

FOR THOSE WHO CHOOSE TO LIVE WELL DESPITE MIGRAINE

# Migraineur

MAGAZINE

Issue 01 | Winter 2016/2017



## THE TRUTH ABOUT TRIGGERS

Plus

THE  
GENETICS  
OF MIGRAINE

TAKING  
YOUR MIGRAINE  
SKIING

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# LETTER FROM THE EDITOR



In this and subsequent issues we will attempt to dispel the many myths that surround migraine...



Welcome to the inaugural issue of a magazine that is intended to both educate and entertain the many millions of Americans who suffer from migraine. As a physician and fellow migraineur who has treated thousands of migraine patients, conducted research in the field and assisted in the development of virtually every new treatment for headache since the emergence of sumatriptan (Imitrex) in the late '80s, I have a particular allegiance to our readership.

Migraine is a decidedly odd malady. Although rarely life-threatening, it is frequently life-altering. Migraine imposes a tremendous physical, financial and psychosocial burden upon our society, and for those afflicted it may persist, throughout most of their lives.

While common, the disorder is poorly understood both by the public and by healthcare providers, a situation that results all too often in a failure to seek medical care or medical mismanagement and consequent patient frustration when such care is sought.

In this and subsequent issues we will attempt to dispel the many myths that surround migraine, acquaint you with the tremendous strides that have been made in understanding and treating the disorder and, most important, offer some guidance as to how you, the migraineur, may enjoy life more fully and control your headache disorder more effectively.

*John F. Rothrock, MD*

Editor in Chief

## ON THE COVER

Northstar Nordic  
Park, Lake Tahoe, CA

**Diane Rothrock, cross-country  
skiing enthusiast, triathlete and  
migraineur, pauses on a trail  
high in the Sierra Nevada.**

# Migraineur

## Editorial Board Profile

Dr. Rothrock received his medical degree from the University of Virginia and completed his internship and residency training in Neurology at the University of Arizona.

In 1983 he joined the Neurosciences faculty at the University of California, San Diego (UCSD), where he established and directed the UCSD Stroke Center and, subsequently, the UCSD Headache Center. He and his UCSD colleagues assisted in the development of such medications as injectable sumatriptan (Imitrex) for acute migraine treatment and divalproex sodium (Depakote) and topiramate (Topamax) for migraine prophylaxis.

From 2006 to 2012 he served as professor, vice chair and medical director of Neurology at the University of Alabama/Birmingham (UAB). Dr. Rothrock continued his clinical research at UAB in the area of migraine, assisting in the development of onabotulinumtoxinA (BotoxA) for chronic migraine.

Since July 2015 he has served as professor and vice chair for the department of Neurology at the George Washington University School of Medicine. With his colleagues locally, nationally and internationally he is working to develop new treatments for migraine and other headache disorders.

Dr. Rothrock has been listed in America's Top Doctors and Best Doctors in America in each of the past 15 years. He has been cited in Men's Health and Women's Health magazines as one of the 20 top neurologists in America.

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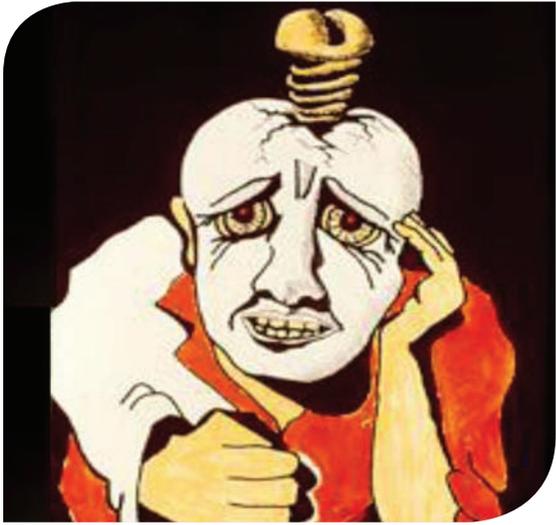
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# MANAGING YOUR MIGRAINE

Here is information that may help you on your journey towards “headache free or nearly so”

## 1 Migraine Tip of the Month: Headache Diary

Individuals who plan to seek medical attention for their migraine should consider keeping a headache diary for a month or two prior to their evaluation. It can be surprisingly difficult to answer the question: “How bad are your headaches?”, and having some objective evidence in hand may be of great assistance to your doctor in working with you to develop an appropriate treatment plan.

Your headache burden is a blend of frequency and severity, often aggravated by varying degrees of nausea, light/sound sensitivity, aura and a host of other unpleasant symptoms. Paradoxically, your efforts to relieve that burden may in fact cause it to increase. Specifically, overuse of medications intended to treat acute headache may produce a gradual worsening of your headache disorder. Although commonly known as “rebound”, a more accurate name for this process is “medication overuse headache” [\[link\]](#).

*a journey of a thousand miles begins with a single step*

THIS INFORMATION MAY SHORTEN YOUR JOURNEY

## 2 Migraine Treatment of the Month: Botox!

In October 2010 the FDA approved onabotulinumtoxinA (BotoxA) for the treatment of chronic migraine, a particularly malignant form of migraine estimated to afflict as many as 1 in 50 Americans. “Chronic” migraine implies that you have a history of typical episodic migraine but that but your previously infrequent headaches have increased to the point where you are experiencing bothersome head pain at least 15 days per month.



Despite the prevalence of chronic migraine, the enormous financial cost to society it imposes and the tremendous degree of pain and suffering it inflicts, the disorder often is underdiagnosed, misdiagnosed and either inadequately treated or not treated at all...simply “lived with”.

Healthcare providers—even specialists trained in handling neurologic disorders—frequently characterize chronic migraine as “sinus headache”, chronic tension-type headache, “mixed” headache (ie, co-existing primary headache disorders: a combination of chronic tension-type headache and episodic migraine) or headache attributable to “stress”, chronic anxiety or depression. This is unfortunate. At worst, such misdiagnosis can lead to the application of medical therapies that are unnecessary, costly, potentially dangerous and of no value in reducing the patient’s headache burden.

The case that follows vividly illustrates these points.

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### Amy is a 33 year old Attorney who lives in Alexandria, VA and works across the Potomac in Washington, D.C.

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Amy is a 33 year old attorney who lives in Alexandria, Virginia and works across the Potomac in Washington, D.C. She is an attractive, personable and highly articulate individual who somewhat ruefully relates her all too familiar story. Amy began experiencing migraine headaches shortly after her first menses at age 13. Over the next 10 years her headaches would recur now and then, usually in association with menses. With law school, however, came a significant increase in her level of chronic stress, and the increased stress was paralleled by a change in her headaches. Her previously paroxysmal “now and



then” headaches became increasingly pervasive, and while her headaches often were not as severe as those of earlier years, they were occurring more days than not. Punctuating her frequent lower intensity headaches she continued to have attacks of her “usual migraine” several times a month.

The chronic headaches interfered with her ability to concentrate on her studies, and the superimposed attacks of her “usual migraine” caused her to miss classes and group study sessions. She found herself falling ever further behind at school, her stress consequently increased and she eventually began experiencing headaches on a daily basis.

Believing her headaches to result from stress and associated anxiety, her primary care provider prescribed escitalopram (Lexapro), a selective serotonin re-uptake inhibitor (SSRI). That drug’s only effect was to eliminate completely her already waning libido, leading to estrangement from her boyfriend and yet more stress.

She was referred to a neurologist who prescribed amitriptyline (Elavil), an older antidepressant also widely used for prevention of migraine and tension-type headaches. This drug caused Amy to gain weight and to experience dry mouth and

daytime sedation. Her headaches persisted unchanged.

At that point, having dropped out of law school, broken up with her boyfriend and moved back home to live with her parents, Amy sought a second neurologic opinion. The second neurologist diagnosed her as having chronic migraine, prescribed various medications for her to use for acute headache treatment and began serial BotoxA injection therapy.

Within three months and following 2 sets of BotoxA injections, Amy had experienced a 50% reduction in her headache burden. Within another 6 months and following a total of 4 sets of injections she was experiencing only occasional “headache days”, and her headaches on those days were controlled with the medications she had been prescribed for acute treatment. After a total of 6 sets of BotoxA injections administered over a period of 15 months, Botox therapy was discontinued. Six months following this she continues to do well, with infrequent headaches and no need for migraine prevention therapy. She is about to graduate from law school, and she is living-happily-with a new boyfriend. The total “direct” (medical) cost of Amy’s headache management prior to the diagnosis of chronic migraine exceeded \$250,000. The “indirect” costs (ie, those resulting from her pain and emotional suffering)

are more difficult to calculate. Amy's case is in no way unusual. Every day, in subspecialty headache clinics across America and globally, healthcare providers encounter many thousands of patients with stories no less compelling than Amy's. Particularly disheartening in Amy's case is that her experience occurred in a major metropolitan center chock-full of well-trained and generally knowledgeable physicians and physician specialists.

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### BotoxA is currently the only therapy specifically approved by the FDA for the prevention/suppression of chronic migraine...

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BotoxA is currently the only therapy specifically approved by the FDA for the prevention/suppression of chronic migraine, and with the exception of topiramate (eg, Topamax), the only treatment with a solid base of scientific evidence to support its use in treating this disorder. Studies comparing the two therapies—BotoxA and topiramate—have suggested they are more or less equally effective in treating chronic migraine but that in part because of its more appealing side effect profile patients prefer BotoxA. A large national study intended to settle the issues of relative effectiveness and patient preference presently is being conducted ([www.clinicaltrials.org](http://www.clinicaltrials.org)).

Botulinum toxin is naturally produced by a bacterium of the *Clostridium* species, and human ingestion of large amounts of the toxin can produce botulism, a serious and potentially fatal acute neurologic illness involving diffuse muscle paralysis. The dose of botulinum toxin used to treat chronic migraine is much, much lower than that involved in cases of botulism, and to date there have been

no reports of systemic spread of the toxin causing clinically significant neuromuscular disease when BotoxA has been used to treat headache.

The first hints that BotoxA might convey a beneficial treatment effect on migraine came primarily from two sources. First, there came a rising tide of anecdotes that individuals with migraine who were receiving BotoxA injections for cosmetic purposes were reporting reductions in their headache burden. Second, patients with receiving BotoxA injections for their painful dystonias (ie, involuntary, sustained contraction of large muscles or groups of muscles) reported a reduction in their dystonia-related pain even before there occurred any appreciable improvement in their dystonias.

The specifics of how Botox suppresses chronic migraine remain unclear, but the effect does not appear to be mediated through paralysis/relaxation of the muscles injected. In one large national study, BotoxA was safe but therapeutically ineffective in treating chronic tension-type headache. Instead, BotoxA appears to have a direct anti-nociceptive (“anti-pain”) effect that in chronic migraine involves “short-circuiting” the biophysiological pathway that generates the headache disorder.

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### Will I Lose My Wrinkles as Well as My Headaches? Will I Look Like a Freak?

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BotoxA does exert its cosmetic effect via muscle relaxation, and using the toxin to suppress chronic migraine can produce cosmetic changes. On rare occasions, treatment will provoke a transient, reversible drooping of one eyelid or (very rarely) both. More commonly, injection of BotoxA into the muscles of the forehead will result in “smoothing out” of any wrinkles in the area of injection, an effect

that tends to persist for 3 to 6 months. While use of BotoxA for the treatment of chronic migraine may cause the patient to experience cosmetic changes he or she may find pleasing, it should be



BEFORE BOTOX



AFTER BOTOX?

emphasized that the dose and injection paradigms for BotoxA mandated by the FDA are quite different than those typically employed when the toxin is injected specifically for cosmetic purposes.

To learn more about BOTOXA, check out this [\[Link\]](#).

## 3 Migraine Myth of the Month

**Myth:** Migraine results from stress, depression, anxiety or some acquired or inherent deficiency of personality.

**Reality:** Migraine is co-morbid with a number of other medical disorders (ie, the disorder occurs in migraineurs at a higher frequency than in non-migraineurs), and these co-morbidities presumably are often genetic in origin. Migraineurs are more prone than non-migraineurs to bipolar disorder, depression, chronic anxiety disorder and panic attacks. These associations – egs, migraine and depression – do not necessarily indicate a causal relationship. When migraine and depression co-exist, one disorder may aggravate the other, but migraine doesn't create depression de novo, and depression biologically does not generate migraine.

This last point is an important one. It's all too easy for the frustrated third party (be it spouse, parent, child or co-worker) to detect the mood disorder that may accompany migraine and to identify that disorder

as the source of the patient's headaches. From there it's a short jump to equating the mood disorder (and thus the migraine itself) with some personal deficiency that the migraineur is perpetuating voluntarily. Too often – and to the detriment of any treatment plan developed – physicians and even the patients themselves buy into this misperception. One common result of the ensuing confusion is that the physician and patient may engage in a verbal jousting match, with the physician maintaining that depression is causing the headaches, and the patient insisting that it is the headaches that have caused the depression.

Such a waste of time. As stated already, the conditions, migraine and depression, are co-morbid, and what this implies for clinical management is that physicians evaluating migraine patients should take particular care to keep their eyes and ears attuned to detect the presence of a mood disorder that requires treatment. It seems a bit silly when you think about it. Physicians don't waste time debating with a severely depressed stroke patient whether the stroke caused the depression or the depression caused the stroke; instead, they

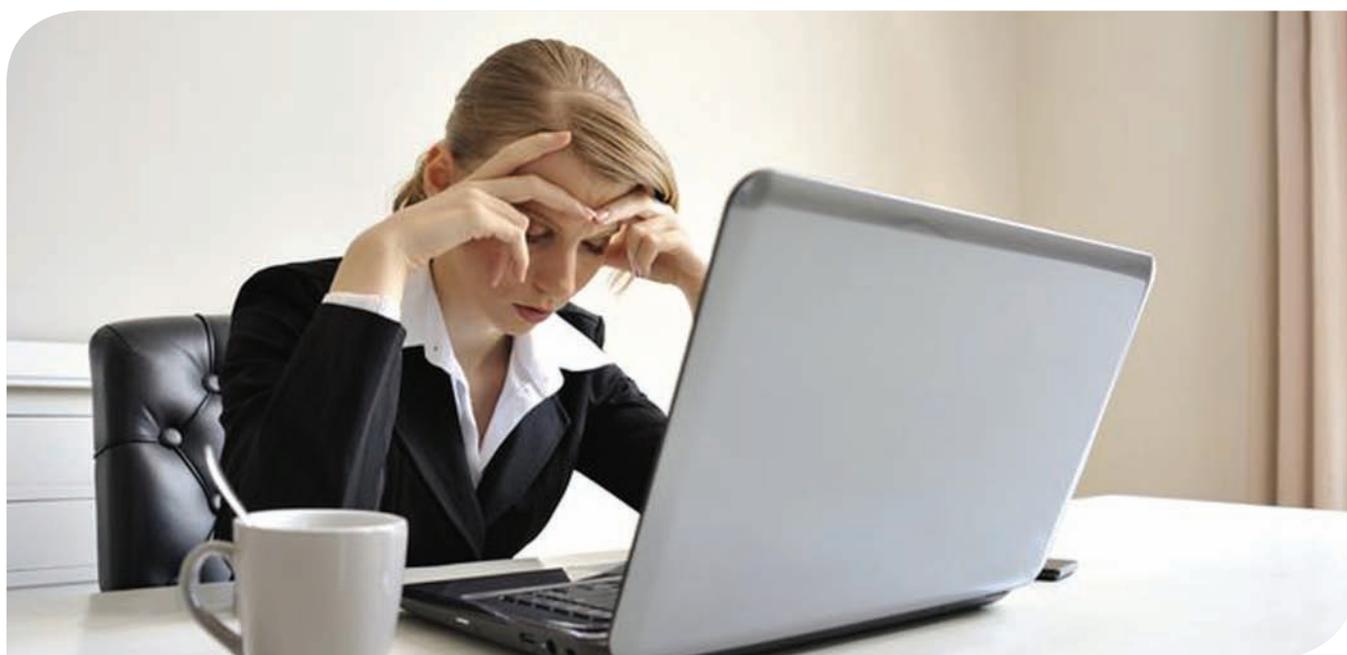
treat the depression and simultaneously prescribe treatment intended to prevent recurrent stroke.

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Patients may confound the situation further by minimizing their active depression or anxiety when speaking with their physicians.

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It's unfortunately true that many physicians either are not especially adept at detecting mood disorders or are reluctant even to explore the possibility of their presence. Patients may confound the situation further by minimizing their active depression or anxiety when speaking with their physicians. If you do the latter, you are working against your own efforts to improve your health, and, specifically, to reduce your migraine. If you are depressed, chronically anxious or experience acute attacks of inexplicable anxiety, ask for help. Depression is like a wound infection: diagnosed and treated early, it's relatively easy to eradicate; left to fester, it's much more difficult to treat...and can even be fatal.



# CELEBRITY MIGRAINE US GRANT

## Grant's Postdrome: the migraine that changed the course of American history

**A**s evidenced by the ancient writings from the Fertile Crescent, migraine has existed within humankind for millennia. Given migraine's high prevalence, with approximately 10% of the general population afflicted by the disorder, and the profound effect migraine may have on one's mood and behavior, it should come as no surprise that migraine has influenced our culture and history. One striking example involves Ulysses S. Grant, military hero and America's 18th president.

Like his commander-in-chief, Abraham Lincoln, Grant suffered from attacks of clinically severe migraine throughout the years of the American Civil War. In April 1865, at Appomattox Courthouse (Virginia), Grant finally had managed to corner the sparse remnants of Robert E. Lee's once-mighty Army of Northern Virginia. Even with final victory seemingly so close at hand, Grant feared that Lee would slip from his grasp, unite his troops with a Confederate army in North Carolina and potentially prolong the war by a year or more.

But Lee realized his army was at last defeated, and he sent across the lines a note requesting terms of surrender. He did so with some trepidation, as Grant was a known for his harsh treatment of defeated foes. It seemed to Lee quite possible that he and his lieutenants would endure the humiliation of imprisonment, trial on charges of treason and, ultimately, the gallows.

Racked by anxiety and impatient to bring his pursuit of Lee to a close, Grant had developed a migraine. In his memoirs he wrote, "I was suffering very severely with a sick headache... I spent the night in bathing my feet in hot water and mustard, and putting mustard plasters on my wrists and the back part of my neck." Despite these efforts, his "sick head-

ache" still persisted the following morning. Then Lee's message arrived, and even writing decades later Grant recalled that "the instant I saw the contents of the note, I was cured."

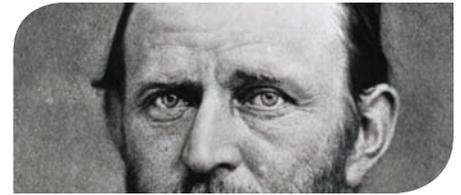
Grant's mood was oddly muted when later on that Palm Sunday he sat opposite Lee in Wilmer McLean's parlor, drawing up the formal terms of surrender. He wrote that "...my feelings which had been quite jubilant on the receipt of his letter were sad and depressed. I felt like anything but rejoicing at the downfall of a foe who had fought so long and valiantly, and had suffered so much for a cause, though that cause was, I believe, one of the worst for which a people ever fought and for which there was the least excuse." Such emotional depletion and "flatness" is typical of the postdrome that immediately follows the headache phase of a migraine attack (see the Comment that follows).

His terms of surrender reflected his subdued mood. Lee's officers would keep their side arms and all cavalry their horses so as "to work their little farms". There would be no arrests, imprisonment or public spectacle. When the Union batteries began to roar in celebration after the surrender ceremony, Grant sent word to have the guns silenced. "The war is over," he told his staff. "The rebels are our countrymen again."

The war indeed was over. The Union was preserved. What Lincoln described as the "great experiment" in social democracy would not fail, and the South would retain its place in the national community.

How much of Grant's behavior on April 9, 1865 was rooted in migrainous biology? Did his generous terms of surrender result from the dysphoria of a migraine postdrome? If not for his acute migraine, how much compassion would he have shown his enemy? In contemplating history, be it that of a nation or an individual, it's no simple task to separate the "psycho" from the "somatic".

**Comment** In its most fully developed clinical form, a migraine attack consists of 4 distinct phases: prodrome, aura, headache and postdrome. The prodromal symptoms signal the



migraineur that an attack is imminent. These symptoms differ from person to person and can be difficult to describe. They may include a feeling of euphoria, uncharacteristic clumsiness, a craving for sweets or agitation.

The aura involves a much more specific neurologic symptom, most likely commonly visual but also extending to include sensory disturbance ("numbness and tingling"), difficulty expressing words, face or limb weakness and a variety of other focal neurologic misfires. The aura typically lasts 15-30 minutes and is immediately followed by the headache phase; occasionally aura may persist for an hour or more, and in roughly a third of migraineurs the aura occurs during the headache phase. Only 20-25% of migraineurs ever experience aura, and very few have aura with every migraine attack.

While the pain experienced during the headache phase may vary widely in its intensity and character, for many it is throbbing, sickening, localized to one side of the head or centered on the eye and accompanied by light and sound sensitivity, nausea and vomiting.

The postdrome follows on the heels of the headache phase. Although some head discomfort may persist, it is typically of low intensity. Many migraineurs liken the postdrome to the hangover one experiences after over-indulging in alcohol. Despite the welcome relief from migrainous headache, postdromal symptoms may include a pervasive sense of melancholy or a feeling of being "let him down".

This postdrome is precisely what Grant describes having experienced immediately following the abrupt cessation of the migraine headache he suffered at Appomattox. That his postdrome contributed to the generous terms of surrender and treatment he extended to the defeated Confederates seems quite plausible. If so, then Grant's migraine-influenced behavior served to ease the nation's difficult transition from war to peace.

# THE TRUTH ABOUT TRIGGERS

it's all too clear that this evening is a bust, and you're destined for a prolonged exile to the tomb-like silence of your darkened bedroom.

**Y**ou and your beloved have picked an especially fine restaurant to celebrate a happy occasion in your life together. Seated at the best corner table in the softly lit dining room, you both are enjoying the spectacular view of the city lights below and the bay beyond and looking forward eagerly to a fine meal and this long-anticipated romantic evening together. To enhance your enjoyment, you splurge and order an expensive bottle of merlot. As you toast your love for one another and raise your glass to your lips, you find the wine deliciously aromatic, and the first sip caresses your palate with its deep, smooth flavor. You sigh and look up from your glass to find your beloved regarding you with obvious adoration...and desire. What could be more perfect? you think.

Twenty minutes later that nagging pressure behind your right eye has built into a throbbing pain so severe that you find it difficult to concentrate on what your beloved is saying. You're feeling increasingly nauseated, and the spectacular meal arrayed before you has all the gustatory appeal of a bowl of cold oatmeal. Within another ten minutes you're in the restroom, acquainting yourself at close range with the facility's toilet, and when you finally emerge-exhausted, sick and head pounding ever more painfully –it's all too clear that this evening is a bust, and you're destined for a prolonged exile (solo) to your bed within the tomb-like silence of your darkened bedroom.

Ugh. While no sane person willingly would invite such cruel punishment, who wants to give up savoring a glass of a great red wine...forever...while your migraineur kid sister can drink like a sailor and remain headache-free? Why does your migraine serve as a more accurate predictor of a change in barometric



pressure than the Weather Channel? What about caffeine...Chinese food...flickering neon lights...strong perfume? Is one doomed by migraine to live like the Boy in a Bubble, insulated from all external stimuli and existing on a diet of lettuce, water and melba toast? What's the truth about these so-called "migraine triggers", anyway?

Individuals with migraine frequently report that their attacks may be precipitated by "triggers". In one recent survey of 200 consecutive migraine patients referred to the University of Alabama Headache Treatment and Research Program, over 90% identified at least one migraine attack trigger; those triggers most commonly cited were physical or emotional stress (77%), menses (72% of actively cycling females), exposure to bright or flickering light (65%) and certain (specified by the patients) odors (61%). Sleep deprivation (or "oversleeping"), fasting or skipping meals, weather changes and alcoholic drinks (especially red wine or other aromatic alcohol-containing beverages) also are commonly cited triggers.

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Before we explore the more specific aspects of migraine triggers, some important general caveats deserve mention:

1. No single entity, however "classic" (eggs, red wine, chocolate, "stress"), acts as a trigger in all migraineurs.
2. In the individual migraineur, rarely does a trigger consistently provoke an attack.
3. As corollary to #2, simultaneous exposure to 2 or more triggers may be required to provoke an attack (see below).
4. In a given migraineur, what serves as a trigger may also serve as a treatment (eg, caffeine).

Current theory holds that the clinical symptomatology we define as “migraine” reflects a relatively hypersensitive brain, with that hypersensitivity likely to be genetic in origin. The migrainous brain appears inherently sensitive to changes in the individual’s “internal” or “external” environment; examples of internal change include the abrupt decline in estrogen levels occurring with menses, sudden stress (or, paradoxically, release from stress) or a change in one’s usual sleep pattern (eg, oversleeping on the weekend or vacation), whereas external changes commonly cited as triggers include weather changes, ingestion of alcohol or exposure to bright or flickering light.

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Following exposure to a sufficient trigger, the genetically primed migrainous brain -cocked and ready - acutely responds by initiating a cascade of clinical and electrical events that clinically are expressed as “migraine”: headache, often accompanied by nausea and sensitivity to light and sound.

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Again, no single trigger - however potent - is common for all migraineurs, and an established trigger rarely triggers a migraine attack each and every time in the affected individual. Furthermore, when attacks are triggered, they may involve a spectrum of migraine symptoms that extends from no headache whatsoever (ie, aura only) to a veritable pit of physical and emotional misery. Stated at a more pragmatic level, ingestion of red wine at times may induce you to suffer a migraine, but if you maintain a passionate devotion to red wine, because the wine/attack association may not be invariable and because the attacks you do experience consequent to indulging your passion may involve only minimal headache...you may choose to play your cards and take your chances.

Or perhaps not if that glass (“or two”) of savory rioja is to be followed immediately by a sweet dessert; if that combination invariably produces annoying or even debilitating migrainous symptoms, it’s best to leave well enough alone. As another example, female migraineurs may find that ingestion of red wine invariably produces migraine only when the wine is drunk in association with another common migraine trigger: menses. As noted previously, over two-thirds of our actively cycling clinic patients report menstrual aggravation of their migraine. That what has proven to be a trigger at other points within the menstrual cycle may serve as a more consistent and potent trigger during menses is not surprising.

A word about caffeine. Finding that caffeine may trigger an attack - or learning of this potential risk from a physician,



friend or another source - a migraineur may take pains to eliminate caffeine use entirely... and recoil in horror when it’s suggested that whatever oral medication is being used for acute migraine be taken with a caffeinated beverage. In reality, while caffeine can trigger migraine in some individuals, and although caffeine overuse can cause migraine progressively to worsen, caffeine can be a surprisingly effective ally in treating acute migraine. During migraine attacks the stomach’s characteristic motility may stall, and oral medications thus helplessly may linger in that organ...unable to progress down into the small intestine where they could be absorbed, into the bloodstream and exert their therapeutic effect. Caffeine can assist in restoring the stomach’s motility, and beyond simply promoting absorption of oral medications, may itself exert a more direct therapeutic effect on the migraine process. Not by coincidence is caffeine a component of so many of the preparations available for acute headache treatment, both over-the-counter and prescription (egs, Excedrin, Goody powders, Esgic, Fioricet, Fiorinal, Cafergot).

Finally, what about elimination diets? Such diets have both their diehard advocates and cold-eyed skeptics. Bottom line: (a) there are virtually no scientific data available to support an extremist position, for or against such diets; (b) by their own life experiences, most migraineurs have identified what for them are clear triggers, dietary or otherwise, and have learned to avoid those dietary components that frequently provoke attacks; (c) to maintain regular eating habits - and specifically to avoid skipping meals - is likely to be of more benefit in controlling migraine than any specific diet; and (d) adopting a migraine “elimination diet” that is inherently healthful (eg, diets “Mediterranean” in composition) makes good sense whether it helps reduce migraine or not.

# THE GENETICS OF MIGRAINE



## What About My Kids?

**M**igraine sufferers often express their concern that they will pass on their affliction to their children.

Sally (Bethesda, Maryland):

Jim, the man I eventually married, is a wonderful guy, a great husband and father, but after our first date I wasn't so sure we were going to work out. Midway through the movie we were watching he told me he wasn't feeling well and asked me to help him get back to his apartment. We'd taken the Metro, but he didn't think he could manage the walk to the Cleveland Park station, just a couple of blocks away. I got us a cab, and on the way to his apartment he vomited twice in the back seat. He was having a migraine, he told me. He was very embarrassed. And he looked terrible.

This scenario was repeated a half dozen times over the next few months; we'd be enjoying ourselves, and then within just a matter of minutes we'd have to leave the restaurant, club, party, etc. On one particularly memorable occasion we were celebrating Valentine's Day at my place, feeding each other chocolate-dipped strawberries by candlelight, when he suddenly vaulted from the bed and spent the next half-hour over the toilet in my bathroom. Not the most romantic of evenings.

I have migraine myself and found it easy enough to sympathize, but I knew the disorder could be inherited. When we got married, I worried that between us we would pass on to any children we had such a gigantic genetic dose of migraine that it



could really affect their lives.

Sure enough, our six year old daughter has always been extremely prone to car-sickness, and now she's beginning to complain of headaches. She loves school and is a good student, but three times last month I was called away from work to bring her home early due to her "sick headaches".

We're ready to have a second child now, but I'm worried what we might pass on to that child in the way of migraine. Would we be dooming him or her to a life compromised by frequent attacks of crippling migraine?

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### MIGRAINE & GENETICS: THE FACTS

- Genetic predisposition is not synonymous with clinical expression.
- Some portions of the inherited genome are static (e.g. bb=blue eyes throughout one's life)
- Some portions of the genome are dynamic (e.g. from family member to family member, the clinical expression of a genetic predisposition to migraine may vary widely)
- ...and even in the given individual, the clinical expression of his/her genetic predisposition to migraine changes over time
- Throughout our lives, what we experience will influence how much or how little our genetic predisposition migraine is expressed symptomatically; Epigenetics!

## THE ORIGIN OF MIGRAINE

Blood Vessel or Brain? For much of the last half of the 20th century, migraine was assumed to be a vascular headache. For whatever mysterious reason (as the theory went), in the arteries of the head would dilate inappropriately to cause attacks of throbbing, sickening pain. Treatment was directed at preventing the arteries from dilating or, in the case of acute attacks, at constricting the dilated vessels.

Starting in the 1980s, there began to accumulate ever more convincing evidence that this so-called “vascular hypothesis” was oversimplified or even inaccurate. We now believe migraine to be a brain disorder, with the recurrent headaches and associated symptoms of migraine reflecting a genetically hypersensitive brain. Either spontaneously or in response to various environmental stimuli, internal (eg, drop in estrogen level at menses) or external (eg, change in barometric pressure), genetically primed brain cells-neurons-fire off and trigger a series of electrochemical events that result in...an attack of migraine.

## THE MIGRAINE GENE

If migraine is a genetic disorder, great! We’ve mapped the human genome, so why not just go find the cursed gene that causes all this misery and fix it!

Would that it were so simple. Unfortunately, we already have identified no fewer than 47(!) genetic permutations that each are capable of producing the symptoms we refer to as “migraine”, and more such mutations undoubtedly are to come. To complicate matters further, genetic predisposition is not synonymous with clinical expression; in two children who possess the same genetic “load” for migraine, one may experience little or nothing in the way of migrainous symptoms, while for the other migraine will be an all-pervasive and life-long adversary.

## EPIGENETICS

Why this striking difference in two genetically similar individuals? At least in part the answer lies in epigenetics. Although the genetic hand of cards we are dealt at conception remains with us unchanged throughout our lives, what we experience in life-what we do and what is done to us-will influence how that hand is played. In our pair of youngsters with an equal genetic predisposition for migraine, for example, research performed by Dr. Gretchen Tietjen and her colleagues at the University of Toledo has demonstrated that the child subjected to emotional neglect will experience the onset of migraine at an earlier age and a higher likelihood of eventually

developing chronic migraine. In short, your genome is the piano, your epigenome is the pianist and you are the music they combine to produce.

## SO...WHAT ABOUT MY KIDS?

- 1 It's important to remember that migraine's clinical course varies widely from one person to another, even between family members; your migraine is unlikely to be your mother's migraine.
- 2 Related to this variability, simply having a genetic predisposition to migraine does not doom one to a lifetime spent in darkened rooms, suffering from relentless headache.
- 3 There are worse chronic disorders to have than migraine; rarely does migraine cause irreversible physical harm, and the arsenal of effective therapies for dealing with migraine is already large and rapidly continuing to expand.

Finally, if it's any consolation to you as a migraineur, this is a disorder that has been with humankind for no less than 5,000 years. If migraine conveyed only harm and nothing in the way of benefit, would not the sweeping broom of evolution and natural selection have whisked it away long ago? While it's not easy to recall when in the throes of an acute migraine, perhaps there's something about this peculiar disorder which marks you as a special contributor to the tribe's common good.

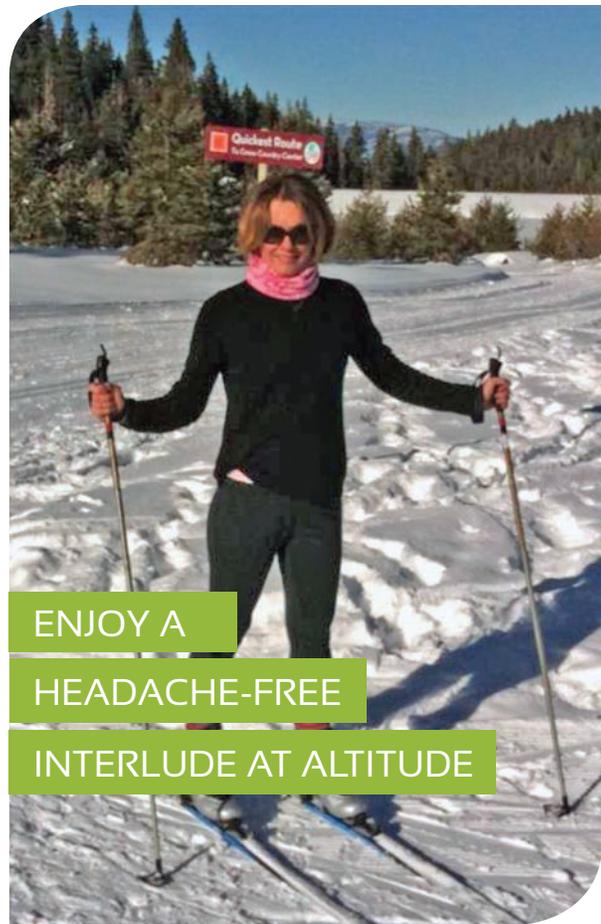


# SO YOU WANT TO TAKE YOUR MIGRAINE AND... GO SKIING!



Follow this advise and you will increase your chances of enjoying a pleasant and headache-free interlude at altitude

Speaking to her physician, LM, a 35-year-old female migraineur, reports: “I’m taking a week off to go skiing with friends at Park City, and instead of looking forward to my vacation, I’m dreading it. Every time I’ve gone skiing in the past, I seem to fall apart physically. I stay exhausted. My skin and mucous membranes get so dry, and I can’t quench my thirst. I’m up all night because I have to urinate so frequently, but that doesn’t really matter because I can’t sleep anyway. And my migraines go ballistic! I usually wind up spending most of the so-called vacation in bed-alone-trying to deal with my headache and wishing I was home.” No doubt about it, a skiing vacation can exact a physical toll from anyone, and the



ENJOY A  
HEADACHE-FREE  
INTERLUDE AT ALTITUDE

abrupt changes and peculiar environmental conditions associated with such vacations may make them particularly challenging for the migraineur. The effects of an uncharacteristic climate, physical exertion and alterations in one’s eating, drinking and sleeping habits can wreak havoc, leading the poor migraineur to wonder why he/she didn’t opt instead for a relaxing vacation on the sea-level beaches of Jamaica. Try following the advice offered here, however, and you will increase your chances of enjoying a pleasant and headache-free interlude at altitude.

## HIGH ALTITUDE ILLNESS

**Altitude sickness:** commonly afflicts flatlanders who suddenly transport themselves to the mountains. The symptoms of high altitude illness include insomnia, frequent urination, unquenchable thirst, fatigue, shortness of breath and headache, and they occur in migraineurs and non-migraineurs alike. Interestingly, the likelihood of one’s developing high altitude illness is unrelated to his/her degree of physical fitness. Well-conditioned athletes who run, swim and cycle regularly at sea level may find themselves helplessly gasping for breath while an obviously unfit individual cheerfully vaults past them up the stairs to the ski lodge with nary a pause. The best way to avoid high altitude illness is to acclimate gradually; for example, if you live in Baltimore and plan to ski at 12,000 feet in Colorado, first spend a day or two visiting mile-high Denver. Unfortunately, the luxury of gradual acclimatization is not an option for those of us whose vacation days are limited; we prefer to get to the ski slopes without delay.



THE BEST WAY TO  
AVOID HIGH ALTITUDE  
ILLNESS IS TO  
ACCLIMATE GRADUALLY

## MEDICATIONS

**Symptom Suppression:** Medications may assist in preventing or suppressing the symptoms of altitude sickness, and the drug most commonly used for that purpose is acetazolamide (Diamox). Aside from occasionally inducing some transient numbness and tingling of the face or extremities and also inducing carbonated beverages – including beer – to taste discouragingly “flat”, short term use of acetazolamide is unlikely to provoke any side effects. The drug appears to work best when begun several days in advance of the anticipated trip and continued throughout the time spent at altitude. The usual dose of acetazolamide in this setting is 250 mg twice or three times daily. Remember, if you are taking topiramate (Topamax) chronically for migraine prevention, that drug has effects similar to those of acetazolamide and possibly may serve in itself as an adequate substitute for the latter. Regardless, when you ask your physician for a prescription for acetazolamide, list for him or her the other medications you currently are taking.



## INSOMNIA

**Sleep Distruption:** Insomnia is a common complication of travel across time zones and of a sudden translocation to high altitude. Disruption of one’s normal sleep pattern is notorious for triggering migraine, and it’s consequently wise for the migraineur to plan in advance for this complication and head it off at the pass. Use of a “prn” (ie, taken as needed) sleep promoter such as eszopiclone (Lunesta), zolpidem (Ambien) or temazepam (Restoril) can make an enormous difference, allowing you to enjoy a well-rested, headache-free interlude at altitude.



## MIGRAINE RX

**Specific Prescription:** When it comes to your usual migraine medications, don’t get caught short while on vacation. Make sure well before you leave that you have quantities of those medications sufficient to last for the time you are away . . . especially those drugs you normally take for acute migraine treatment. And if in the recent past you’ve had attacks of severe, disabling migraine that failed your usual self-administered therapy and required a trip to the doctor’s office or ED, it’s not a bad idea to bring with you on your trip a written statement by your physician that briefly summarizes your medical history, migraine history in particular and the medications that have been required to treat your migraine. Any migraineur who has undergone the experience will tell you that to seek treatment for acute headache at an unfamiliar medical facility can be a frustrating and even humiliating experience; to do so bearing a statement from your regular physician may go a long ways towards lessening the hassle.



## DEHYDRATION

**Fluid Volume:** Hydrate. In fact, over hydrate . . . even to the point where you’re feeling a bit soggy and consistently producing urine that is clear and colorless. The dryness and low humidity at high altitude subtly deplete your fluid volume, and the physical exertion associated with skiing-not to mention simply carrying out one’s usual routine activities at 10,000 feet-further compounds the problem. Don’t let the absence of sweating fool you; that bracing high mountain air dries your sweat as rapidly as it forms. As you take pains to maintain adequate hydration, avoid fluids that contain alcohol or caffeine; as does the rapid shift to high altitude itself, both chemicals promote

frequent urination, and the fluids you take in will make only a brief stopover within your cardiovascular system before exiting. Finally, if you start to get a migraine, don’t panic; the same medications that worked back home in San Francisco will work in Aspen or Sun Valley. And as always with acute migraine treatment, treat early, and use an adequate dose.



## RELAX!

**Don’t Overdo:** Flushed with the excitement of having shed home and work, one’s natural temptation is immediately to attack the slopes with wild abandon: first in line at the lifts when they open and last to come off the mountain, cramming in as many runs as possible. And afterwards, what better way to celebrate your alpine heroics than with a huge dinner and a long night spent dancing at the club afterwards, the evening of course punctuated by many glasses of wine and perhaps an exotic martini or three. Give yourself a break! The mountains, restaurants and clubs aren’t going anywhere, and to knock yourself out of action for the duration of the trip by overindulging on your first day and night makes little sense. This is supposed to be fun . . . not a competition to determine who can become the most exhausted. Consider initially skiing a half-day; take the morning at a leisurely pace, getting accustomed to your new surroundings and performing some stretching exercises in anticipation of the afternoon’s skiing. Go easy on the caffeine and alcohol, and, once again, don’t forget to hydrate with free water throughout the day and evening. Go to bed early, and use your medication if you have difficulty falling asleep. Save something for the rest of the vacation. Who wants to turn what could be an idyllic interlude into just another bout of prolonged migraine?



# DOCTOR ON CALL

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**M**ary, a single twenty-three year old graduate student in Boston writes:

*“I have a long history of migraine headaches, but two weeks ago I had what was for me a unique and very scary symptom that occurred along with one of my typical headaches.*

*I was sitting in the lecture hall and feeling just fine, when out of nowhere I began to see flashes of light in the periphery of my vision on the right. Then I began to lose vision on that side, and it progressed to the point that for a few minutes I couldn't see the right side of the slides that were being projected on the screen. Within 20 minutes my vision was back to normal, but then almost immediately I began to have a really severe migraine headache and felt so nauseated that I had to leave the lecture hall and go back to my apartment.*

*When I saw my doctor two days later, he told me that I'd had a “visual aura” and that I might have a stroke if I didn't stop the birth control pill I was taking. I usually take Maxalt [rizatriptan] for my migraines, but he also told me that I could never take it or any other “triptan” again.*

*What gives? Am I going to have a stroke? Do I really have to go off the pill? Is it dangerous for me to take Maxalt?”*



## THE DOCTOR'S REPLY

In answer to your specific questions: highly unlikely; probably in your best interest; and...no.

For both males and females, having migraine conveys a 2 to 3-fold increase in the risk of stroke relative to the age and gender-matched general population. Both smoking and the occurrence of aura-experienced by approximately 25% of migraineurs-further increase stroke risk, and in women who have migraine with aura the use of an estrogen-containing oral contraceptive (OC) raises stroke risk yet higher. For women ages 25-29 the 10 year risk of stroke in those who have migraine with aura (MwA) and are taking an estrogen-based OC is roughly 8 times that of age-matched females in the general population.

While this 8-fold relative risk may appear quite frightening, the absolute risk of stroke in the young female population is extremely low; even in those with OCP use and MwA, only 23 out of 10,000 will suffer a stroke over a period of 10 years. In other words, use of an OC will increase your risk of stroke if you have MwA, but the risk remains very low. Because that (very low) additional risk may be eliminated entirely, however, females with MwA who wish to practice contraception should consider using an IUD (hormonal or non-hormonal) or another alternative to the OCP. As for the rizatriptan (Maxalt)/stroke question, there is no evidence to suggest that use of this drug or any other triptan increases the risk of stroke in females (or males) with MwA.

Your special  
moments  
should never  
be ruined  
by a migraine.

We have  
your back,  
no matter where  
the trail leads you.



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