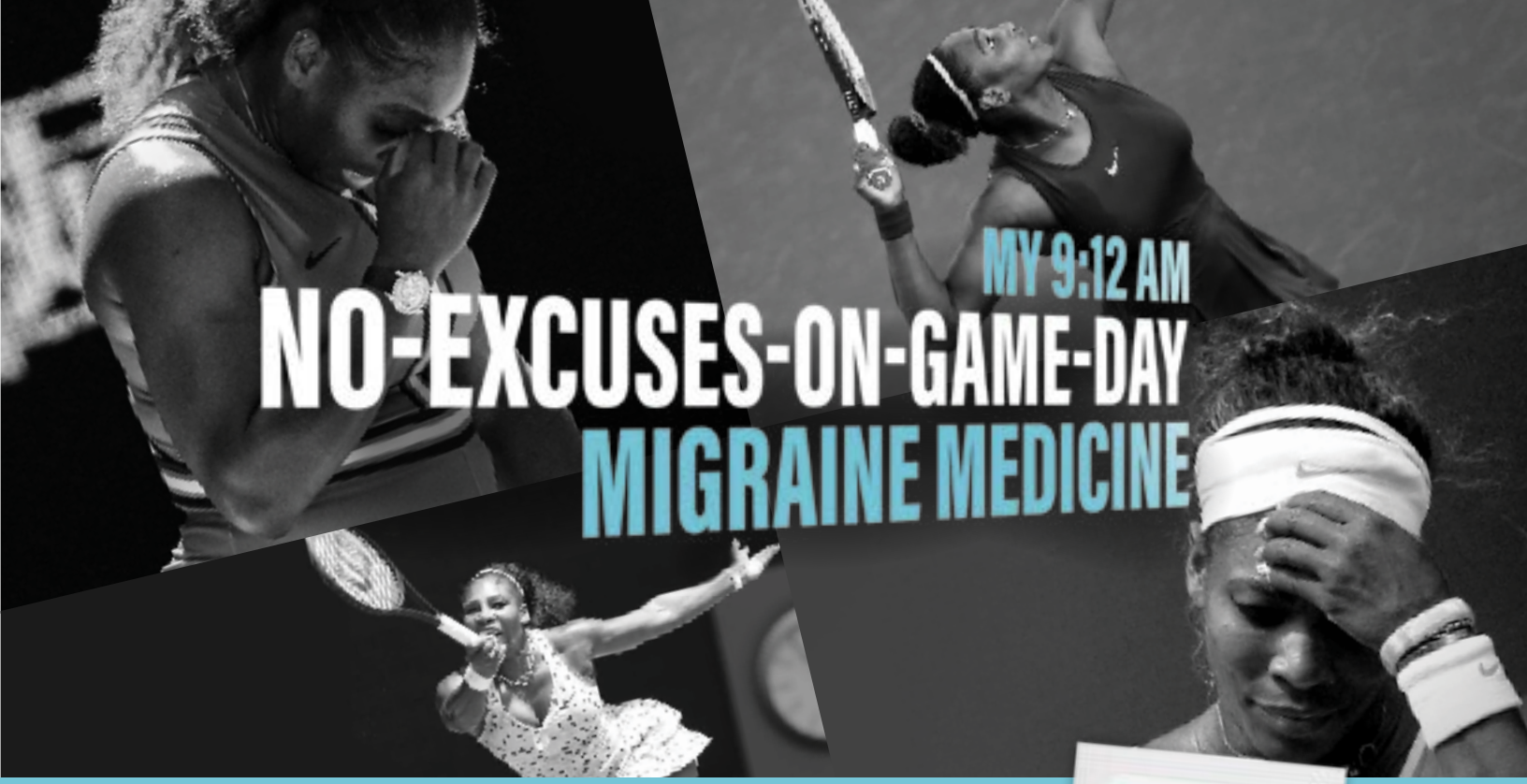
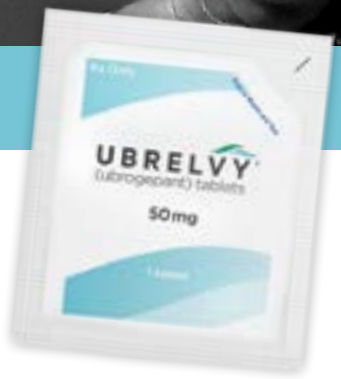


UBRELVY CAN QUICKLY STOP MIGRAINE IN ITS TRACKS.



When I took UBRELVY for the first time, I forgot I even had a migraine.
—Serena Williams

One dose of UBRELVY works fast. In clinical studies, many people had pain relief and some even had pain freedom within 2 hours. Unlike older medicines, UBRELVY directly blocks CGRP protein, which is believed to be a cause of migraine.

UBRELVY. The migraine medicine for anytime, anywhere migraine strikes, without worrying if it's too late to take it or where you happen to be.*

*People took UBRELVY within 4 hours of a migraine attack.

Eligible patients may pay as little as $0 a month†

ASK YOUR HEALTHCARE PROVIDER ABOUT UBRELVY.

LEARN MORE AT **UBRELVY.COM**.

What is UBRELVY® (ubrogepant)?
UBRELVY is a prescription medicine used for the acute treatment of migraine attacks with or without aura in adults. UBRELVY is not used to prevent migraine headaches.

IMPORTANT SAFETY INFORMATION

Who should not take UBRELVY (ubrogepant)?
Do not take UBRELVY if you are taking medicines known as strong CYP3A4 inhibitors, such as ketoconazole, clarithromycin, itraconazole.

What should I tell my healthcare provider before taking UBRELVY?
Tell your healthcare provider about all your medical conditions, including if you:
- Have liver problems
- Have kidney problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Your healthcare provider can tell you if it is safe to take UBRELVY with other medicines.

What are the most common side effects of UBRELVY?
The most common side effects are nausea (4%) and sleepiness (3%). These are not all of the possible side effects of UBRELVY.

You may report side effects to the FDA at 1-800-FDA-1088.

Please see full Patient Information on the following page.

†Patient out-of-pocket costs may vary. Terms and Conditions apply. This offer is only valid for commercially insured patients. Offer not valid for patients enrolled in Medicare, Medicaid, or other federal or state healthcare programs. Please see full Program Terms, Conditions, and Eligibility Criteria at UBRELVY.com.

UBRELVY® (ubrogepant) tablets

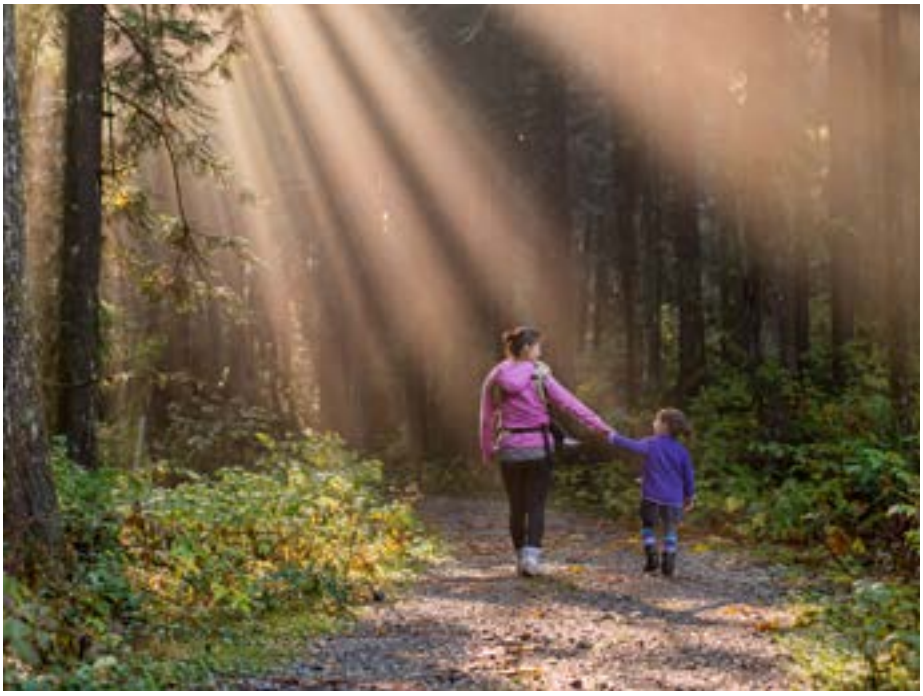
THE ANYTIME, ANYWHERE MIGRAINE MEDICINE

Non-Pharmacologic Treatment of Migraine

*What **YOU** can do to reduce your migraine*

Many of the newer medications for prevention of episodic migraine, suppression of chronic migraine and treatment of acute migraine headache are thankfully both safe and typically well tolerated. Of the newer medications for migraine prevention or suppression, onabotulinumtoxinA (BotoxA) and the anti-CGRP monoclonal antibodies (mabs) are particularly "clean" in terms of their low likelihood of producing side effects; approximately 1% of Botox treatments may be complicated by transient and reversible droop of an eyelid, and the mabs occasionally may cause an injection site reaction or, less often, severe constipation, but when compared to older medications such as topiramate, amitriptyline and beta blockers (eg, propranolol), their side effect profiles are far more favorable. Much the same can be said for the newer medications for acute headache treatment. Ubrogepant (Ubrelvy), remigepant (Nurtec), and, in particular, lasmiditan (Reyvow) are somewhat more prone to cause side effects, but for patients who either fail to respond to or cannot tolerate the triptans or nonsteroidal anti-inflammatory drugs (NSAIDs), they often represent a very effective and well-tolerated alternative.

Even so, many migraineurs would prefer to avoid taking medication altogether, and even those more inclined to take medication can achieve a greater reduction in headache and migraine burden if their treatment strategy includes non-pharmacologic components. We broached this topic in a previous issue, but here we will try to offer more detailed and specific suggestions.



Triggers

Some options for non-pharmacologic management of migraine are listed in the Table. Avoidance of migraine attack triggers is strongly advocated by many headache subspecialists, but to a certain extent such management appears inherently obvious. If ingestion of red wine consistently produces a severe migraine headache within 30 minutes of ingesting that wine, then it's probably wise to skip the wine. If it does so less consistently or the triggered headache often is less intense, then drink your wine and take your chances. On the other hand, if the trigger is more difficult to avoid and cannot be controlled (for example, a change in barometric pressure), short of immediately flying to a destination with friendlier weather, about all you can do is be prepared and keep whatever medication(s) you use for acute migraine treatment close at hand.

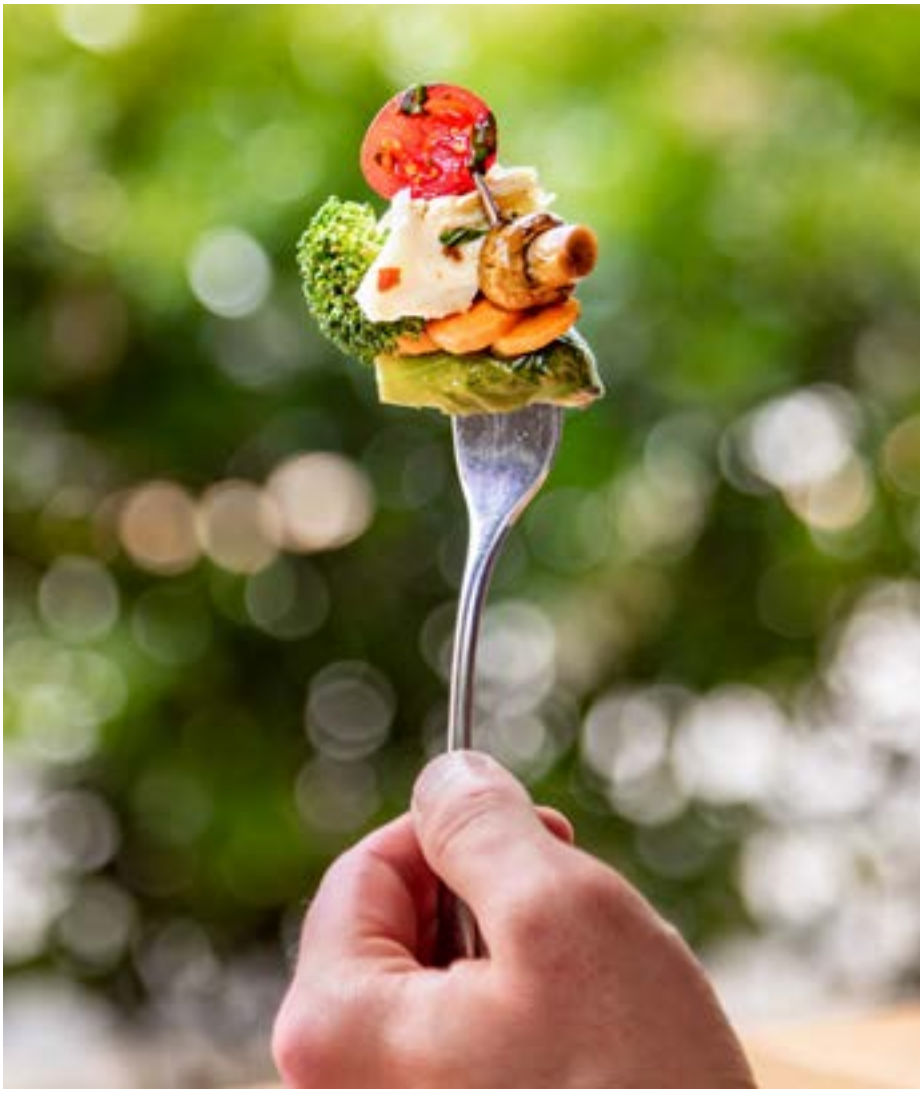
Menses poses a similar problem. Migraine thrives on change, and the rapid decline in estrogen level occurring with the onset of menses can serve as a potent migraine trigger. About two-thirds of actively cycling female migraineurs experience a menstrual aggravation of their migraine, and much as is the case with weather changes this is not necessarily an easy trigger to be avoided or controlled. Elimination of menses by use of an active oral contraceptive throughout the month or use of a hormone-secreting IUD may be quite helpful in controlling or even eliminating menstrually-associated migraine, but this is not necessarily an acceptable alternative for many women and may be medically contraindicated in others.

Diet

What about other triggers/aggravators that lack such a clear temporal link and thus may be less easily identified? For example, does gluten aggravate migraine? How about dairy products? Are food elimination diets a reasonable treatment intervention for migraine stabilization? Do there exist effective "migraine diets"? Difficult to say. Any answer to these questions almost inevitably provokes dissension…a sure-fire indication that no one knows "the answer". There are those who enthusiastically extol the virtue of their gluten-free diet and speak of the tremendous improvement in migraine control that occurred when they eliminated gluten or another component common in American diets, but the evidence to support the value of elimination diets is conflicting. Again, because migraine thrives on change, perhaps the best dietary advice to the migraineur who desires a lower migraine burden is to eat healthfully and to do so with meals that are regularly spaced. If you want to try a food elimination diet, then by all means do so…but stick to dietary plans that are nutritionally sound and do not involve prolonged fasting or other techniques that promote either dehydration or irregularly spaced meals.

Sleep

Much the same can be said for sleep hygiene. Avoid sleep deprivation or its opposite, oversleeping; do not try to make up for a week of late nights/little sleep by oversleeping on the weekend. If you have a sleep disorder such as sleep apnea, a common and well-recognized aggravator of migraine, seek treatment for the disorder.



Exercise

It's difficult to overestimate the value of aerobic conditioning towards maintaining optimal brain and systemic health. Numerous studies have demonstrated the effectiveness of regular aerobic exercise in reducing migraine burden. If you are not already committed to an aerobic conditioning program, start one, pick something that will not bore you to death and begin slowly, gradually increasing your activity. If you have no significant heart disorder or other medical contraindication to vigorous exercise, start with an activity that increases your resting heart rate by at least 50% and maintains it at that level for at least 20 minutes sustained. Do this at least three times per week. At first, simply walking on level ground may be sufficient to increase your resting pulse rate of, say, 80, to 120 or more, but you will find after a few weeks that it may require walking up an incline to achieve that same effect. The good news: this indicates you are becoming aerobically more fit and improving your cardiovascular status. More to the point, you also may begin to experience a progressive reduction in migraine burden.

"Alternative" therapies

Migraine patients often ask their doctors about the potential value of acupuncture, chiropractic medicine, craniosacral therapy or other therapies involving active or passive physical manipulation. An "MD" (doctor of medicine) is trained in what is termed *allopathic* medicine, and very few allopathic physicians have a clear understanding of – let alone training in - chiropractic medicine, traditional Chinese medicine or other alternative forms of medical care. As such, allopathic physicians are probably better off telling patients that they simply cannot provide an informed opinion regarding the value of an alternative means of managing their headache disorders and to limit their comments to expressing concern that the patient not expend an exorbitant amount of money on such therapy if they do not

feel they are receiving significant benefit. Many of my own patients have reported improvement from such therapy, and many others have reported no improvement. I generally advise my patients that there does not exist in the peer-reviewed allopathic medical literature convincing evidence to establish or refute a role for these therapies in treating migraine and, in particular, explain that with the exception of avoiding forced neck manipulation* I do not hold any particular opinion regarding the safety or value of chiropractic intervention. [*while such manipulations are performed frequently and without any adverse result, there are reports that link this particular procedure with the production of trauma to major arteries in the neck that supply blood to the brain and consequent stroke).

Massage

In my own management of patients, and even before the term "evidence-based medicine" came into vogue, I always have felt it important to distinguish between what I *feel* to be true and what I *know* to be true. For example, I know from the results of well-designed and scientifically rigorous clinical research studies that the serial injection of onabotulinumtoxinA is safe and effective for suppressing chronic migraine. On the other hand, I feel (but do not know) that virtually all of us would benefit from massage therapy received on a regular basis. For one of my previous headache clinics that was part of the University of Alabama healthcare system I frequently referred patients to massage therapists based in the clinic, especially those patients whose chronic migraine or chronic tension-type headaches sounded by history to have a prominent musculoskeletal component and whose exams were notable for obvious spasm in the muscles of the neck and shoulders. While many of the patients so referred expressed to me their conviction that the regular massage therapy they received was instrumental in reducing their headache burden and associated symptoms, such anecdotal reports are obviously not equivalent to a prospective, randomized trial required to provide any given therapy with a viable scientific evidence base.

I continue to feel that regular massage therapy would be beneficial for many of my headache patients, but the main factor prohibiting me from greater use of that intervention is financial. In most cases, about the only way to achieve authorization for massage therapy by an insurer is to refer the patient to a conventional physical therapist and specifically request a treatment such as deep tissue massage. Even then, however, the treatments may be too infrequent or the course of therapy too short to provide any enduring benefit.

"Non-pharmacologic" pharmaceuticals

While none of the "supplements and nutraceuticals" commonly used to treat migraine are really any less "non-pharmacologic" than Excedrin or even a prescription medication, many patients are more comfortable using this class of medications for migraine control. While a number have been touted for their effectiveness in treating migraine, those which possess at least a reasonably sound scientific evidence base include vitamin B2 (riboflavin), coenzyme Q 10, *Petasites* (butter-burr extract) and magnesium. For a more detailed and excellent description of these medications and the non-pharmacologic interventions discussed previously, I strongly recommend a migraine "self-help" manual, The End of Migraines, authored by Dr. Alexander Mauskop.

Stress reduction

Returning to the "holistic" headache clinic which my colleagues and I established in Alabama, we retained there and frequently utilized the services of a clinical psychologist who was particularly adept at what in those years was termed "self-hypnosis" and which now more generally is included under the rubric of "relaxation techniques". Once again, taken as a group migraineurs consistently rank "stress" as their top migraine trigger/aggravator, and a host of interventions – meditation, cognitive behavioral therapy (CBT), conventional psychotherapy, yoga and many more – may assist in reducing stress and associated migraine burden.

Devices

There currently are four devices which have been approved by the FDA for migraine treatment. All involve electrical stimulation at a relatively low level of intensity, all are safe and all have been demonstrated to be effective for treatment of acute migraine headache.

The first to arrive on the scene was the Cephaly device, and it is applied to the forehead to produce mild electrical stimulation to the nerves in that region. The smartphone-controlled Nervio device provides electrical pulses to the upper arm, and the intensity of the pulses may be adjusted according to your degree of comfort; it is approved for use by adolescents as well as adults. The Relivion MG device wraps around the head, delivers electrical stimulation to that area and may be used with a smartphone app to generate treatment and response data that may be shared with your HCP. Lastly, gammaCore is a handheld device that delivers low level electrical stimulation to the vagus nerve in your neck. It is notable for having FDA approval as a treatment for both acute migraine headache and for migraine prevention. While none of these devices is "indicated" for use in pregnancy, many clinicians advise their patients to try one of them as a substitute for migraine drug therapy during attempted conception or pregnancy.

You can see that much of what is suggested here for non-pharmacological management of migraine in some way involves stress reduction. Aerobic conditioning, avoiding sleep deprivation, eating healthfully and at regular intervals and, obviously, specific interventions such as meditation and CBT all help to reduce stress.

In my career, I've lived and practiced medicine both in a beachside community heavily populated by dedicated surfers and, subsequently, in a crowded, traffic-congested metropolitan blob in the lower Northeast heavily populated by hyperintense overachievers. Often, I've wondered how much one's environment may influence the prevalence of migraine within a population or, perhaps more accurately, the degree of migraine burden experienced by that population.

Both in the peer-reviewed medical literature and in a previous issue of this magazine, I've reported upon the high volume of chronic tension-type headache patients I have seen in my Pennsylvania Avenue clinic as opposed to my previous clinics based in southern California and Alabama. To my knowledge, no one (including me) has systematically assessed the migraine burden afflicting the general population in these widely diverse areas, but I would hypothesize that living in a metropolitan area that requires three hours of commuting daily is associated with a much higher burden than living on the beach in San Diego, biking to work and surfing at sunset.

Interestingly, and in line with previous comments regarding migraine's affinity for sudden change, release from stress can be as much of a trigger/aggravator as is experiencing chronic stress. I had a good friend in San Diego, a busy orthopedic surgeon who routinely worked as much as 80 hours per week. At intervals he and his movie star beautiful wife would fly off to Switzerland or some other such exotic locale for a long weekend, and when he returned, he invariably would complain to me that he spent the entire vacation in their darkened (and very expensive) hotel room miserable with acute migraine. *Why,* he would ask me, *do I have no problem with migraine when I'm working so hard and never sleeping and then suffer from terrible migraine when I take a few days off?* Even allowing for the triggers of air travel and across time zones, the answer is that for him a abrupt reduction in stress served as a potent migraine trigger.

Unfortunately, few of us can afford the luxury of moving from a high stress environment to enjoy the laid-back lifestyle offered by a beachside surfing community in San Diego, Sayulita (Mexico) or coastal Portugal. Even so, to minimize migraine burden (and to enhance our humanity) we should do what we can to insulate ourselves from the stress inherent within the places we live and work. As the surfers say, life is a short ride. Make it a good one.

- JFR

Table

Assorted Non-Pharmacologic Treatment of Migraine