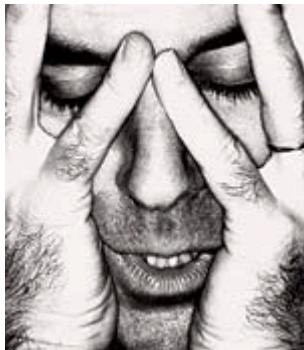


LE Magazine February 2004

## REPORT

**Natural Agents Offer Relief from the Misery of Migraines**

By Romy Fox



*Almost everyone gets a headache once in a while, and for most people an aspirin or two is usually enough to make it go away.*

*But for 45 million Americans, the headaches keep coming back—monthly, weekly, and even daily. By the numbers, the problem of recurrent headaches is quite serious. Every year, headache-driven absenteeism and medical expenses cost the US some \$50 billion. Americans spend more than \$4 billion a year just on over-the-counter headache pain relievers.<sup>1</sup>*

*Of the different types of headache, perhaps the most dreaded and disabling is migraine headaches. In this article, we will focus on migraines—their symptoms, several theories that have been advanced to explain what causes migraines, and research that suggests magnesium, riboflavin,*

*and other natural agents may be effective aids in preventing and treating migraine headaches.*

**A Headache “Sampler”**

Migraines are just one of several different kinds of headache, each having its own causes, symptoms, and treatments.

**Tension headaches** account for about three-quarters or more of all headaches. “Tension-type” headaches produce mild-to-moderate pain on both sides of the head. The pain is steady and comes gradually rather than all at once, and later fades away. Tension headaches are commonly associated with stress, but also may be linked to emotional problems such as depression. Most tension headaches respond to standard over-the-counter painkillers.

**Migraine headaches** afflict approximately 28 million Americans and produce excruciating pain that can leave victims nearly crippled for hours or days at a time. Some people experience symptoms besides pain. The migraine may be heralded by an aura, a strange feeling marked by flashing lights or other visual disturbances. Dizziness and nausea, chills or sweat, and double vision or slurred speech may accompany migraines. Noise or light may make everything feel worse. Women are more than twice as likely as men to suffer from migraines. “Migraineurs” (those with migraines) continue to suffer despite the numerous medications prescribed by their physicians.



**Cluster headaches** arrive in groups. For days, weeks, or even months on end, they strike one or more times a day. Each headache may be relatively brief, lasting perhaps 30 to 90 minutes. The pain begins mildly, but quickly becomes unbearable. One side of the face at a time is typically affected, with the pain centering around the eye on the affected side. Some 1 million Americans suffer from cluster headaches, which typically attack men; 90% of victims are male, with most in their twenties, thirties, and forties.

**Exertion headaches** are linked to physical activities such as exercise, sex, laughing, and coughing. They often strike during or just after strenuous activity. While not considered dangerous per se, exertion headaches may indicate a stroke or other problem and therefore should be brought to the attention of a physician immediately.

**Organic headaches** are messengers telling you that something is amiss, and that could be anything from elevated blood pressure to a brain tumor. The headache pain may be accompanied by fever, neck stiffness, confusion, difficulty in speaking or moving, or other symptoms. The pain tends to grow worse, either increasing with each headache or striking more frequently. Organic headaches account for fewer than 1% of all headaches.

**Other kinds of headaches**, such as those associated with hangovers, constipation, and low blood sugar, often can be cured by attacking their underlying causes.

Because headaches can signal a serious underlying illness, it is best not to self-diagnose them. If you experience unexplained, unusual, or particularly severe headaches, if they strike more often or in different ways than in the past, or if your headaches are associated with any other symptoms, you should consult your physician immediately.

## Focus on Migraines

Migraine symptoms range in severity from miserable to crippling; migraines can ruin an afternoon or immobilize their sufferers for days on end.

Migraines come in several varieties. The classical migraine strikes a small percentage of sufferers, and is heralded by the visual disturbances known as the aura. Most migraines, however, are common migraines, and lack the aura. Other types include: basilar migraines, which can trigger fainting, poor coordination, and double vision; hemiplegic migraines, which make it difficult to move one side of the body; ophthalmoplegic migraines, which interfere with vision; retinal migraines, which darken or completely obliterate vision during an attack; and menstrual migraines, which are tied to a woman's monthly cycle.

Although researchers have not yet determined the cause of migraines, they have offered several theories:

**Vascular theory.** Blood vessels in the brain and head are supposed to contract and expand on command, thereby reducing or increasing blood flow to the brain at the appropriate times. The vascular theory argues that for migraine sufferers, the contraction-expansion mechanism in the blood vessels goes awry, interfering with blood flow in the brain and head. Eventually, these vessels become too relaxed and their walls too permeable, allowing fluid from the blood to leak into surrounding tissues, triggering pain and inflammation.

**Serotonin theory.** A neurotransmitter called serotonin helps control pain sensations, sleep, mood, and other bodily actions and feelings. A deficiency of this neurotransmitter can trigger migraines by encouraging inappropriate contraction and relaxation of the arteries. A lack of serotonin may also lower the pain threshold, making everything hurt more.

**Neural theory.** Migraines begin when certain regions of the brain become irritated. The body responds to the irritation by releasing chemicals that, among other things, cause the blood vessels to become inflamed and irritate the nerves.

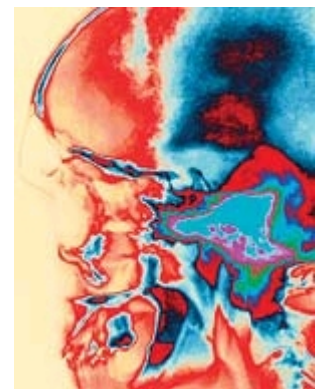
Still other theories have been advanced to explain the genesis of migraines. Deficiencies in brain energy metabolism, both between and during migraine attacks, may be to blame.<sup>2</sup> Some studies point to platelets, the tiny substances that help blood clot; platelets may be structured differently in migraineurs, making them more likely to aggregate.<sup>3</sup> Nutritional imbalances and deficiencies also have been suggested as a cause of migraines. Indeed, a mounting body of research suggests that magnesium and other natural agents can play an important role in the prevention of migraines.

## Magnesium for Migraines

Magnesium helps muscles, including those surrounding arteries, to relax, and this may be why a deficiency of this mineral is linked to migraines. Researchers have learned that some of the same things that deplete the body's supply of magnesium—including stress, alcohol, and pregnancy—can trigger migraines in susceptible people. They also have discovered that certain medicines that successfully treat migraines mimic magnesium's actions by:

- Keeping open blood vessels in the brain
- Preventing sudden spasms that “clamp down” on arteries
- Keeping the blood thin and flowing by preventing platelets from sticking together inappropriately
- Helping to maintain the stability of cell membranes
- Interfering with the inflammation-producing substances released at the onset of a migraine.

While magnesium may help ease migraines, not just any kind of magnesium will do. The two forms of magnesium that circulate in the blood are “bound” and “free.” The bound form is “tied” to other substances and is relatively inactive. The free form is not bound to other substances and remains active, a characteristic that researchers believe enables it to counteract the effects of migraines.



## REPORT

### Natural Agents Offer Relief from the Misery of Migraines

By Romy Fox

Up to half of the people who suffer migraines are deficient in the free and active form of magnesium, which is known as serum ionized magnesium.<sup>4</sup> If free magnesium levels fall too low, the vessels supplying blood to the head may “clamp down” inappropriately, hindering blood flow in the head and triggering a migraine. These vessels may become “stuck” in the contracted state, leaving the “pain switch” jammed in the “on” position. Inflammatory substances may be released that heighten pain sensations.

Through the 1990s, the relationship between migraines and magnesium was unclear. Some studies showed that magnesium prevents migraines, others did not. This confusion was due to problems involved in measuring magnesium—researchers were able to measure only the total magnesium in the blood, not the free form. When a technique for measuring free magnesium was finally developed, it became clear that a deficiency in free magnesium was a definite risk factor for migraines.

In 1993, two different studies were performed at the New York Headache Center by Alexander Mauskop, MD, one of the nation’s leading authorities on migraines and author of *What Your Doctor May Not Tell You About Migraines*.<sup>5,6</sup> Mauskop and his team found that people in the throes of a migraine had lower levels of free magnesium in their blood.

Their next step was to determine whether replacing the missing magnesium would stop the headaches. In 1995, Mauskop and his colleagues gave intravenous injections of magnesium to patients who were in the throes of a migraine and also had low levels of free magnesium.<sup>7</sup> The magnesium injections brought the migraines to a halt, sometimes in as little as 15 minutes. Mauskop found that the lower the initial level of free magnesium in migraine sufferers, the more substantial and long lasting was the relief offered by the injections. The following year, Mauskop published a study reporting equally good results among 40 people suffering from several types of severe headaches, not just migraines.<sup>8</sup>

After learning that an intravenous infusion of magnesium could halt a migraine in progress, researchers wondered whether taking daily magnesium supplements could keep migraines from striking in the first place. German researchers addressed that question in a study of 81 migraineurs.<sup>9</sup> The volunteers in this randomized, double-blind, placebo-controlled study suffered an average of 3.6 migraines each month. For 12 weeks, half of the patients were given 600 mg of magnesium daily, while the other half received a placebo. The results were encouraging: among those taking the magnesium, the number of migraines, days lost to migraines, and anti-migraine medications required all dropped significantly. An earlier Italian study, performed exclusively on women suffering from menstrual migraines, also found that magnesium supplementation could prevent migraines from striking.<sup>10</sup>

Dr. Mauskop agreed that magnesium supplements could indeed make migraines less frequent, noting, “a trial of oral magnesium supplementation can be recommended to a majority of migraine sufferers.”<sup>4</sup>

Minor deficiencies of magnesium are widespread, and 15-20% of Americans suffer from chronic magnesium deficiency.<sup>11</sup> Even minor magnesium deficiencies may be enough to trigger migraines in susceptible people. A daily dose of 300-400 mg of supplemental magnesium appears to be effective for many migraineurs. Some experts recommend splitting the dose and taking each half with a meal, one early in the day and the other later.

#### Alexander Mauskop, MD, Discusses Anti-Migraine Supplements

“As a physician specializing in treating headaches, I’ve been particularly impressed by the efficacy of magnesium, which I have been researching for the past 12 years. Fifty percent of those with migraines are deficient in magnesium and can enjoy dramatic improvement if they supplement their diet with this mineral. I know they can, because I’ve seen it happen over and over again.

“Although the results with riboflavin alone are not as impressive as those seen with magnesium, the combination of the vitamin and the mineral is potentially strong. You need to take megadoses of riboflavin, 400 mg, and should be prepared to wait two to three months to enjoy the benefits.

“Feverfew has been tested in five double-blind studies. There is a clear trend showing that it is better than placebo, which means it has definite benefits. As for butterbur, one of the two major studies on the butterbur root extract was centered here at my New York Headache Center. The test showed that it was much more effective than a placebo.

“We can always use more study, but it’s safe to say that a large percentage of migraine sufferers can be helped by supplements such as magnesium, riboflavin, feverfew, and butterbur.”

Alexander Mauskop, MD, is one of the nation’s leading authorities on migraines and other types of headache. A neurologist with 20 years’ experience treating patients, Dr. Mauskop is director of the New York Headache Center, and an associate professor of neurology at the State University of New York (SUNY) Downstate Medical Center in Brooklyn, NY.

### **Riboflavin for Migraines**

Riboflavin, also known as vitamin B2, has a variety of functions, from aiding in the manufacture of red blood cells to assisting in the extraction of energy from carbohydrates, protein, and fat.

Riboflavin may be related to migraines via tiny “energy factories” in the brain cells called mitochondria. Low mitochondrial energy production in migraineurs may trigger the headaches, and having additional supplies of the vitamin on hand may help increase cellular energy production and reduce migraine risk.

In 1994, researchers from Belgium’s University of Liege studied 49 migraineurs.<sup>12</sup> The volunteers were given 400 mg of riboflavin with breakfast every day for at least three months. By the end of the study period, participants reported an average of 67% fewer migraine attacks, as well as less-severe attacks.

Four years later, the same researchers conducted a second study in which 55 migraineurs were given either riboflavin or a placebo for three months.<sup>13</sup> Those taking the vitamin saw a decrease in the frequency of attacks and number of days lost to migraines compared to those who received the placebo.

It apparently is necessary to take large doses of riboflavin—perhaps 400 mg daily—to obtain its anti-migraine benefits. A few months may pass before results are seen. Because many foods contain riboflavin, serious cases of deficiency are uncommon; however, for a large percentage of the population, riboflavin intake is either substandard or barely adequate, with elderly people and the poor especially likely to be deficient.<sup>14</sup>



### **Feverfew for Migraines**

In the 17th century, a British herbalist wrote that an herb called feverfew (*Tanacetum parthenium*) was helpful in treating “all pains in the head.” Despite a centuries-old tradition of using this member of the aster family for headaches, fever, and other ailments, today it is mostly used as an ornamental shrub in gardens or along roadways. Nevertheless, several studies concerning feverfew’s ability to prevent migraines have appeared since the late 1970s.

In 1985, researchers looked at 17 migraineurs who were already using feverfew to prevent headaches.<sup>15</sup> In this double-blind, placebo-controlled study, eight people continued to receive feverfew, while nine were given a placebo. Those who no longer received the feverfew reported having more, and more-serious, migraines. The study results suggest feverfew does indeed prevent migraines.

In 1988, an intriguing report appeared in the prestigious British medical journal *The Lancet*.<sup>16</sup> Seventy-two migraineurs participated in a double-blind, placebo-controlled crossover study. When the volunteers took a daily capsule of dried feverfew leaves, the frequency and severity of their migraines fell, and they experienced less nausea and vomiting.

More recently, scientists in Poland studied 24 women, aged 19-61.<sup>17</sup> After feverfew was administered for 1-2 months, one-third of the women reported a significant reduction in migraine severity, with only minor side effects.

In their review of the published literature on feverfew and migraines, researchers from England’s University of Exter concluded that feverfew is “likely to be effective in the prevention of migraine” headaches and presents no major safety issues.<sup>18</sup>

## REPORT

### Natural Agents Offer Relief from the Misery of Migraines

By Romy Fox

Why feverfew helps prevent migraines remains unknown. Some researchers attribute the herb's anti-migraine properties to its parthenolide, which may hinder the inflammatory process,<sup>19</sup> or to the release of serotonin from certain white blood cells and platelets, which in turn can reduce the frequency and severity of migraines by keeping the blood vessels properly toned.<sup>20</sup> Other substances in feverfew may interfere with the actions of arachidonic acid and histamine, which can contribute to migraine pain and other symptoms.<sup>21</sup>



Feverfew has been approved in Britain and Canada as a treatment for migraines, with a generally recommended dose of 100 mg per day.

#### Butterbur for Migraines

Butterbur (*Petasites hybridus*) is a shrub native to Europe and parts of Asia and Africa. For the past 30 years, it has been prescribed to migraineurs in Germany. Butterbur contains petasin and isopetasin,<sup>22</sup> which are believed to slow the body's production of leukotriene. With less leukotriene present, blood vessels are less likely to become inflamed and migraines less likely to develop.

A standardized extract of butterbur called Petadolex® was used in two randomized, double-blind, placebo-controlled studies to test whether butterbur could prevent migraines. In the first study, 60 migraineurs were divided into two groups. For 12 weeks, one group received 100 mg of Petadolex® a day, the other a placebo. By the end of the first month, those taking the butterbur extract reported significantly fewer migraine headaches compared to those taking the placebo. By the third month, the butterbur group had 60% fewer migraine attacks than did the control group. Migraine-related symptoms also were reduced, and no significant side effects were reported among those taking the Petadolex®.

The second study, involving 233 migraineurs, produced equally encouraging results.<sup>22</sup> The volunteers received either 100 mg of Petadolex®, 150 mg of Petadolex®, or a placebo every day for 16 weeks. Those taking 150 mg of Petadolex® daily saw significantly fewer migraines compared to the placebo group, with mild gastrointestinal problems being the only reported side effect. The study results suggest that 75 mg of butterbur extract taken twice a day with food may be the optimal dosage.

#### Other Intriguing Therapies

While physicians continue to explore how magnesium, riboflavin, feverfew, and butterbur work to counteract migraines, several other therapies also are under study.

**Glucosamine.** Doctors at Canada's Brampton Pain Clinic studied 10 people. All suffered migraines or migraine-like headaches and none had been helped by previous standard treatments.<sup>23</sup> After they took glucosamine for 4-6 weeks, the volunteers reported a drop in the number and intensity of migraines. The researchers theorize that glucosamine works through white blood cells called mast cells to boost the production of heparin, which helps to reduce blood clotting, thus reducing nerve-mediated inflammation and pain. How much glucosamine is required to prevent migraines is unknown, but the therapeutic dose may be similar to that used to treat osteoarthritis (approximately 1,800 mg per day).

**Coenzyme Q10 (CoQ10).** This vitamin-like substance may aid migraineurs by stimulating the mitochondria to produce more energy. A 2002 study published in the journal *Cephalgia* reported on 32 migraine patients treated with a daily dose of 150 mg of CoQ10 for four months.<sup>24</sup> By the study's end, the average number of migraine attacks per month fell from 4.85 to 2.81, and CoQ10 did not trigger any reported side effects. If the results of this preliminary study are confirmed by double-blind studies, 150 mg per day of CoQ10 may become the recommended dose.

**Melatonin.** Secreted by the pineal gland at night to aid in sleep, this hormone also may play a role in the genesis of migraines. French researchers noted abnormal melatonin levels in the blood of four of six women who suffer from migraines (compared to nine healthy people serving as controls).<sup>25</sup> The scientists theorized that problems with the pineal gland may be responsible for migraines in some people, thus explaining why melatonin may help reduce the incidence of migraines.

According to the American Migraine Study II conducted by the National Headache Foundation, migraine headaches are underdiagnosed and undertreated.<sup>26</sup> Despite new understanding of the disease and new “medications designed specifically for the treatment of migraine, many patients continue to experience needless pain and disability,” the study reported.

Some 28 million Americans suffer migraines, which means you can find a migraineur in one of every four households. While standard medications are helpful, millions may find additional relief in natural, readily available substances such as magnesium, riboflavin, feverfew, butterbur, glucosamine, CoQ10, and melatonin.



---

## References

---

1. Educational Resources: NHF Headache Fact Sheet page. National Headache Foundation web site. Available at: <http://www.headaches.org/consumer/generalinfo/factsheet.html>. Accessed November 25, 2003.
2. CoQ10's possible new target: migraines. Life Extension magazine, April 2003:28.
3. Khosh F. Natural approach to migraine headaches. Townsend Letter for Doctors and Patients, Aug-Sep 2002.
4. Mauskop A, Altura BM. Role of magnesium in the pathogenesis and treatment of migraines. Clin Neurosci 1998;5(1):24-7.
5. Mauskop A, Altura BT, Cracco RQ, Altura BM. Serum ionized magnesium levels in patients with tension-type headaches. Olesen J and Schoenen J, eds. In: Tension-type Headache: Classification, Mechanisms, and Treatment. New York: Raven Press; 1993: 137-40.
6. Mauskop A, Altura BT, Cracco RQ, Altura BM. Deficiency in serum ionized magnesium but not total magnesium in patients with migraines. Possible role of  $ICa^{2+}/IMg^{2+}$  ratio. Headache 1993 Mar;33(3):135-8.
7. Mauskop A, Altura BT, Cracco RQ, Altura BM. Intravenous magnesium sulphate relieves migraine attacks in patients with low serum ionized magnesium levels: a pilot study. Clin Sci (Lond) 1995 Dec;89(6):633-6.
8. Mauskop A, Altura BT, Cracco RQ, Altura BM. Intravenous magnesium sulfate rapidly alleviates headaches of various types. Headache 1996(Mar);36(3):154-60.
9. Peikert A, Wilimzig C, Kohne-Volland R. Prophylaxis of migraine with oral magnesium: results from a prospective, multi-center, placebo-controlled and double-blind randomized study. Cephalgia 1996 Jun;16(4):257-63.
10. Facchinetti F, Sances G, Borella P, Genazzani AR, Nappi G. Magnesium prophylaxis of menstrual migraine: effects on intracellular magnesium. Headache 1991 May;31(5):298-301.
11. Durlach J, Durlach V, Bac P, Bara M, Guiet-Bara A. Magnesium and therapeutics. Magnes Res 1994 Dec;7(3-4):313-28.
12. Schoenen J, Lenaerts M, Bastings E. High-dose riboflavin as a prophylactic treatment of migraine: results of an open pilot study. Cephalgia 1994 Oct;14(5):328-9.
13. Schoenen J, Jacqy J, Lenaerts M. Effectiveness of high-dose riboflavin in migraine prophylaxis. A randomized controlled trial. Neurology 1998 Feb;50(2):466-70.
14. Southon S, Bailey AI, Wright AJ, Belsten J, Finglas PM. Micronutrient undernutrition in British schoolchildren. Proc Nutr Soc 1993 Feb;52(1):155-63.
15. Johnson ES, Kadam NP, Hylands DM, Hylands PJ. Efficacy of feverfew as prophylactic treatment of migraine. Br Med J (Clin Res Ed) 1985 Aug 31;291(6495):569-73.
16. Murphy JJ, Heptinstall S, Nitchell JR. Randomized double-blind placebo-controlled trial of feverfew in migraine prevention. Lancet 1988 Jul 23;2(8604):189-92.
17. Prusinski A, Durko A, Niczyporuk-Turek A. Feverfew as prophylactic treatment of migraine. Neurol Neurochir Pol 1999;33 Suppl 5:89-95.

18. Ernst E, Pittler MH. The efficacy and safety of feverfew (*Tanacetum parthenium* L): an update of a systematic review. *Public Health Nutr* 2000 Dec;3(4A):509-14.
19. Cutlan AR, Bonilla LE, Simon JE, Erwin JE. Intra-specific variability of feverfew: correlations between parthenolide, morphological traits and seen origin. *Planta Med* 2000 Oct;66(7):612-7.
20. Mauskop A, Fox B. *What Your Doctor May Not Tell You About Migraines*. New York: Warner Books; 2001:79.
21. Mauskop A, Fox B. *What Your Doctor May Not Tell You About Migraines*. New York: Warner Books; 2001:52.
22. Brown DJ. Standardized butterbur extract Petadolex®—herbal approach to migraine prophylaxis. *Townsend Letter for Doctors and Patients*, Oct 2002.
23. Russell AL, McCarty MF. Glucosamine for migraine prophylaxis? *Med Hypotheses* 2000 Sep;55(3):195-8.
24. Rozen TD, Oshinsky ML, Gebeline CA, et al. Open label trial of coenzyme Q10 as a migraine preventive. *Cephalgia* 2002 Mar;22(2):137-41.
25. Claustrat B, Brun J, Geoffriau M, Zaidan R, Mallo C, Chazot G. Nocturnal plasma melatonin profile and melatonin kinetics during infusion in status migrainosus. *Cephalgia* 1997 Jun;17(4):511-7.
26. New Results Available from the American Migraine Study II [press release]. Chicago: National Headache Foundation, February 22, 2000.

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

**LifeExtension®**

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.