Dr. Michael Teixido, MD – Jefferson Medical College
Dr. John Carey, MD - Johns Hopkins Otolaryngology-Head & Neck Surgery
Updated May 14, 2014

Migraine – More than a Headache

by Drs. Michael Teixido and John Carey

Introduction

Migraine is a common clinical problem characterized by episodic attacks of head pain and associated symptoms such as nausea, sensitivity to light, sound, or head movement. It is generally thought of as a headache problem, but it has become apparent in recent years that many patients suffer symptoms from migraine who do not have severe headaches as a dominant symptom. These patients may have a primary complaint of dizziness, of ear pain, of ear or head fullness, "sinus" pressure, and even fluctuating hearing loss. Fortunately, treatment regimens long established for the treatment of "classic" migraine headaches are generally effective against these "atypical" symptoms of migraine.

How Common is Migraine?

There are currently 28 million Americans with "classic" migraine headaches. In a room with 100 people, 13 are likely to have migraine. This is as common as diabetes and asthma combined. The number of people suffering with atypical forms of migraine is unknown. Females are 3 times more likely to have migraine than males. Although any person can have migraine at any age, migraine is most common between ages 30 and 50. The peak incidence of migraine in females occurs at 35 years of age—at this age, 28% of all females have migraine headaches. The peak incidence of migraine in men occurs at 30 years of age—at this age, about 10% of all males have migraine headaches.

Migraine is a lifelong problem. It may start in childhood and disappear and reappear in new forms throughout an individual's life. In general, there is a decrease in headache intensity and an increase in the incidence of atypical symptoms of migraine (vertigo, ear pain, bowel symptoms, etc) as patients mature. Migraine tends to run in families, so having a relative with migraine makes it more likely that you will have migraine as well.

Surveys show that only 48% of people with migraine headaches have had a diagnosis and are being treated for their headaches. Unfortunately, only 29% of US migraine sufferers are very satisfied with their treatment. This is usually a reflection of a lack of understanding of the nature of migraine and its treatment, or lack of commitment to effective treatments. We hope this material will help you to achieve better control of your migraine symptoms, whatever they are, and improve your quality of life.

How are People with Migraine Different?

Evidence suggests that migraine is an inherited problem of ion channels in the brain. This may result in what is best described as a "sensitive brain". Most individuals exposed to loud noise, bright light, or excessive motion can adapt to these strong stimuli within minutes, but in the brain of a "migraineur" (migraine patient), the strength of the stimulus continues to grow, and a migraine crisis can

occur. This lack of ability to adapt to strong sensory stimulation helps us understand why so many patients have migraine headache or other migraine symptoms that can be provoked by bright light, excessive noise, strong smells, excessive motion, and painful stimuli.

What Happens During a Migraine Attack?

Abnormal electrical activity may occur in the brain tissues during a migraine attack. Areas of altered activity have been found on brain imaging studies in patients having migraine attacks. This activity is called "spreading depression," and it represents a wave of increased activity of nerve cells, followed by decreased activity. Originally it was thought that blood vessel spasms caused this abnormal activity, but more recently we have learned that this is not the case. The electrical disturbance is the primary event, and the blood flow changes are a response to the electrical disturbance.

The tendency to generate this electrical disturbance is probably enhanced by inheriting certain forms of the ion channels that set the electrical activity in these nerve cells. Ion channels are like chemical gates – they control the flow of sodium, potassium, and other elements in and out of nerve cells. Migraine may represent a set of biochemical abnormalities of these gates. In a sense, individuals with abnormalities are "primed" to generate this abnormal electrical activity. The addition of something else may push them over the edge and generate the electrical disturbance that underlies migraine attacks. This is where other triggers come to play a role: certain foods, weather changes, stress, hormonal changes, sleep disruptions, etc.

The electrical disturbance may cause very obvious symptoms. For example, spreading depression in the vision areas of the brain may result in unusual visual phenomena such as the appearance of spark-like bursts, wavy lines, blind spots, or even complete visual loss in rare cases. Abnormal cortical brain activity over other regions of the cortex can result in temporary confusion, inability to speak, numbness, or even paralysis of any part of the body. These symptoms, which occur due to electrical disturbances at the surface of the brain, typically are brief, lasting no longer than 20 minutes.

The electrical disturbance of migraine frequently involves deeper parts of the brain that are important processing centers for the senses. We believe that these centers become "hypersensitized." This means a person having a migraine who senses pain, motion, or sound will tend to have an exaggerated, distorted experience of the pain, motion, or sound that may be so intense that it is difficult to tolerate. A hallmark of migraine headache – rare but telltale when it happens – is allodynia, the experience of just simply touching the scalp or even the hair as intolerably painful. Light, sound, motion, or odors can also become intolerable. The patient may become so sensitive that he or she has no choice but to withdraw to a quiet, dark place and sleep until the episode has passed.

Another element in migraine is the release of chemicals by the trigeminal nerve. This nerve supplies sensation to the entire face, scalp, lining of the eyes, nasal cavity and sinuses, teeth and gums, jaw joints, parts of the neck and ears, even shoulders. This nerve releases inflammatory peptides – short pieces of

proteins – into the tissues nearby. These peptides (CGRP, substance P, etc.) can cause the local blood vessels to become "leaky," losing their serum into surrounding tissues. The tissues can even swell and become painful on this basis. Classic migraine headache may occur when branches of the trigeminal nerve going to the lining of the brain get inflamed, causing painful throbbing headache due to sensitization of the blood vessels around the brain by the inflammatory peptides. But if branches going to the sinuses are involved instead of those going to the lining of the brain, the symptoms may not seem like classic migraine headache, but instead may be sinus congestion and runny nose. These patients often feel that they have sinusitis, but scans show no anatomic abnormality of the sinuses.

Other symptoms of migraine activity in the brain may include retention of fluid, lethargy, nausea, fainting, anxiety, fever, and even (rarely) seizures.

What is a Migraine Trigger?

A migraine trigger is any environmental, dietary, or physiologic factor that can provoke migraine activity in the brain.

Environmental triggers

Examples of environmental triggers include odors, bright lights, noise, and other excessive sensory stimuli. Painful stimuli that trigger migraine usually occur in the head and neck. The most common of these are neck injury and spasm, temporomandibular joint pain, and sinus inflammation. Forty percent of migraineurs report that they are affected by weather changes. The mechanism of this trigger is not currently understood.

Food triggers

There are hundreds of potential food triggers for migraine. Comprehensive lists of foods that may contribute to triggering migraine can easily be found on the Web. In general, these foods fall into two main categories: 1) byproducts of food aging and 2) foods with chemicals similar to the neurotransmitters that our brains use. Byproducts of food aging are found in fermented products like red wine, aged cheeses, and yeast in fresh bread and yogurt. Foods with chemicals similar to our own neurotransmitters that may aggravate migraine are coffee, chocolate, MSG, and the nitrates used as preservatives in many of our prepackaged foods. Dietary triggers are generally not the result of allergies, but are direct sensitivities to chemicals in foods and beverages.

There is a common misconception that if a person is sensitive to a food item, they will know it, because they will have migraine symptoms within an hour of eating the particular food item. In fact, some effects may come immediately, but some may be delayed for days. Added to this confusion is the reality that many real food triggers may not cause migraine alone, but only in combination with other partial triggers, which together may provoke an attack of migraine headache or symptoms. For example, some migraineurs can eat chocolate or

drink red wine alone with no problem, but will suffer a migraine attack if chocolate and red wine are taken together.

We generally recommend an initial dietary trial that avoids only the most common migraine triggers. If good results are not achieved within a few weeks, a comprehensive diet which eliminates all potential migraine triggers is recommended. It may take 6-10 weeks for a patient suffering from severe and debilitating migraine symptoms to respond, but most do. After an improvement in symptoms is achieved, suspected foods can be added to the diet – but slowly, and one at a time, to see whether they are an important triggers for that patient. Despite the difficulty of this kind of a trial, we have found that even the most severely affected migraineurs tend to respond and are generously rewarded for their efforts.

Physiologic triggers

Perhaps the most common trigger of migraine is stress. Patients commonly report increased symptoms when they are fatigued, suffer lack of sleep, or alter their sleep schedule. Many other physiologic stresses can also trigger migraine, such as hunger, exercise, and pain. Some patients suffer migraine from sleeping too much, and cannot understand why most of their weekends are ruined by headaches or dizziness. It is not unusual for unsuspected sleep apnea to trigger migraines. Migraines are commonly triggered by hormone changes, like the drop in estrogen levels before the menstrual period or after menopause.

Treatment of Migraine

It seems easy to take pain medications or abortive medications such as narcotics or triptans to suppress symptoms, but when taken frequently, these can worsen the problem by causing rebound symptoms more intense than the original attack. It is unfortunately common that patients get themselves into a vicious cycle, resulting in decreased functioning at work and at home with the expected emotional consequences before preventative treatment is sought. The best treatment results will be obtained by those patients who work to understand what migraine is and how migraine is affecting their lives. This allows a teamwork approach with the physician and better outcomes.

The mainstay of treatment for migraine headache and atypical migraine symptoms is **trigger identification and avoidance**. This requires education about migraine triggers and the use of a migraine diary in which the patient is asked to record their symptoms and the probable trigger for that particular episode. Unlike many environmental and physiologic triggers, dietary triggers can be avoided. In general, an attempt to improve lifestyle by reducing stress, improving sleep habits, and adding regular exercise are beneficial. When done maximally, many patients will obtain near complete freedom from their migraines with this treatment alone.

At times, symptoms may be so constant that individual events and their triggers cannot be easily identified. In these cases, it may be helpful to give **medications to elevate the threshold** above which migraine triggering in the

brain occurs. These may be medications originally used for blood pressure control, depression, or seizures which have been found to be easily tolerated and very good at preventing frequent migraine attacks. When this is successful, the breakthrough attacks which do occur are usually easily attributed to some particular trigger or aggravating factor, which can then be avoided. It may take 6-8 weeks to respond to a medication, and it is not uncommon for a patient to have to try more than one medication. Patients requiring medications to elevate migraine threshold can realistically expect a 50-80% reduction in symptom intensity and frequency.

If after maximizing the benefits of trigger identification and avoidance and medications to elevate the threshold of migraine, breakthrough headaches are still occurring, **medications to abort acute attacks** may be prescribed. There are now excellent medications which can help improve migraine symptoms both deep in the brain and those painful symptoms associated with sensitized blood vessels around the brain. These new medications are called triptans. Because they can cause rebound, they should not be used more than a few times a month. Doctors' opinions may vary on this.

Some patients will have occasional severe headaches which can be aborted effectively with triptans without the risk of rebound. These patients should always be on the lookout for an increase in headache frequency and intensity that are the first signs of rebound. Long term treatment of acute headaches with narcotics generally leads to increasing medication needs and must be considered very cautiously, especially in patients with histories of chemical dependency.

Migraine and Meniere's Disease

There is increasing interest among ENT physicians in the connection between migraine and Meniere's disease. Meniere's disease is a disorder of the inner ear characterized by episodic fullness, tinnitus (ringing), hearing loss, and vertigo whose cause is poorly understood. It has classically been associated with a pattern of fluid buildup in a portion of the inner ear. While the prevalence of migraine in the US population is 13%, the prevalence of migraine in patients with Meniere's disease is 56%, and the prevalence of migraine in patients with bilateral Meniere's disease is 85%.

It has recently been discovered that the tiny blood vessels in the inner ear are innervated by branches of the trigeminal nerve that innervates the intracranial blood vessels. We have already seen how this nerve releases peptides in migraine that can cause inflammation of local blood vessels. Interestingly, experiments have shown that electrical stimulation of the trigeminal nerve has caused blood vessels in the inner ear to become "leaky" as well. Could it be that this leads to fluid changes in the inner ear, which could affect it severely enough to cause a problem like Meniere's disease? This is presently speculative, but we find that many patients with migraine and Meniere's disease who are treated effectively for migraine have experienced an improvement in their Meniere's symptoms.

Dr. Michael Teixido, MD – Jefferson Medical College
Dr. John Carey, MD - Johns Hopkins Otolaryngology-Head & Neck Surgery
Updated May 14, 2014

Migraine and Vertigo

Twenty-five percent of migraineurs experience vertigo along with their other migraine symptoms. In many patients seen at our balance clinics, vertigo is the predominant feature of their migraine. We typically find that they have had more classic migraine headaches at some time in the past, or have a family history of migraine. Migraine symptoms of new onset in a patient with no personal or family history of migraine can also occur. This is particularly common after head injury or whiplash with chronic neck symptoms. Neck symptoms and spasm tend to increase weeks to months after an initial whiplash injury, causing headache and associated episodes of vertigo. These symptoms are generally not associated with pressure in the ear or hearing changes and may originate in the brainstem from faulty central processing of balance information from the inner ears. These patients are often best treated with physical therapy to decrease neck muscle stiffness and pain, medications to decrease neck muscle stiffness and pain, as well as traditional migraine therapy.

Migraine and Otalgia (Ear pain)

Up to 40% of migraineurs report ear pain that lasts anywhere from seconds to months on end. Ear pain has many causes, including infection and Eustachian tube problems in the ear, TMJ, and referred pain from the extensive lining of the throat. Migraineurs who present to the doctor with ear pains frequently complain that their ears are hypersensitive to touch, to wind, and to cold. When an otolaryngologist has ruled out all of these other causes of ear pain in a patient with a history of migraine, migraine treatment is often effective in eliminating the pain.

Migraine and Sinus Pressure

A great deal of confusion exists among patients and their physicians regarding the source of symptoms of facial pressure. While facial pressure is indeed a cardinal symptom of "true" sinusitis, up to 45% of migraine patients report attack-related "sinus" symptoms, including tearing, runny nose, and nasal congestion. In migraine, these symptoms may be caused by a release of peptides by the trigeminal nerve branches going to the mucous membranes in the nasal cavity and sinuses. These symptoms may last only a few minutes or hours during the migraine episode. Sinus symptoms caused by colds or sinus infections tend to last for days.

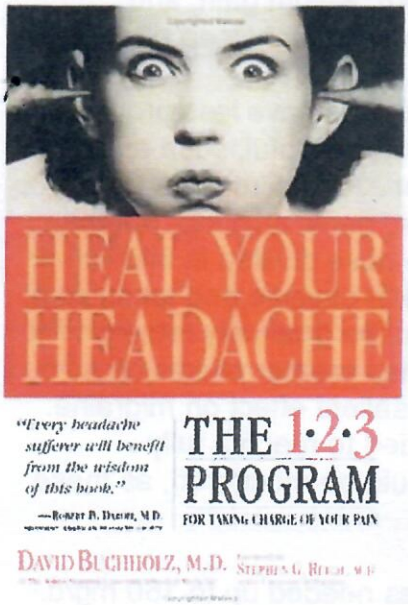
Sinus pain, which feels like pressure, is also commonly associated with migraine, and may be the only "headache" experienced in a migraine. In migraine, symptoms tend to last minutes to hours rather than for days, as in sinus infections. Fifty percent of migraine patients report that their headaches are influenced by weather.

Dr. Michael Teixido, MD – Jefferson Medical College
Dr. John Carey, MD - Johns Hopkins Otolaryngology-Head & Neck Surgery
Updated May 14, 2014

Where can I Learn More about Migraine?

Several websites provide valuable information. Dr. Timothy Hain maintains an excellent website on vertigo and imbalance disorders at www.dizziness-and-balance.com. A website specifically devoted to migraine-associated vertigo can be found at www.mvertigo.org.

In addition, we typically recommend that my patients read the book, *Heal your Headache the 1-2-3 Program* by David Buchholz, MD. This book provides a comprehensive diet plan composed completely of foods that do not trigger migraine. It is much easier to follow this diet than to be suspicious of every food of every food you have in your cabinet at home or that you see in the supermarket. It also teaches and emphasizes the concepts of rebound and the additive character of migraine triggers. Patients who have severe migraine-related vertigo may not be able to read a whole book because of their condition. They will benefit greatly from reading the book together with a family member who can help them to stay on track and to understand all the concepts in the book.



Those patients who do love to read and who have very atypical manifestations of migraine often find great comfort in the experiences of Oliver Sacks, MD, in his book, *Migraine*. Dr. Sacks is an extremely insightful neurologist with a gift for writing and who himself had migraines beginning at age 2. He has collected an astonishing series of patient stories with both common and extremely unusual symptoms, all attributable to migraine mechanisms.

Treatment Guidelines for Physicians

For treatment we first encourage a strict migraine control diet, eliminating common migraine culprits including chocolate, wines, caffeine, certain cheeses, monosodium glutamate (MSG) as well as less frequently recognized problem foods containing yeast (yoghurt, sourdough, freshly made bread), nuts, and nut products. Glutamate can occur in foods not only through the addition of MSG, but also by hydrolyzing (breaking down) proteins. So labels that include "hydrolyzed casein," "hydrolyzed yeast extract," etc., are likely to include glutamate.

We also encourage a regular sleep schedule and aerobic exercise program. Patients are also counseled to avoid vasoconstrictive medications such as psuedoephedrine, and to minimize the use of triptans, which may cause rebound symptoms.

Dr. Michael Teixido, MD – Jefferson Medical College
Dr. John Carey, MD - Johns Hopkins Otolaryngology-Head & Neck Surgery
Updated May 14, 2014

When patients follow these guidelines and still have migraine-associated symptoms, we emphasize prophylactic medications in preference to the "quick fix" agents such as fiorinal, triptans, narcotics, or steroids. Effective prophylactic medications are chosen based on the patient's other medical problems and tolerance of side effects. Some suggested regimens follow:

Calcium channel blockers: Diltiazem CD 120 mg/d increasing as tolerated to 240-480 mg total/d, often in two divided doses. Constipation and hypotension are the most common side effects, but this is often the best-tolerated regimen.

Antidepressants: Nortriptyline starting at LOW doses (10 mg/d) and slowly increasing to 50-100 mg at night. Higher doses (100-200 mg) may occasionally be needed. Levels can help guide therapy. Dry mouth, weight gain, and sedation are the most common side effects. Patients with poor sleep often benefit the most from these agents.

Selective serotonin reuptake inhibitor (SSRI) agents have less proven benefit in migraine control. We have found mixed agents helpful, such as venlafaxine (Effexor). The full starting dose of Effexor XR 37.5 mg can have prominent serotonergic effects, including, on occasion, panic attacks. But the Effexor XR 37.5mg capsules can be opened, and the dose divided in into two or three parts. Each part can be placed in a closed gelatin capsule and taken as a low starting dose once daily for a week. The dose can be gradually increased to the full 37.5 mg. As the dose is increased, the drug has greater effects on blocking norepinephrine reuptake, which may be the salient effect on migraine. So patience is necessary as a long time may be needed to reach a fully therapeutic dose. Heart rate and blood pressure should be monitored, as these can be dose-limiting

Beta-blockers: Propranolol LA 60 mg/d increasing as needed up to 160 mg/d. Reactive airway disease (e.g., asthma) and diabetes are usually contraindications. Depression may be worsened by beta-blockers. Nadolol has fewer such CNS side effects; it is started at 20 mg/d and increased as needed up to 120 mg/d.

Anticonvulsants: Topiramate has been shown to be a very effective migraine prophylactic agent. It is started at 25 mg daily and increased weekly to a goal of 100-200 mg twice daily. Patients often report cognitive slowing ("brain fog") when they start this medication, but this usually resolves over a few weeks with this plan for a slow increase in the dose. The main side effect at higher doses is a tingling sensation. Rarely, patients can develop kidney issues - metabolic acidosis or kidney stones. If there is a history of stones, regular monitoring of the urine may be necessary.

Sodium valproate 250-500 mg BID is usually well tolerated, but liver function tests and platelets should be monitored. Gabapentin is usually well tolerated. It is started at a low dose of 300 mg a day, with weekly escalating

doses to a first target dose of 300 mg three times a day (900 mg total). Then it can be increased gradually to another target dose of 1800 mg total a day (in 3 divided doses), or until side effects (usually sedation) appear. It has the inconvenience of frequent dosing, but with a low adverse effect profile. Dosing adjustments are necessary for renal insufficiency, and the medication should not be used in children under 12 years old.

All patients are cautioned that migraine symptoms often do not respond quickly to these interventions. Great patience is required of the patient and physician as 6-8 weeks of diet changes or the full dose of any new medication may be needed before benefits are seen.

Anxiety, depression, and even panic attacks are frequent accompanying diagnoses in these patients. These diagnoses should be recognized and discussed. The choice of a prophylactic medication may also be influenced by these other conditions.

One of the best resources for migraine therapeutics currently available is Lawrence Robbins' *Management of Headache and Headache Medications*. It very clearly outlines strategies for first line, second line, and combination therapy for migraine and other headache types in an easy-to-use handbook format.

BIBLIOGRAPHY

1. Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2001;41(7):646-657.
2. http://www.cdc.gov/nedss/
3. http://www.arthritis.org
4. http://www.census.gov
5. Lipton RB, Stewart WF. Migraine in the United States: a review of epidemiology and health care use. *Neurology*. 1993;43 (suppl 3):S6-S10.
6. Stewart WF, Linet MS, Celantano DD, et al. Age- and sex-specific incidence rates of migraine with and without visual aura. *Am J Epidemiology*. 1991;134:1111-1120.
7. Lipton RB, Stewart WF, Simon D. Medical consultation for migraine: results from the American Migraine Study. *Headache*. 1998;38:87-96.
8. Lipton RB, Scher AI, Kolodner K, et al. Migraine in the United States: epidemiology and patterns of health care use. *Neurology*. 2002;58(6):885-894.
9. Vinson DR. Treatment patterns of isolated benign headache in US emergency departments. *Ann Emerg Med*. 2002;39(3):215-222.
10. Lipton RB, Stewart WF. Acute migraine therapy: do doctors understand what patients with migraine want from therapy? *Headache*. 1999;39 (suppl 2):S20-S26.
11. Lance JW, Goadsby PJ. *Mechanism and Management of Headache*. London, England: Butterworth-Heinemann; 1998.
12. Silberstein SD, Lipton RB, Goadsby PJ. *Headache in Clinical Practice*. 2nd ed. London, England: Martin Dunitz; 2002.

13. Olesen J, Tfelt-Hansen P, Welch KMA. *The Headaches*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000.
14. Honkasalo ML, Kaprio J, Winter T, et al. Migraine and concomitant symptoms among 8167 adult twin pairs. *Headache*. 1995;35:70-78.
15. Ophoff RA, Terwindt GM, Vergouwe GM, et al. Familial hemiplegic migraine and episodic ataxia type-2 are caused by mutations in the Ca2+ channel gene CACNL1A4. *Cell*.1996;87:543-552.
16. May A, Ophoff, RA, Terwindt GM, et al. Familial hemiplegic migraine locus on chromosome 19p13 is involved in common forms of migraine with and without aura. *Hum Genet*. 1995;96(5):604-608.
17. Nyholt DR, Lea RA, Goadsby PJ, et al. Familial typical migraine: linkage to chromosome 19p13 and evidence for genetic heterogeneity. *Neurology*. 1998;50:1428-1432.
18. Peroutka SJ, Wilhoit T, Jones K. Clinical susceptibility to migraine with aura is modified by dopamine D2 receptor (DRD2) NcoI alleles. *Neurology*. 1997;49:201-206.
19. Welch KM, D'Andrea G, Tepley N, et al. The concept of migraine as a state of central neuronal hyperexcitability. *Neurol Clin*. 1990;8(4):817-828.
20. D'Andrea G, Cananzi AR, Joseph R, et al. Platelet excitatory amino acids in migraine. *Cephalalgia*. 1989;9 (Suppl 10):105-106. [Poster Presentation]
21. Ferrari MD, Odink J, Bos KD, et al. Neuroexcitatory plasma amino acids are elevated in migraine. *Neurology*. 1990;40(10):1582-1586.
22. Wang W, Schoenen J. Interictal potentiation of passive "oddball" auditory event-related potentials in migraine. *Cephalalgia*. 1998;18(5):261-265.
23. Aurora SK, CaoY, Bowyer SM, Welch KM. The occipital cortex is hyperexcitable in migraine: experimental evidence. *Headache*. 1999;39(7):469-476.
24. Wray SH, Mijovic-Prelec D, Kosslyn SM.Visual processing in migraineurs. *Brain*. 1995;118 (Pt 1):25-35.
25. Afridi SK, Matharu MS, Lee L et al. A PET study exploring the laterality of brainstem activation in migraine using glyceryl trinitrate. *Brain*. 2005;128:932-939.
26. Lashley KS. Patterns of cerebral integration indicated by the scotomas of migraine. *Arch Neurol Psych*. 1941;46:331-339.
27. Lauritzen M. Pathophysiology of the migraine aura. The spreading depression theory. *Brain*. 1994;117(Pt 1):199-210.
28. Olesen J, Friberg L, Olsen TS, et al. Timing and topography of cerebral blood flow, aura, and headache during migraine attacks. *Ann Neurol*. 1990;28(6):791-798.
29. Woods RP, Iacoboni M, Mazziotta JC. Brief report: bilateral spreading cerebral hypoperfusion during spontaneous migraine headache. *N Engl J Med*. 1994;331(25):1689-1692.
30. Hadjikhani N, Sanchez Del Rio M, Wu O, et al. Mechanisms of migraine aura revealed by functional MRI in human visual cortex. *Proc Natl Acad Sci USA*. 2001;98(8):4687-4692.

31. Cutrer FM, Sorensen AG, Weisskoff RM, et al. Perfusion-weighted imaging defects during spontaneous migrainous aura. *Ann Neurol.* 1998;43(1):25-31.
32. Goadsby, PJ, Lipton RB, Ferrari, MD. Migraine. Current Understanding and Treatment, Jan. 24, 2002 New England Journal of Medicine, No. 4, Volume 346:257-270 Copyright (C) 2002. Massachusetts Medical Society. All rights reserved.
33. Knight YE, Edvinsson L, Goadsby PJ. Blockade of calcitonin-gene-related peptide release after superior sagittal stimulation in cat: a comparison of avitriptan and CP122,288. *Neuropeptides.* 1999;33(1):41-46.
34. Ray BS, Wolff HG. Experimental studies on headache. Pain sensitive structures of the head and their significance in headache. *Arch Surg.* 1940;41:813-856.
35. Goadsby PJ. Pathophysiology of headache. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain.* 7th ed. New York, NY: Oxford University Press; 2001:57-72.
36. Cutrer FM, Limmroth V, Woeber C, et al. New targets for antimigraine drug development. In: Goadsby PJ, Silberstein SD, eds. *Headache: Bluebooks of Practical Neurology. Vol. 17.* Philadelphia, PA: Butterworth-Heinemann; 1997:59-120.
37. Burstein R, Cutrer MF, Yarnitsky D. The development of cutaneous allodynia during a migraine attack: clinical evidence for the sequential recruitment of spinal and supraspinal nociceptive neurons in migraine. *Brain.* 2000;123 (Pt 8):1703-1709.
38. Diener HC et al. A practical guide to the management and prevention of migraine. *Drugs.* 1998; 56(5):811-824.
39. Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2000;55(6):754-762.
40. Lipton RB, Stewart WF, Ryan RE. Efficacy and safety of acetaminophen, aspirin, and caffeine in alleviating migraine headache pain: three double-blind, randomized, placebo-controlled trials. *Arch Neurol.* 1998;55(2):210-217.
41. Goadsby PJ. The pharmacology of headache. *Prog Neurobiol.* 2000;62(5):509-525.
42. Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT(1B/1D) agonists) in acute migraine treatment: a meta-analysis of 53 trials. *Lancet.* 2001;358(9294):1668-1675.
43. Worldwide Product Safety and Pharmacovigilance Document. December 1999.
44. Gray RN, Goslin RE, McCrory DC, et al. *Drug Treatments for the Prevention of Migraine Headache.* Technical Review 2.3. Duke University: US Department of Health and Human Services, Agency for Health Care Policy and Research; February 1999. NTIS Accession No. PB99-127953. Available at: http://www.clinpol.mc.duke.edu/.
45. Lipton RB, Diamond S, Reed M, et al. Migraine diagnosis and treatment: Results from the American Migraine Study II. *Headache.* 2001;41(7):638-645.

46. Rasmussen BK, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population – a prevalence study. *J Clin Epidemiol.* 1991;44:1147-1157.
47. Raskin NH. *Headache.* 2nd ed. New York: Churchill Livingstone; 1988.
48. Barbanti P, Fabbrini G, Pesare M, Cerbo R. Neurovascular symptoms during migraine attacks. [abstract] *Cephalalgia.* 2001;21(4):295.
49. Kaniecki R. Migraine headache exacerbation with sumatriptan injection: a sign of supratherapeutic dosing? [abstract] Cephalalgia. 2001;21(4):413.
50. Kayan A, Hood JD. Neuro-otological manifestations of migraine. *Brain.* 1984;107:1123.
51. Wladislavosky-Waserman P, Facer G et al. Meniere's disease: a 30-year epidemiologic and clinical study in Rochester, MN, 1951-*1980. Laryngoscope.* 1996;94:1098-1102.
52. Vass Z, Dai CF et al. Co-localization of the vanilloid capsaicin receptor and substance P in sensory nerve fibers innervating cochlear and vertebro-basilar arteries. *Neuroscience.* 2004;124:919-927.
53. Buchholz D. *Heal your Headache the 1-2-3 Program.* Workman Publishing Company, New York, NY. 2002.
54. Sacks O. *Migraine.* Vintage Books, New York, NY. 1992.
55. Robbins L. *Management of Headache and Headache Medications, 2nd Edition.* Springer-Verlag, New York, NY. 2000.

The following website compiles many of the references related to migraine associated vertigo and has an active forum on the subject:
www.mvertigo.org

The Headache Center

Migraine Diet

(Thanks to Dr. Jason Rosenberg and the Johns Hopkins Headache Center for this compilation, which we have modified from our experience.)

Food may play a significant role in the frequency of migraine. Although some migraine patients find that eating certain foods will provoke symptoms every single time, the effect of diet may be less obvious. In general, the more "trigger" foods you consume, the more symptoms you may have. The hope is that by avoiding these possible triggers, the better off you will be. Eating regularly timed meals, avoiding hunger, avoiding dehydration, and avoiding skipping meals is probably more important than the specific foods you do or do not eat. Try following this list as strictly as possible for at least two months. If it helps, you may gradually add back your favorite foods one at a time, keeping track of your headaches as you do so.

Category	Foods to Avoid, Reduce, or Limit	Foods that are OK
Caffeine	No more than 2 servings / day. Do not vary the amount or timing from day to day. Coffee, tea, colas, Mountain Dew, Sunkist, certain medications (Anacin, Excedrin)	Decaffeinated coffee, herbal or green tea, caffeine-free sodas, fruit juice (see below)
Snacks / Desserts	**Chocolate**, **nuts** (peanuts, especially), **peanut butter**, seeds	Fruits listed below, sherbet, ice cream, cakes, pudding, Jello, sugar, jam, jelly, honey, hard candy, cookies made w/o chocolate or nuts
Alcohol	Avoid all, especially: ales, Burgundy, chianti, malted **beers**, **red wine**, sherry, vermouth. Note: some medications contain alcohol (Nyquil)	Non-alcoholic beverages
Dairy	**Aged cheeses**: Brie, blue, boursault, brick, Camembert, cheddar, Emmenlalaer, gouda, mozzarella, Parmesan, Provolone, Romano, Roquefort, stilton, Swiss, etc. Buttermilk, chocolate milk, sour cream Eggs and **yogurt** should be limited to 2-3 times per week	Other cheeses: American, cottage, cream cheese, farmer, ricotta, Velveeta. Milk, Egg substitute
Cereals & Grains	Fresh breads and **yeast products**, fresh bagels, fresh doughnuts, yeast extracts, brewer's yeast, sourdough (*freezing bread may inactivate yeast)	Commercial breads (white, wheat, rye, multi-grain, Italian), English Muffins, crackers, rye, toast, bagels, potatoes, rice, spaghetti, noodles, hot or dried cereals, oatmeal
Meats	Aged, canned, cured, or **processed meats** (bologna, pepperoni, salami, other pre-packaged deli meats), pickled meats or fish, salted or dried meats or poultry, hot dogs, sausages, jerky	Fresh / unprocessed meats, poultry, fish, lamb, pork, veal, lamb, tuna
MSG (monosodium glutamate)	Avoid **glutamate** in all its multiple forms: MSG, "natural flavoring," "flavor enhancer," etc. Soy sauce, foods containing "hydrolyzed protein products" or "autolyzed yeast", canned soups, bouillon cubes, Accent, meat tenderizers, seasoned salts. Pickled, preserved or marinated foods	Salt and other spices, butter, margarine, cooking oil, white vinegar, salad dressing (small amounts)
Sweeteners	Aspartame (Equal, Nutrasweet) (somewhat controversial)	Sucrose (sugar), high fructose corn syrup, sucralose (Splenda), saccharin (Sweet 'n Low)
Vegetables	Pole or broad beans, lima beans, Italian beans, lentils, snow peas, fava beans, Navy beans, pinto beans, pea pods, sauerkraut, garbanzo beans, **onions**, **olives**, pickles	Asparagus, beets, broccoli, carrots, corn, lettuce, pumpkins, spinach, squash, string beans, tomatoes– all those not listed
Fruit	**Avocados**, figs, papaya, passion fruit, raisins, red plums. Limit **bananas** and **citrus fruit** & juice (orange, lemon, lime, grapefruit, tangerines) to ½ cup per day	Apples, berries, peaches, pears, prunes, fruit cocktail
Mixed Dishes	Beef stroganoff, cheese blintzes, frozen meals / TV diners, lasagna, macaroni and cheese, pizza	

Note that tyramine, nitrites, nitrates, and MSG are found in many foods and may be difficult to avoid. Learn to read labels.

While there are few consistent scientific studies of the effect of food on headaches, there is a general consensus about which foods may be important to avoid. The above list is drawn from various sources including the National Headache Foundation, journal articles, websites and books (such as David Buchholz's *Heal Your Headache: The 1-2-3 Program for Taking Charge of Your Pain*).

The Headache Center

Vitamins and Dietary Supplements

Certain vitamins and food supplements may provide a benefit in terms of headache prevention. Many unsubstantiated claims can be found on the internet and at health food stores. The best evidence exists for the agents below (published peer reviewed, randomized controlled trials, albeit small ones in some cases). Side effects are typically mild.

- B2/Riboflavin – up to 400mg / day
- Magnesium – up to 400mg 2x / day (diarrhea possible)
- Coenzyme Q_{10} – up to 100mg 3x / day (expensive)

Note: There are a few companies that package more than one of the above vitamins / supplements into a single pill for convenience. One such product is "Migravent", info. available at http://www.migravent.com.; another is "MigreLief", info. available at http://www.migrelief.com.

- Melatonin – There is some weaker evidence that melatonin, a hormone that helps regulate sleep, may help headaches if 3–6 mg is taken an hour or so before bedtime. Significant side effects are rare. Probably most useful in treating cluster headaches.

The following are used in Europe more commonly, but are less regulated or reliable in the US:

- Butterburr (*Petasites hybridus*) extract, Petadolex brand (pyrrolizidine alkaloid free), 50–75mg twice a day with food (expensive)
- Feverfew (*Parthenium integrifolium*) 50mg+ per day (inexpensive)

We do not specifically endorse any brand name item, nor do we have any financial interest in any of these products.