

# Migraine Headaches

## WHAT IS HEADACHE?

### General Definition of Headaches

When a person has a headache, the pain does not originate in the brain itself (which is insensitive to pain) but in one or more of the following locations:

- The tissues covering the brain.
- The attaching structures at the base of the brain.
- Muscles and blood vessels around the scalp, face, and neck.

Headache is generally categorized as primary or secondary.

*Primary Headache.* A headache is considered primary when a disease or other medical condition does not cause it.

- Tension headache is the most common primary headache and accounts for 90% of all headaches.
- Neurovascular headaches are the second most frequently occurring primary headaches and include migraines (the more common) and cluster headaches. Such headaches are caused by an interaction between blood vessel and nerve abnormalities.

*Secondary Headache.* Secondary headaches are caused by other medical conditions, such as sinusitis infection, neck injuries or abnormalities, and stroke. About 2% of headaches are secondary headaches caused by abnormalities or infections in the nasal or sinus passages (sinus headaches). [See *Box Causes of Secondary Headache.*]

It is not uncommon for someone to experience a combination of headache types.

### Migraine Headaches: General Description of its Course

Migraine is now recognized as a chronic illness, not simply as a headache. Migraines are defined by whether auras accompany them or not:

- *Common migraines* are without auras. About 75% of migraines are the common type.
- *Classic migraines* are those with auras.

A person may experience one or the other at different times. [For a more detailed description see *Box Definitions of Classic and Common Migraine Attacks.*]

In general, there are four symptom phases to a migraine (although they may not all occur in every

patient): the prodrome, auras, the attack, and the postdrome phase.

*Prodrome.* The prodrome phase is a group of vague symptoms that may precede a migraine attack by several hours, or even a day or two. Such prodrome symptoms can include the following:

- Sensitivity to light or sound.
- Changes in appetite.
- Fatigue and yawning.
- Malaise.
- Mood changes.
- Food cravings.

*Auras.* Auras are sensory disturbances that occur before the migraine attack in between 20% and 25% of patients. Visually, auras are referred to as being positive or negative:

- Positive auras include bright or shimmering light or shapes at the edge of their field of vision called *scintillating scotoma*. They can enlarge and fill the line of vision. Other positive aura experiences are zigzag lines or stars.
- Negative auras are dark holes, blind spots, or tunnel vision (inability to see to the side).
- Patients may have mixed positive and negative auras. This is a visual experience that is sometimes described as a fortress with sharp angles around a dark center.

Other neurologic symptoms may occur at the same time as the aura, although they are less common. They include the following:

- Speech disturbances.
- Tingling, numbness, or weakness in an arm or leg.
- Perceptual disturbances such as space or size distortions.
- Confusion.

*Migraine Attack.* If untreated, attacks usually last from four to 72 hours. A typical migraine attack produces the following symptoms:

- Throbbing pain on one side of the head. The word migraine, in fact, is derived from the Greek word *hemikrania*, meaning "half of the head" because the pain of migraine often occurs on one side. Pain also sometimes spreads to affect the entire head.
- Pain worsened by physical activity.
- Nausea, sometimes with vomiting.
- Visual symptoms.

- Facial tingling or numbness.
- Extreme sensitivity to light and noise.
- Looking pale and feeling cold.

*Postdrome.* After a migraine attack, there is usually a postdrome phase, in which patients may feel exhausted and mentally foggy for a while.

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## **DEFINITIONS OF CLASSIC AND COMMON MIGRAINE ATTACKS**

### **Migraines without Auras (Common Migraine)**

*Definition of Migraine Without Auras.* To be defined as a migraine without aura, a patient should have at least five attacks that have the following characteristics:

- A. Each untreated, or unsuccessfully treated, attack must last four to 73 hours.
- B. It must have at least two of the following four qualities:

minutes or two or more aura symptoms occur in succession.

- No single aura symptom lasts more than an hour. (There may be successive aura symptoms, however, that extend that time, but each one should not last more than 60 minutes.)
- The headache itself may begin before, at the same time, or at an interval of no more than an hour after the hour.

As with common migraines, other neurologic or medical conditions that might be causing this pain must be ruled out or if they occur, they are not related in time to the suspected migraine.

## Other Migraine Variations

Although migraine is considered to be a specific chronic illness, it has a number of various presentations that occur in different individuals.

*Ophthalmoplegic Migraine.* This very rare headache tends to occur in younger adults. The pain centers around one eye and is usually less intense than in a standard migraine. It may be accompanied by vomiting, double vision, a droopy eyelid, and paralysis of eye muscles. Attacks can last from hours to months. A CT or MRI scan may be needed to rule out an aneurysm (a rupture blood vessel) in the brain.

*Retinal Migraine.* Symptoms of retinal migraine are short-term blind spots or total blindness in one eye that lasts less than an hour. A headache may precede or occur with the eye symptoms. Sometimes retinal migraines develop without headache. Other eye and neurologic disorders must be ruled out.

*Basilar Migraine.* Considered a subtype of migraine with aura, this migraine starts in the basilar artery, which forms at the base of the skull. It occurs mainly in young people. Symptoms may include vertigo (the room spins), ringing in the ears, slurred speech, unsteadiness, possibly loss of consciousness, and severe headaches.

*Familial Hemiplegic Migraine.* This is a very rare inherited genetic migraine disease. It can cause temporary paralysis on one side of the body, vision problems, and vertigo. These symptoms occur about 10 to 90 minutes before the headache.

*Status Migrainosus.* This is a serious and rare migraine that is so severe and prolonged that it requires hospitalization.

*Menstrual Migraines.* About half of women with migraines report an association with menstruation. Experts believe, however, that *true* menstrual migraines are less common than thought. True menstrual migraines tend not to have auras and to increase in prevalence between two days before and five days after the onset of their period.

## Persistent Migraines

In some cases, migraine patients eventually experience on-going and chronic headaches. They may be caused by the following conditions.

*Rebound Headache.* The most common cause of chronic migraine is the so-called rebound effect, which is a cycle caused by overuse of migraine medications. The process involves the following:

- Patients typically have taken pain medication for more than three days a week on an ongoing basis.
- When the patients stop taking them, they experience a rebound headaches.
- They start taking the drugs again.
- Eventually the headache simply persists and medications are no longer effective.

Medications implicated in rebound migraines include simple painkillers (e.g., acetaminophen, aspirin, ibuprofen), barbiturates, sedatives, narcotics, and migraine medications, particularly those that also contain caffeine. (Heavy caffeine use can also cause this condition.)

*Transformed Migraines.* In some cases, migraines themselves evolve into chronic, daily headaches called transformed migraines. Such headaches resemble tension headaches but are more likely to be accompanied by gastrointestinal distress and mental or visual disturbances and, in women, to be affected by menstrual cycles.

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## **OTHER PRIMARY HEADACHES**

*Tension Headache.* Tension headache is often experienced in the following locations:

- In the forehead.
- In the back of the head and neck.
- In both regions.

It is typically described as a tight feeling, as if the head were in a vise. Soreness in the shoulders or neck is common. These headaches can last minutes to days and may occur daily in some sufferers. Tension headaches do not cause nausea or limit activities as migraine headaches do, although depression, anxiety, and sleeping problems may accompany persistent headaches. They sometimes evolve in people who initially experience migraines, and, in such cases, can become chronic and difficult to treat. [For more information on tension headaches see *Headache*.]

*Cluster Headache.* Cluster headaches are very painful events. Patients typically

- Feelings of intense restlessness are common. People in the throes of a cluster headache may pace the floor or may even bang their heads against the wall in an attempt to cope with the pain.
- Cluster headaches often have a cycle with the following pattern:
- Attacks themselves are usually brief, lasting between 30 and 90 minutes, although they can persist for up to three hours.
- During an active period, sufferers can experience as few as one attack every other day to one or more daily. In a rare form of cluster headache, known as chronic paroxysmal hemicrania, as many as six attacks per day can occur.
- An active period of recurrent cluster attacks typically extends over four to 12 weeks.
- Headache-free periods last several months to even years.

[For more information on cluster headaches see *Headache*.]

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## CAUSES OF SECONDARY HEADACHES

About 90% of people seeking help for headaches have a primary headache disorder. The balance of secondary headaches, however, is caused by an underlying disorder that produces the headache as a symptom. Many conditions cause headache as a symptom. Some of the most common are listed below.

*Sinus Headache.* Many primary headaches, including migraine, are misdiagnosed as sinus headache. Sinus headaches can occur in the front of the face, usually around the eyes, across the cheeks, or over the forehead. They are usually mild in the morning and increase during the day and are usually accompanied by fever, runny nose, congestion, and general debilitation. Sinus headaches spread over a larger area of the head than migraines, but it is often difficult to tell them apart, particularly if headache is the only symptom of sinusitis; they even coexist in many cases. Often, the visual changes associated with migraine can rule out sinusitis, but such visual changes do not occur with all migraines. (In rare cases, sinusitis can cause double vision and even vision loss, a sign of very serious infection.) [For more information, see *Well-Connected Report #62, Sinusitis*.]

*Headache Due to Neck Problems.* Some headaches may be caused by abnormalities of the neck muscles resulting from prolonged poor posture (such as that caused by sitting in front of a computer keyboard or driving daily for long periods), arthritis, injuries of the upper spine, or abnormalities in the cervical spine (the spinal bones in the neck). Nerves in the neck converge in the

trigeminal nerve in the face and can generate pain signals that the brain may interpret as headache. Pain is usually on one side; even if it affects both sides of the head it is usually more severe on one side. The quality of the headache may be similar to an aching tension headache or a mild migraine without aura.

*Temporomandibular Joint Dysfunction (TMJ).* TMJ is caused by clenching the jaws or grinding the teeth (usually during sleep), or by abnormalities in the jaw joints themselves. The diagnosis is easy if chewing produces pain or if jaw motion is restricted or noisy. TMJ pain can occur in the ear, cheek, temples, neck, or shoulders.

*Glaucoma.* Acute glaucoma is caused by increased pressure in the eye and requires immediate medical attention. Throbbing pain may be felt around or behind the eyes or in the forehead. Patients have redness in the eye and may see halos or rings around lights.

*Brain Tumor.* Fear of brain tumor is common among people with headaches, but headache is almost never the first or only sign of a tumor. Changes in personality and mental functioning, vomiting, seizures, and other symptoms are more likely to appear first. When the headache does develop, it is often worse early in the morning or may awaken sufferers during the night.

*Neuralgia.* Neuralgia is pain due to nerve abnormalities, which can occur in the facial area and resemble migraine or sinus headaches.

*Hypertension.* Although many people attribute headaches to high blood pressure, the two are rarely associated. An exception is malignant hypertension, an uncommon medical emergency, in which the blood pressure abruptly rises to extreme levels, causing damage to blood vessels in the brain, heart, and kidneys.

*Strokes Caused by Blood Clots or Hemorrhages.* A blood clot or hemorrhage in the brain leading to a stroke can cause a severe headache, sometimes referred to as a thunderclap headache when it is very sudden and severe. The onset of such a headache, particularly if it is associated with confusion, stupor, or other neurologic symptoms, mandates prompt medical attention. It is important to determine if a clot or bleeding is causing the stroke, since treatments are very different.

*Head Injuries.* It is obvious that a significant blow to the head will cause pain. Post-injury headaches, however, can reflect serious damage, ranging from skull fractures to internal bleeding.

*Disorders of the Meninges.* The meninges are the membranes covering the brain and the spinal cord. In very rare instances, ordinary physical strain may injure or weaken the meninges, causing a leakage of cerebrovascular fluid (the fluid that bathes the brain). This can cause severe headache and nausea, which are relieved by lying flat. The condition is very treatable. Meningitis, which is an infection or irritation of these membranes, is an uncommon but potentially serious cause of severe headache. Other symptoms include nausea and stiffness or pain in the neck.

*Gynecologic Problems.* Many clinicians have anecdotally linked gynecologic problems, such as ovarian cysts and menstrual disorders, to chronic

headaches, and new data are emerging to support this association.

*Temporal (Giant Cell) Arteritis.* Certain causes of headaches are unique to the elderly, such as temporal arteritis, also called giant cell arteritis. Inflammation in arteries that carry blood to the head, neck, and sometimes the upper part of the body can cause very severe headaches. The risk for this headache is highest in people over age 70, especially among women, people of European heritage, and patients with polymyalgia rheumatica.

*Miscellaneous Causes of Benign Headaches.* Rapid consumption of ice cream or other very cold foods or beverages is the most common trigger of sudden headache pain, which may be prevented by warming the food or drink for a few seconds in the front of the mouth before swallowing. Other common benign causes of headache include eyestrain, dental problems, allergies, systemic infections, and caffeine withdrawal. Headaches may be induced by sexual activity or intense physical exertion. Leakage from spinal cord fluid is rare but can cause headaches that may be mistaken for brain tumors.

## **HOW SERIOUS ARE MIGRAINES?**

### **Possibility for Remission**

In many people migraines eventually go into remission and sometimes disappear completely, particularly as people age. Estrogen decline after menopause may be responsible for remission in some older women. One study reported that the following people with migraines (called *migraineurs*) have a better chance of remission:

- Those with a family history of migraine with aura.
- People with migraines that are not triggered by light.
- People with no other primary headaches.

According to another study a history of head trauma or oral contraceptive use predicted a *poorer* long-term outlook.

### **Risk for Stroke**

Studies have found that migraine or severe headache is a risk factor for stroke in both men and women, especially before age 50. About 19% of all strokes occur in people with a history of migraine. Migraine with aura carries a higher risk for stroke than without auras. Interestingly, a 2001 study reported that in people who experienced migraine-related stroke, the frequency of migraines declined afterward.

The actual risk itself for migraineurs is low, however, as indicated by one study:

- Women with migraines had a 2.7% risk of stroke, with the time of greatest risk between the ages of 45 and 65.



- Men with migraines had a 4.6% risk and their greatest time of risk was before age 45.

In both genders, the risk diminished with age.

Studies suggest specific risk factors for younger women with migraines, particularly those with auras:

- Taking high-estrogen oral contraceptives (OCs). (Whether progesterone-alone contraceptives carry any risk is unknown.)

In migraineurs who take OCs, the risk increases with one or more of the following:

- High blood pressure.
- Smoking.

## **Emotional Disorders and Quality of Life**

Anxiety (particularly panic disorders) and major depression are strongly associated with migraines. In one 2000 study, for example, 47% of migraine patients had depression. There does not appear to be any causal relationship, although headache and emotional disorders may have some common biologic factors.

In any case, the negative impact of migraines on quality of life, families, and even work productivity is significant and often underrated as a serious complication. Studies indicate that people with migraines have poorer social interactions and emotional health than patients with chronic medical illnesses, including asthma, diabetes, and arthritis.

## **Migraine and Pregnancy**

*Effect of Pregnancy on Migraines.* In one study, pregnant women with tension or migraine headaches experienced 80% fewer headaches, usually after the end of the first trimester.

*Effect of Migraine on the Pregnant Woman or Fetus.* Migraine headaches do not pose any added risks during pregnancy to the mother or the fetus, although women with migraines may be at higher risk for having smaller (but not premature) babies.

## **WHAT CAUSES MIGRAINE HEADACHES?**

Until recently, the general theory on the migraine process rested solely on the idea that abnormalities of blood vessel (vascular) systems in the head were responsible for migraines. Now, however, experts tend to believe that migraine starts with an underlying central nervous system disorder, which, when triggered by various stimuli, sets off a chain of neurologic and biochemical events, some of which subsequently affect the brain's vascular system. No experimental model fully explains the migraine process.

There is certainly a strong genetic component in migraine with or without auras. Researchers

have located a single genetic mutation responsible for the very rare familial hemiplegic migraine, but a number of genes are likely to be involved in the great majority of migraine cases. A number of chemicals, structures, nerve pathways, and other players involved in the process are under investigation.

## General Theories to Explain Migraine

*Central Nervous Disorder.* One theory that attempts to integrate many of the known events in the migraine process is as follows:

- Stress or some unknown factor triggers the release of certain protein fragments called peptides (e.g., Substance P, calcitonin gene-related peptide, and others).
- These peptides dilate blood vessels and produce an inflammatory response that triggers over-excitation of the nerve cells in the *trigeminal pathway*. (This nerve pathway runs from the brain stem to the head and face. These nerves spread to the *meninges* (the membrane covering of the brain).)
- While the brain itself is insensitive to pain, the meninges and blood vessels around the brain are sensitive to pain. Some experts suggest that pain occurs when blood drains from the center of the head to the blood vessels around the brain.
- Auras are believed to be a response to blood flow changes that cause a rapid reduction in brain activity that reaches the cerebral cortex (the outer layer of the brain), referred to as *spreading depression*. This effect may be visualized as an electrical wave spreading through the brain just as a wave of water is caused by the dropping of a pebble. Some research suggests that in people with auras, the cortical spreading depression itself activates the inflammation in the trigeminal nerves that triggers pain in the meninges.

*Abnormal Calcium Channels.* Some migraines may be due to abnormalities in the channels within cells that transport the electrical ions calcium, magnesium, sodium, and potassium. Calcium channels appear to play a particularly critical role in migraine patients:

- Calcium channels regulate the release of serotonin, an important *neurotransmitter* in the migraine process. (A neurotransmitter is a chemical messenger that allows communication between nerves in the brain.)
- Magnesium interacts with calcium channels and magnesium deficiencies have been detected in the brains of migraine patients.
- Calcium channels also play a major role in cortical spreading depression, the brain event that appears to be important in migraine symptoms.

Some patients with migraine may inherit one or more factors that impair calcium channels, making them susceptible to headaches. For example, mutations in a gene that encodes calcium channels appears to be responsible for familial hemiplegic migraine.

## The Role of Serotonin and Other Neurotransmitters

Neurotransmitters are chemical messengers in the brain. Two important ones, serotonin and dopamine, appear to be critical in the processes leading to migraine.

*Serotonin.* Serotonin (also called 5-hydroxytryptamine or 5-HT) is involved in regulation of pain perception and depression, among other important functions.

The receptors for serotonin implicated in migraine are found on the trigeminal nerve endings. Serotonin appears to block the peptides involved in over-stimulating these nerves and producing inflammation. A number of studies have reported the following findings to suggest that serotonin serves as a brake in the migraine process:

- Higher-than-normal levels of a serotonin compound are excreted in urine.
- Levels of serotonin in the blood decline.
- Drugs that target receptors in the brain for serotonin are generally effective in stopping a migraine.

*Dopamine.* Dopamine, another important neurotransmitter, may act as a *stimulant* of the migraine process. Some evidence suggests that certain genetic factors make people over-sensitive to the effects of dopamine, which include nerve cell excitation. Such nerve-cell over-activity could trigger the events in the brain leading to migraine. The prodromal symptoms (mood changes, yawning, drowsiness), for example, have been associated with increased dopamine activity. Dopamine receptors are also involved in regulation of blood flow in the brain.

## **Other Factors Involved in Migraine**

*Reduced Magnesium Levels.* Researchers have also noted a drop in magnesium levels before or during a migraine attack. Magnesium plays a role in nerve cell function; reduced levels could be a destabilizing factor, causing the nerves in the brain to misfire, possibly even accounting for the auras that many sufferers experience.

*Hypotension.* One study suggested that some migraine headaches might be precipitated by a sudden drop in blood pressure (hypotension). (Conversely, some cases have suggested that migraine may *cause* hypotension.)

## **Migraine Triggers**

A wide range of events and conditions can alter conditions in the brain that bring on nerve excitation and trigger migraines. They include, but are not limited to the following:

- Emotional stress (although the headaches often erupt after the stress has eased).
- Intense physical exertion (such as after lifting, athletic endeavor, and even bowel movements or sexual activity).
- The female hormones progesterone and estrogen. Most likely hormone *fluctuation*, rather than whether levels are elevated or low, are the triggers of migraines. More research is needed to determine each hormone's precise effects.
- Abrupt weather changes (such as Chinook winds).
- Bright or flickering lights.

- High altitude.
- Travel motion.
- Changes in sleep patterns.
- Low blood sugar has been known to trigger headaches and fasting can often precipitate migraines.

**Chemicals found in certain foods may trigger headaches in some people. More than 100 foods have the capacity to trigger migraine headache. [ See Table Foods That May Trigger Migraines under How Can Migraine Headaches Be Prevented?.]WHO GETS MIGRAINE HEADACHES?**

## Gender

Migraine affects between 15% to 20% of women and 6% to 14% of men. This significantly greater incidence in women holds throughout the world and in every culture. Although the incidence of migraine is similar for boys and girls during childhood, it increases in girls after puberty.

*Hormone Fluctuations in Women.* Most migraines in women develop during the hormonally active years between adolescence and menopause. Fluctuations of estrogen and progesterone, rather than their presence, appear to increase the risk for migraines and their severity in some women.

- About half of women with migraines report headaches associated with their menstrual cycle, although true menstrual migraines may actually be less common. So-called true menstrual migraines tend not to have auras and to increase in prevalence between two days before and five days after the onset of period.
- The first three months of pregnancy can exacerbate migraines in some women, although one study reported that pregnancy had little effect one way or the other on severity in most women with chronic headaches.
- Women whose migraines are affected by pregnancy or menstruation are also likely to have worse migraines if they take oral contraceptives or hormone replacement therapies.

## Age

*General Age of Onset.* More than 20% of adults with migraine report that their headaches started before age 10 and over 45% say they started under age 20. The prevalence of migraine declines in both men and women after age 40.

*Migraine in Children.* Migraine headaches occur in all ages and can appear in children as young as four years of age. Migraines in children are equally prevalent in boys and girls. Migraine is common in children and may be underdiagnosed. Some studies estimate prevalence in children of 5% to 10%. [ See Box Guidelines for Migraines in Children.]

In one Greek study of children, researchers reported a prevalence of migraine of 6.2%. Of the children who had migraines, 3.4% reported headaches without aura and 2.8% experienced aura with at least some of their headaches.

*Migraine Onset in Older Adults.* Although uncommon, late-life migraine occurs in about 1% of the population, usually in men. In such cases, it often occurs as migraine with visual disturbances but without headache.

## **Family History**

Research indicates that slightly over half of migraine cases may be inherited.

## **Ethnic Differences**

Caucasians have a higher risk than either African Americans or Asians. Worldwide, one study reported that migraines are most common in North America. They are slightly less prevalent in South America and Europe and far less common in Asia and Africa. Investigators believe that the differences are due to genetic variations, not environmental factors.

## **Other Medical Conditions Associated with Migraines**

People with migraine have a higher incidence of other, including the following:

- Asthma and allergies. Some studies have reported an association between migraine and asthma. One observed that parents with migraines had a greater chance of having children with asthma and allergies.
- *H. pylori* Infection. People who are infected with the bacteria *H. pylori*, the major cause of peptic ulcers, are at higher risk for migraines.
- Epilepsy. Patients with epilepsy are twice as likely to have migraines as the general population.
- Fibromyalgia.
- Systemic lupus erythematosus.
- Raynaud's syndrome.
- Mitral valve prolapse.

## **Personality Traits**

One study suggested that women with migraine tend to over-respond to stressful situations. In the study, they were more likely than other women to be diligent, conscientious, and overly sensitive to pressure from others. More likely, however, a

person's family history of migraine, rather than any personality tic, is the important risk factor.

## **WHAT TESTS ARE REQUIRED TO ESTABLISH THE CAUSE OF HEADACHE?**

Anyone, including children, with recurring or persistent headaches should consult a physician. There are no blood tests or imaging techniques that can be used to diagnose migraine headaches. A diagnosis will be made on the basis of history and physical exam, and, if necessary, ruling out other diseases or conditions that may be causing the headaches. (Tests may be necessary to rule out other conditions.) It is important to choose a doctor who is sensitive to the needs of headache sufferers and aware of the latest advances in treatment.

### **Description of Symptoms**

For accurate diagnosis, the patient should describe the following:

- The duration and frequency of headaches.
- Recent changes in character of the headaches.
- The location of the pain.
- The type (e.g., throbbing or steady pressure).
- The intensity.
- Any associated symptoms, such as nausea and vomiting.
- Describe clearly any visual disturbances, including auras.

It should be noted that the presence of auras or other disturbances do not always identify migraine sufferers:

- For instance, patients with severe sinus infections may experience double vision or visual loss. (This is an emergency condition, since it indicates the infection has spread to areas around the eyes.)
- Many migraine sufferers have no auras.
- Many elderly people with late-onset migraine have auras but no pain.

### **Headache Diary to Identify Triggers**

The patient should try to recall what seems to bring on the headache and anything that relieves it. Keeping a headache diary is a useful way to identify triggers that bring on headaches. Some tips include the following:

- Include all conditions, including any foods eaten, preceding an attack. Often two or more triggers interact to produce a headache. For example, a combination of weather changes and fatigue can make headaches more likely than the presence of just one of these

events.

- Keep a migraine record for at least three menstrual cycles. In women this can help to confirm or refute a diagnosis of menstrual migraine.
- Track medications. This is important for identifying possible rebound headache or transformed migraine.
- Attempt to define the intensity of the headache using a number system, such as the following:

1 = mild, barely noticeable.

2 = noticeable, but does not interfere with work/activities.

3 = distracts from work/activities.

4 = makes work/activities very difficult.

5 = incapacitating.

## **Medical and Personal History**

The patient should report any other conditions that might be associated with headache, including but not limited to the following:

- Any chronic or recent illness and their treatments.
- Any injuries, particularly head or back injuries.
- Any uncharacteristic dietary changes.
- Any current medications or recent withdrawals from any drugs, including over-the-counter or so-called natural remedies.
- Any history of caffeine, alcohol, or drug abuse.
- Any serious stress, depression, and anxiety.

The physician will also need a general medical and family history of headaches or diseases, such as epilepsy, that may increase their risk. Migraine, in particular, tends to run in families.

## **Physical Examination**

In order to diagnose a chronic headache, the physician will examine the head and neck and will usually perform a neurologic examination, which includes a series of simple exercises to test strength, reflexes, coordination, and sensation. The physician may ask questions to test short-term memory and related aspects of mental function.

## **Diagnosing the Cause of Persistent Migraines**

Extensive testing may be advised for anyone with a chronic, daily headache. Tracking times of

medications, withdrawal, and headache, using the headache diary, is usually very helpful in diagnosis.

*Differentiating Rebound Headache from Transformed Migraines.* Migraines that evolve to chronic headache must be first differentiated between natural transformed migraines and rebound headache (the most common cause of persistent migraines):

- A transformed migraines is usually more consistent in its severity and its location than a rebound headache.
- Transformed migraines are less sensitive to triggers than rebound headaches.

*Differentiating Transformed from Tension Headaches.* Once rebound headache is ruled out, the physician must then differentiate natural transformed migraines from tension headaches:

- In most cases of transformed migraine (but not tension headache) gastrointestinal or neurologic symptoms are present.
- Transformed migraine is also frequently associated with menstrual fluctuations in women.

## **Imaging Tests**

Imaging tests of the brain may be recommended under the following circumstances:

- If the results of the history and physical examination suggest neurologic problems.
- For patients with headache that wakes them at night.
- For new headaches in the elderly. In this age group, it is particularly important to first rule out age-related disorders, including stroke, hypoglycemia, hydrocephalus, and head injuries (usually from falls).
- For patients with worsening headache.

They are not recommended for patients with migraine and with no other abnormal indications. [ See *Box*, Headache Symptoms that Could Indicate Serious Underlying Disorders.]

The following tests may be used:

- A CT (computed tomography) scan may be ordered to rule out brain disorders or headaches caused by chronic sinusitis.
- X-rays and other tests may also be used if sinusitis is strongly suspected.
- A neck x-ray can reveal arthritis or spinal problems.
- Other tests include an MRI (magnetic resonance imaging), EEG (electroencephalogram), lumbar puncture, ultrasound testing, and cerebral angiography, which are only performed if there is reason to suspect an underlying disease.



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## **Headache Symptoms that Could Indicate Serious Underlying Disorders**

Headaches indicating a serious underlying problem, such as cerebrovascular disorder or malignant hypertension, are uncommon. (It should again be emphasized that a headache is not a common symptom of a brain tumor.) People with existing chronic headaches, however, might miss a more serious condition believing it to be one of their usual headaches. Such patients should call a physician promptly if the quality of a headache or accompanying symptoms has changed. Everyone should call a physician for any of the following symptoms:

- Sudden, severe headache that persists or increases in intensity over the following hours, sometimes accompanied by nausea, vomiting, or altered mental states (possible hemorrhagic stroke).
- Sudden, very severe headache, worse than any headache ever experienced (possible indication of hemorrhage or a ruptured aneurysm).
- Chronic or severe headaches that begin after age 50.
- Headaches in the back of the head accompanied by other symptoms, such as memory loss, confusion, loss of balance, changes in speech or vision, or loss of strength in or numbness or tingling in arms or legs (possibility of small stroke in the base of the skull).
- Headaches after head injury, especially if drowsiness or nausea are present (possibility of hemorrhage).
- Headaches accompanied by fever, stiff neck, nausea and vomiting (possibility of spinal meningitis).
- Headaches that increase with coughing or straining (possibility of brain swelling).
- A throbbing pain around or behind the eyes or in the forehead accompanied by redness in the eye and perceptions of halos or rings around lights (possibility of acute glaucoma).
- A one-sided headache in the temple in elderly people; the artery in the temple is firm and knotty and has no pulse; scalp is tender (possibility of temporal arteritis, which can cause blindness or even stroke if not treated).
- Sudden onset and then persistent, throbbing pain around the eye possibly spreading to the ear or neck unrelieved by pain medication (possibility of blood clot in one of the sinus veins of the brain).

## **WHAT ARE THE GUIDELINES FOR TREATING A MIGRAINE ATTACK**

Many effective headache remedies are now available for treating a migraine attack. Still, a 2000 survey of European migraineurs found that half seek no treatment from a doctor, perhaps because of the stigma of migraine. And only 27% of patients were given medications that were consistently effective. It should be noted that as many as 30% of migraine sufferers also have accompanying headaches resulting from tension, drugs, infections, or other causes. It is important to distinguish between headache types in order to determine appropriate treatment. [ *See Table Drugs Used for Migraines.* ]

*General Guidelines.* The general goals of treatment are the following:

- On the advice of the physician, choose drugs with as few side effects as possible. Patients should discuss various methods for administering the medication (pills, injections, nasal spray, or rectal suppositories) and begin with one they believe will be the least distressing.
- Treat the attack rapidly, within an hour of symptom onset if possible. Start with low doses first and build up dosage slowly.
- Try to minimize the use of back-up or rescue medications. (A rescue medication is typically an opiate, which the patient uses at home for pain relief when other medications fail.)
- Try to guard against rebound effect. Nearly all drugs used for migraine can cause rebound headache and none of the drugs should be taken for longer than two days per week. (Dihydroergotamine and newer triptans may pose a much lower risk for rebound than others, although evidence for this is not certain.)
- It may take two to four months for an agent to be effective.

*Stepped-Up Treatment Approach .* Some experts have advocated a stepped-up treatment course for an acute migraine attack. This involves starting with the least potent treatments and taking increasingly more potent drugs until the pain stops. In this approach some patients need up to five different medications to achieve pain relief. A typical stepped approach is the following:

- Patients first try general pain relievers (NSAIDs, Exedrin Migraine) and stress-reduction techniques.
- If these are not effective within two hours, migraine-specific agents should be tried next. Triptans are the first choice, then ergot derivatives (dihydroergotamine [DHE]).
- Injected or rectally administered drugs may be used for patients with migraines associated with severe nausea or vomiting. Nausea itself should be treated with specific anti-nausea drugs, such as metoclopramide (Reglan).
- If migraine medications fail to relieve symptoms within four hours, rescue drugs (opiates, corticosteroids) may be used.

*Stratified Approach.* Many physicians and patients now prefer the stratified approach. The doctor first estimates the severity of the patient's condition based on his or her

history. Then, based on the severity of a typical attack, the physician decides whether the patient should start with more or less potent agents at the first signs of the migraine:

- Patients with less disabling migraines start with general pain relievers.
- Patients with a history of moderate to severe migraines start with migraine-specific prescription medicine at the onset of mild pain.

Some studies report dramatic relief with the stratified approach. Side effects may be more severe, although newer agents, such as the recent-generation triptans, may provide effective early relief without significant adverse effects.

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## **GUIDELINES FOR MIGRAINES IN CHILDREN**

Some studies estimate that between 5% and 10% of children may experience migraines but that the disorder is underdiagnosed in children.

### **Symptoms in Children**

The standard diagnostic criteria for migraine in adults, however, may apply to only about two-thirds of migraines in children and adolescents. For example, the following differences have been observed:

- Headaches tend to last for a shorter time (as little as an hour) in children.
- Migraine tends to occur in the front of the face and occurs on both sides in two-thirds of child patients.
- Children may often have a form of migraine known as a migraine equivalent or abdominal migraine, which does not cause a headache at all. Instead children experience periodic bouts of nausea and vomiting (called *cyclic vomiting syndrome* ) or other secondary symptoms found in adult migraine, such as a reaction against light or sound. Cyclic vomiting may actually occur in nearly 2% of school-aged children with or without a migraine association.
- Migraine triggers in children are similar to those in adults, but common ones in children are eating ice cream and anxiety and fear.

### **Outlook in Children**

Migraine in children is disabling, as it is in adults, and they tend to lose more school days than other children. Children with frequent headaches may also be at higher risk for headaches in adulthood and also for other physical and psychiatric problems.

### **Treatments in Children**

For most children with migraines, mild pain relievers and home remedies may be sufficient.

- The standard approach for migraine in children is to start with ibuprofen (Advil) or acetaminophen (Tylenol) as early as possible. An oral form is recommended but if the child is vomiting, then rectal administration may be used.
- Ginger tea or ginger ale may be helpful and soothing.

In severe cases, more potent agents are used. Some options include the following:

- Dihydroergotamine has been an option for children with severe migraine.
- Non-oral forms of triptans, such as the sumatriptan nasal spray, may prove to be safe and effective in children, although a 2000 study showed effectiveness in only one in 10 adolescents. (Studies on oral sumatriptan have not shown it to be at all effective in children.)
- Intravenous prochlorperazine may be effective in stopping intractable migraines in children.
- For prolonged headache, dexamethasone (an inhaled corticosteroid) may provide relief by reducing inflammation.

### **Preventive Measures in Children**

- Non-medication methods, including biofeedback and muscle relaxation techniques may be helpful. In one study of children with migraines and poor sleep habits, instructions in improving sleep without using medications reduced migraine attacks significantly.
- If these methods fail, then preventive drugs may be used, although evidence is weak on the effectiveness of standard migraine preventive agents in children. Flunarizine, an anti-seizure agent that also blocks calcium channels, has been effective for children in trials but is not yet approved in the US. The tricyclic antidepressants have been useful for childhood migraine with cyclic vomiting.

### **Withdrawing from Medications**

If rebound migraines develop because of medication overuse, the patients cannot recover without stopping the drugs. (If caffeine is the culprit, a person may only need to reduce coffee or tea drinking to a reasonable level, not necessarily stop drinking it altogether.) The patient usually has the option of stopping abruptly or gradually and should expect the following course:

- Most headache drugs can be stopped abruptly but the patient should be sure to check

with the physician before withdrawal. Certain non-headache medications, such as anti-anxiety drugs or beta-blockers, require gradual withdrawal.

- If the patient chooses to taper off standard headache medications, withdrawal should be completed within three days or shorter. Otherwise the patient may become discouraged.
- Alternative medications may be administered during the first days. Examples of drugs that may be used include dihydroergotamine (with or without metoclopramide), NSAIDs (in mild cases), corticosteroids, or valproate.
- Whatever approach is used for stopping medication, the patient must expect a period of worsening headache afterward. Most people feel better within two weeks, although headache symptoms can persist up to 16 weeks (and in rare cases even longer).
- If the symptoms do not respond to treatment and cause severe nausea and vomiting, the patient may need to be hospitalized.

On the encouraging side, some patients experience dramatic long-term relief from all headaches afterward, and one study reported that 82% of patients significantly improved four months after withdrawal.

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#### **Drugs Used for Treating Migraine**

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Lidocaine	Nasal drops may be effective in 15 minutes. Limited evidence on effectiveness.
Anti-nausea Agents: metoclopramide (Reglan), domperidone (Motilium), Prochlorperazine (Compazine)	Oral combination of NSAIDs and metoclopramide effective in treating migraine. Oral forms of metoclopramide or domperidone reduce nausea and may help absorption of migraine agents. Intravenous administration of prochlorperazine useful for severe prolonged attacks in some patients.
Butalbital (a barbiturate) plus other compounds including aspirin and caffeine (Fiorinal, Issocet, Endolor, Femcet) or acetaminophen (Phenilin, Axocet, Bucet, Fioricet)	Has some proven benefits for acute attack. Can become habit forming over time.
Corticosteroids (dexamethasone, hydrocortisone)	Rescue therapy for patients with status migrainous.
Opioids (oral or nasal spray [Butorphanol])	For rescue treatment in very severe pain that does not respond to other agents.

## WHAT ARE THE SPECIFIC DRUGS AND REMEDIES FOR TREATING A MIGRAINE ATTACK?

### Specific Treatments for Mild Migraine

*Excedrin Migraine.* Some patients with mild migraines respond well to over-the-counter painkillers, particularly if they are administered at the very first warning of an impending attack. Excedrin Migraine, which contains acetaminophen, aspirin, and caffeine, is the first over-the-counter medication to be considered effective for temporary relief of migraines. Studies have reported significant relief in nearly 70% of patients. It may also help menstrual migraines.

*Nonsteroidal Anti-Inflammatory Drugs (NSAIDs).* NSAIDs are also first-line drugs tried for mild to moderate migraines. They are not very effective when used alone against severe migraine headache. Some experts suggest that the effect that the migraine process has on the gastrointestinal (GI) tract may prevent the absorption of NSAIDs. Some studies reporting benefits for specific NSAIDs include the following:

- Aspirin, ibuprofen (Advil Migraine), and naproxen (Anaprox, Aleve) are all available over the counter, and may have some benefits for mild migraine. Naproxen appears to be more effective than other NSAIDs. An investigative ibuprofen gel that has been effective in relieving headaches in early studies.

- A study of children who had migraines compared ibuprofen and acetaminophen. Acetaminophen worked faster, but after three hours, ibuprofen was more effective. Parents of children with migraines should consult with their physicians about using a combination of these drugs.
- Researchers have combined a high-dose NSAID (equivalent to 900 mg of aspirin) with metoclopramide (Reglan), a drug that prevents nausea and vomiting. Several studies show this combination is equal to oral sumatriptan and superior to DHE, two standard migraine drugs. People should not take high doses of NSAIDs without some protective agent since they can cause severe gastrointestinal distress.
- In one study, an NSAID combination, diclofenac-potassium (Cataflam), was as effective as sumatriptan, a standard migraine drug. Cataflam worked more rapidly and helped reduce nausea. The combination is not appropriate for people allergic to aspirin or at risk for bleeding.
- Injectable NSAIDs, particularly ketorolac, are proving in some cases to be equally or more effective than powerful migraine medications used for severe and persistent migraines. It should be noted that ketorolac has a higher risk for gastrointestinal bleeding than many other NSAIDs.

New NSAIDs, called selective COX-2 inhibitors include celecoxib (Celebrex), rofecoxib (Vioxx), and meloxicam (Mobic). These agents may allow high doses without the accompanying gastrointestinal side effects.

*Cooling Pads.* Cooling pads may help during an attack. Some products (Migraine Ice, TheraPatch Headache Cool Gel) employ a pad containing a gel that cools the skin for up to four hours and can be placed on the forehead, temple, or back of the neck.

*Ginger.* In general, herbal medicines should never be used by children or pregnant or nursing women without medical counsel. One exception may be ginger, which has no side effects and can be eaten in powder or fresh form, as long as quantities are not excessive. Some people have reported less pain and frequency of migraines while taking ginger, and children can take it without danger.

## **Triptans**

Triptans (also referred to as serotonin agonists) help maintain serotonin levels in the brain and so specifically target one of the major components in the migraine process. Triptans are the most important migraine agents currently available and are now recommended as first-line agents for many adult patients with moderate to severe migraines when NSAIDs are not effective. Patient satisfaction is high with these agents and they have the following benefits:

- They appear to be effective for most migraine patients.
- They are beneficial for patients with combination tension and migraine headaches.
- They may be effective for preventing menstrual migraines.

- They do not have the sedative effect of other migraine drugs.
- Withdrawal after overuse appears to be of shorter duration and is less severe than with other migraine medications.

*Brands and Success Rates. Brands and Success Rates.* Sumatriptan (Imitrex) was the first drug specifically developed for use against migraine. Newer oral triptans include zolmitriptan (Zomig), naratriptan (Naramig, Amerge), rizatriptan (Maxalt), almotriptan (Axert), frovatriptan (Frova), eletriptan, and avitriptan.

Sumatriptan has the longest track record and is the most studied. It can be administered orally in table form, as an injection, or as nasal spray. Injected sumatriptan works the fastest, but is inconvenient and causes pain at the injection site. The nasal spray form bypasses the stomach and is absorbed more quickly than the oral form. Some patients report relief as soon as 15 minutes after administration. The spray may leave a bad taste and it tends to be less effective when a person has nasal congestion from cold or allergy. Sumatriptan has proven to bring rapid relief to most migraine sufferers. Unfortunately, recurring headaches with sumatriptan develop within the first 24 hours in 20% to 40% of people who have taken the drug.

Studies on the newer agents have reported pain relief within two hours in between 60% and 91% of patients. Comparison studies with sumatriptan are suggesting that the newer agents have fewer side effects and are superior to sumatriptan for providing immediate, sustained, and consistent pain relief. Recurrence rates are also lower. Of these agents, almotriptan is emerging as being both effective and having fewer side effects, particularly chest pain, than other triptans. It may prove to be one of the most cost effective of these agents. Naratriptan also has few side effects and has been referred to as the "gentle" triptan.

### **Combinations of triptans plus NSAIDs may be helpful in preventing recurrence.**

*Side Effects.* Many of the newer triptans may have fewer severe side effects than sumatriptan. Side effects of most triptans, however, can include the following:

- Nausea.
- Dizziness.
- Muscle weakness.
- Heaviness, pain or both in the chest. (About 40% of patients taking sumatriptan experience these symptoms and they are major factors in discontinuing the drug. Newer agents, such as almotriptan, produce fewer chest symptoms.)
- Tingling and numbness in the toes.
- Rapid heart rate.
- Other effects include a warm sensation and discomfort in the ear, nose, and throat.



*Complications of Triptans.* The following are potentially serious problems.

- **Complications on the Heart and Circulation.** Triptans narrow (constrict) blood vessels. Because of this effect, very rarely spasms in the blood vessels may occur and cause serious side effects, including stroke and heart attack. Such events are not only rare but occur primarily in patients with an existing history or risk factors for these conditions.
- **Serotonin Syndrome.** Triptans also affect serotonin and so people taking antidepressants that increase serotonin levels (which are most antidepressants) should avoid taking both. The effects of such combinations may cause a so-called serotonin syndrome, which causes mental changes, restlessness, tremor, chills, sweating, and colitis. Some physicians believe, however, that the risk for the syndrome from taking both classes of drugs is very small.

The following groups should avoid triptans or take them with caution and only with the advisement of a physician:

- Anyone with a history or with any risk factors for stroke, uncontrolled diabetes, high blood pressure, or heart disease.
- People taking antidepressants that increase serotonin levels.
- Pregnant women. Studies on the effects of triptans in this group are limited. One study suggested a higher incidence of preterm deliveries in pregnant women taking sumatriptan. No higher rates of still births or birth defects were reported. In general, pregnant women should avoid any medications if possible.
- Children and adolescents. They may be safe, but controlled studies are needed to confirm this. (Triptans should not, in any case, be the first-line treatment for children.) [ See *Box Migraines in Children.*]
- People with basilar or hemiplegic migraines. (Triptans are not indicated for these migraineurs.)

## **Ergotamine (Ergot)**

Drugs containing ergotamine (commonly called ergots) constrict smooth muscles, including those in blood vessels, and are useful for migraine.

*Forms of Ergotamine.*

- Dihydroergotamine (DHE) is an ergot derivative. It is administered by injection, which can be performed at home. A nasal spray form of DHE (Migranal) may have fewer side effects than the injection. Dihydroergotamine has stopped migraine attacks in up to 90% of cases and is often effective against menstrual migraines.
- Ergotamine itself is available in oral tablets (Ergomar, Wigraine, Ercaf) and in rectal suppositories (Cafergot). Cafergot, Wigraine, and Ercaf contain caffeine.
- An ergotamine inhaler is being investigated.

*Side Effects.* Side effects of ergotamine include the following:

- Nausea.
- Dizziness.
- Tingling sensations.
- Muscle cramps.
- Chest or abdominal pain.
- The following are potentially serious problems:
- Toxicity. Ergotamine is toxic at high levels.
- Complications on the Heart and Circulation. It also causes persistent blood vessel contractions, which may pose a danger for people with heart disease or risk factors for heart attack or stroke.

The following patients should avoid ergots:

- Pregnant women.
- People over 60.
- Those with serious, chronic health problems, particularly those of the heart and circulation.

## **Lidocaine**

Nasal drops containing lidocaine, a local anesthetic, can provide effective pain relief within 15 minutes for many migraine sufferers. One case report suggests that taking it during the aura phase may offer significant protection against developing the full-blown headache. It has certain downsides:

- It is rather difficult to administer. Patients must be lying down with their head dangling.
- The headache often relapses in an hour, and other drugs must then be used.
- Side effects include unpleasant taste, burning sensation, and facial numbness.

However, the drug does not cause drowsiness or heart rhythm disturbances as some other migraine treatments do. And its fast effectiveness and safety make it a promising first drug during a migraine attack. It should not be used for any other form of headache.

## **Opiates**

If the pain is very severe and does not respond to other agents, physicians may try pain killers containing opiates (e.g., morphine, codeine, meperidine [Demerol], or oxycodone

[Oxycontin]). Butorphanol is an opiate in nasal spray form that may be useful as a rescue treatment when others fail. A number of such opiates use combinations of NSAIDs (ibuprofen or aspirin) or acetaminophen with an opioid. One study reported that about half of patients who start opioid therapy for migraine respond well and the benefits persist over time.

*Side Effects.* Side effects for all opioids include drowsiness, impaired judgment, nausea, and constipation. Addiction is a risk. Such drugs should not be prescribed for patients at risk for drug abuse, including those with personality or psychiatric disorders.

### **Agents Used to Prevent Nausea and Vomiting**

Metoclopramide (Reglan) is used in combinations with other agents to treat the nausea and vomiting that occurs with other drugs and with the condition itself. In fact, in one study using only aspirin with metoclopramide had some significant effect on the migraine itself. This and other anti-nausea drugs, such as domperidone (Motilium) may also help the intestine absorb the migraine medications.

### **Investigative Treatments**

*Nerve Protecting Agents.* These investigative agents block nerve pathways in the brain that are responsible for over-exciting nerve cells. One agent called LY293558 is known as an AMPA glutamate receptor antagonist and is showing promise in early trials.

*Intra-Oral Vasoconstriction Device (IVC).* An interesting investigative approach called the intra-oral vasoconstriction device (IVC) is based on the idea that many headaches are associated with inflammation in the areas above the upper molar teeth. This creates swelling and puts pressure on the maxillary nerves, which are behind the cheekbones. IVC employs hollow tubes containing circulating ice water that the patient holds against areas in the mouth thought to be inflamed. A small early study reported that the device was as effective as sumatriptan in relieving headache pain. In addition, it appeared to relieve nausea.

## **WHAT ARE THE GENERAL GUIDELINES FOR PREVENTING MIGRAINE ATTACKS?**

Lifestyle measures and non-drug approaches, such as biofeedback, should be tried first for preventing migraine attacks. [ *See What Are the Non-Medication Measures for Preventing Migraine Headaches?*]

In general, patients should discuss using medications on a daily bases for prevention of migraines when one or more of the following conditions are present:

- When recurring migraines significantly interfere with normal activities, even with treatment.

- It attacks are severe and disabling.
- If drugs used for migraine attack are ineffective.
- If drugs used for treatment are being overused.
- If side effects of treatment are overly severe.
- If migraine attacks are frequent (typically striking more than two or three times a month).
- If the migraines are rare forms (for example, hemiplegic migraine, basilar migraine, migraine with prolonged aura). It is important to determine the migraine type because some of the standard drugs for migraines, such as triptans, are not effective with hemiplegic and basilar migraines.

*Specific Approach.* In most cases, the patient takes medications in the following manner:

- One agent is usually tested at a time, with the patient taking the least powerful drug at the lowest dose first and increasing to greatest potency as agents fails.
- Combinations may be appropriate (such as a nonsteroidal anti-inflammatory drug [NSAID] with an antidepressant) for certain individuals.
- Patients who have certain other medical conditions (e.g., heart disease, history of stroke, epilepsy, anxiety) may be able to choose drugs that are useful for both conditions.
- Patients should use a headache diary to evaluate the effects. It may take two to three months for the patients to experience benefits from a preventive program.
- Once a medication has controlled the migraine, the patient should try tapering the dose after six to 12 months, with the goal of stopping completely.

It should be noted that many of these preventive drugs have potentially serious side effects, and that even with their use, only 10% of patients become completely headache free. (Medications should *never* be taken as preventive measures for tension-type headaches, except for unusual chronic or very predictable types. In these cases, a physician should always be consulted.)

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**Migraine Medications Commonly Used for Prevention**

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Potent prescription NSAIDs are available.	<i>Disadvantage:</i> Gastrointestinal problems, including possible bleeding, with long-term use.  Rebound Effect.
Beta-blockers (propranolol)	Reduce frequency of attacks and severity when they occur.  <i>Disadvantage.</i> Should not be used with patients with asthma and certain heart conditions. Used with caution in those with diabetes.
Valproate (Depakote), gabapentin (Neurontin) or other anticonvulsant agents	Reduce frequency of attacks and severity of migraines without auras. May be useful for patients who cannot take medications that constrict blood vessels.
Antidepressants (tricyclics, SSRIs)	Tricyclics (especially amitriptyline) are particularly useful for combination headaches. They cause frequent side effects, however. SSRIs and newer antidepressants may be helpful in some circumstances, although evidence is weak.
Calcium-Channel blockers (diltiazem, nimodipine, verapamil, flunarizine)	Prevent migraines and cluster. May be particularly useful in migraine patients at risk for stroke.
Triptans	Oral sumatriptan or newer low-dose "gentle" triptans, such as naratriptan, may be useful for preventing menstrual migraines.
Ergots: Ergotamine, dihydroergotamine (DHE), methysergide	Methysergide proving to be useful for prevention. Other ergots are not appropriate.

## WHAT ARE THE SPECIFIC DRUGS USED TO PREVENT MIGRAINES?

### Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) for Prevention

*Standard NSAIDs.* Nonsteroidal anti-inflammatory drugs (common pain relievers that are available over the counter or in prescription form). NSAIDs may be used for prevention of migraine under the following circumstances:

- *Nonprescription NSAIDs.* Regular, preventive use of low-dose aspirin (so-called baby aspirin), ibuprofen (Advil), and naproxen (Aleve) may reduce the occurrence of migraine

headaches by about 20%. (Even with nonprescription NSAIDs, no one should take them regularly without consulting a physician.)

- *Prescription-strength NSAIDs.* Prescription-strength NSAIDs can reduce the frequency of attacks in over half of migraine sufferers. There are many prescription brands available. Mefenamic acid (Ponstel) and naproxen (Anaprox) are particularly useful for preventing migraines associated with menstruation.

Long-term use of these drugs can lead to ulcers and possibly gastrointestinal bleeding. [For more information on NSAIDs *see* How are Headaches Treated? .]

*COX-2 Inhibitors.* Celecoxib (Celebrex), rofecoxib (Vioxx), and valdecoxib (Bextra) are known as COX-2 (cyclooxygenase-2) inhibitors. These NSAIDs have specific actions that appear to reduce the risk for ulcers and bleeding while still relieving pain. Some early evidence suggests they may be useful for preventing migraines. There is some concern, however, about adverse effects on kidney function and a higher incidence of heart attacks in patients taking these agents.

## **Beta-Blockers**

Beta-blockers are usually prescribed to reduce high blood pressure. Some, however, are also useful in reducing the frequency of migraine attacks and their severity when they occur.

- Propranolol (Inderal) and timolol (Blocadren) have been approved specifically for prevention of migraine.
- Others not yet approved may be effective, including atenolol (Tenormin), metoprolol (Lopressor, Toprol XL), and nadolol (Corgard).

There is some suggestion that people with migraines who have had a stroke should avoid beta-blockers.

*Side Effects.* Side effects may include the following:

- Fatigue and lethargy are common.
- Some people experience vivid dreams and nightmares, depression, and memory loss.
- Dizziness and lightheadedness may occur upon standing.
- Exercise capacity may be reduced.
- Other side effects may include cold extremities, asthma, decreased heart function, gastrointestinal problems, and sexual dysfunction.

If side effects occur, the patient should call a physician, but it is extremely important not to stop the drug abruptly.

## Anticonvulsants

*Valproate and Divalproex Sodium.* Valproate (Depakene) and a similar drug divalproex sodium (Depakote) are commonly used for epilepsy or bipolar disease. They are now approved for reducing severity and frequency of severe migraines without auras. Studies report that valproate reduces by 50% or greater by the end of one year, after which the benefits remain stable.

Side effects vary depending on the potency for the drug, but may include the following:

- Stomach and intestinal problems. Divalproex sodium (Depakote) has a lower risk for these side effects than valproate (Depakene).
- Increased appetite with weight gain.
- Temporary hair thinning and loss have occurred; taking zinc and selenium supplements may help reduce the effect.
- Young girls may develop secondary male characteristics and premenopausal women are at increased risk for menstrual irregularities and polycystic ovaries due to elevated male hormones, which are reversible.
- Birth defects when taken during pregnancy. (This is a significant adverse effect.)
- Parkinson's symptoms preceded by hearing loss. These have been reported in people with epilepsy who use valproate for more than a year, but they were reversible when the drug was withdrawn.

*Other Anticonvulsants.* Newer anticonvulsants are also being investigated for migraine, such as gabapentin (Neurontin), topiramate (Topamax), felbamate (Felbatol), and tiagabine (Gabitril). In one study, for example, gabapentin was modestly effective but drop-out rates were high. It may be useful for select groups of patients.

## Antidepressants

Certain antidepressants are quite effective in preventing all forms of headache, including migraine. The most effective ones include the following two classes:

- Tricyclic antidepressants. They include amitriptyline (Elavil, Endep) and protriptyline (Vivactil). The tricyclics may be particularly useful for patients who suffer from both migraines and tension headaches. Low doses may also help prevent cyclic vomiting in childhood migraine.
- Serotonin-reuptake inhibitors (SSRIs). SSRIs are sometimes helpful in reducing migraines. They include fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), and fluvoxamine (Luvox).
- Designer antidepressants. Newer antidepressants target neurotransmitters, such as norepinephrine, alone or in addition to serotonin. Nefazodone (Serzone) and venlafaxine (Effexor), are showing particular promise in preventing migraines.

The effects of any of these antidepressants on headaches are most likely due to their effects on serotonin, a chemical messenger in the brain that influences depression and migraine. [For more extensive information on antidepressants, including side effects, see *Well-Connected Report #8, Depression.*]

## **Calcium-Channel Blockers**

Calcium-channel blockers have been prescribed for preventing both migraine and cluster headaches. They must be taken for weeks to months before any benefit is noticed. Certain calcium-channel blockers may be particularly beneficial for preventing migraines in migraine patients who have experienced stroke.

Verapamil (Calan) is most commonly used for prevention of migraines. Others used or being investigated for migraines include diltiazem (Cardizem), nimodipine (Nimotop), nifedipine (Procardia), amlodipine (Norvasc), felodipine (Plendil), and nisoldipine (Sular). Novel calcium blockers, such as dotarizine and flunarizine, are being investigated and show promise for migraines. Flunarizine, available overseas but not in the US, is effective and may help prevent migraines in children. (Other calcium-channel blockers are not useful for children.)

*Side Effects.* They vary among different preparations. They may cause the following:

- Fluid accumulation in the feet.
- Drop in blood pressure, with accompanying dizziness.
- In some people they cause headaches as severe as the migraines they are preventing.
- Constipation.
- Fatigue.
- Impotence.
- Gingivitis.
- Flushing, and allergic symptoms.

Note: Grapefruit boosts the effects of calcium-channel blocking drugs.

## **Ergots**

Ergotamine and dihydroergotamine (DHE) are known as ergots and are commonly used to treat migraines. They are not generally used for prevention because of the danger of dependency; they may be used occasionally, however, to prevent *predictable* migraine attacks, such as those that occur every month around menstruation. Methysergide is a newer ergot that has multiple actions on serotonin and has been proven to be protective. It has some very severe side effects, however. [For detailed discussion on Ergots, see What



Are the Specific Drugs and Remedies for Treating a Migraine Attack?]

## **Triptans**

Triptans, like ergots, are used to treat migraines. However, some, such as naratriptan, may be protective for women who have predictable menstrual migraines. For example, some patients take naratriptan the day before a typical migraines starts and continue it for one or two days. [For detailed discussion on Triptans, *see* What Are the Specific Drugs and Remedies for Treating a Migraine Attack?]

## **Hormonal Agents**

Hormonal agents, such as oral contraceptives (OCs) or hormone replacement therapy, have a mixed effect on women with migraines. In general agents that keep hormone levels steady may be helpful.

### *Oral Contraceptives.*

- *Negative Effects.* Oral contraceptives (OCs) have been associated with worse headaches in 18% to 50% of women and have also been linked to a higher risk for stroke in women with classic migraines (with auras). Young women should avoid or stop oral contraception if they have classic migraines, migraines that worsen or change character after OCs, if they have close relatives with stroke or heart disease, or if they smoke.
- *Positive Effects.* Some evidence suggests that OCs are effective for preventing menstrual migraines (which do not have auras). In such cases, their benefits may outweigh the low risk of a serious adverse event. Keeping a migraine record for at least three menstrual cycles can help to confirm whether a woman actually has a true menstrual migraine. Progestin-only oral contraception particularly plays no positive role in migraine prevention, although progestin injections (e.g., Depo-Provera) that stop menstruation can be helpful.

*Hormone Replacement Therapy (HRT).* Oral HRT appears to worsen migraines in many women with a history of these headaches, menstrual migraines. Using a HRT patch, however, may not affect migraines as oral HRT does. (Some women report *fewer* migraines after taking hormone replacement therapy.)

## **Other Agents Investigated for Preventing Migraines**

*Angiotensin Converting Enzyme (ACE) Inhibitors.* Commonly used for treating high blood pressure, ACE inhibitors block the production of the protein angiotensin, which constricts blood vessels and may be involved in migraine. Studies using the ACE inhibitor lisinopril (Prinivil, Zestril) are reporting significant reduction in migraine attacks.

*Botulinum.* Botulinum toxin A (Botox) injections are being used for a number of conditions requiring small muscle relaxation, including eliminating wrinkles. Researchers are now reporting complete migraine relief in more than half of patients being tested and

improvement of more than 50% in another 35% of patients. Relief lasted three to four months with no adverse effects.

*Leukotriene-Antagonists.* Leukotriene-antagonists are anti-inflammatory agents that blocks leukotrienes, powerful immune system factors that are important in causing airway constriction. They include zileuton (Ziflo), zafirlukast (Accolate), montelukast (Singulair), and pranlukast (Ultair, Onon). These agents are being used in asthma and some physicians have observed a reduction in migraine frequency in asthmatic patients who also had these headaches. In one study that investigated their use for migraine prevention, more than half of patients experienced a reduction in frequency of severe attacks. They are not approved by the FDA for migraines, however, nor are they routinely used by physicians.

*Dopamine Agonists.* Alpha-dihydroergocryptine is a drug known as a dopamine agonist, which may helpful in preventing common migraine (without aura).

## **WHAT ARE THE LIFESTYLE AND ALTERNATIVE MEASURES FOR PREVENTING MIGRAINE HEADACHES?**

### **Dietary Factors**

*Avoiding Food Triggers.* Avoiding foods that trigger migraine is important in people who are susceptible to these triggers. Keeping a headache diary that includes tracking diet and headache onset can help identify them. [ *See Table Foods That May Trigger Migraines.* ]

*Healthy Diet.* One study indicates that a diet low in fat and high in complex carbohydrates may significantly reduce the frequency, severity, and duration of migraine headaches. Such a diet is healthy in general in any case.

*Eating Regularly.* Eating regularly is important to prevent low blood sugar. People with migraines who fast periodically for religious reasons might consider taking preventive medications.

*Vitamin B2 Supplements.* There is reasonable evidence on the benefits of vitamin B2 for migraine sufferers. In one study, patients who took 400 mg of vitamin B2 (riboflavin) reduced their migraine attacks by half, although the vitamin had no effect on the severity or duration of migraines that did occur. In another study, it helped increase the effectiveness of beta-blockers, drugs used to prevent migraines in some people. Vitamin B2 is generally safe, although some people taking high doses develop diarrhea.

*Smelling Pleasurable Foods.* One interesting study suggested that smelling certain pleasurable foods may reduce migraine pain. (The study used green apples as part of the experiment; patients with headaches who liked the smell of green apples had less pain. The scent had no effect on those who didn't like the fruit.)

<b>Foods That May Trigger Migraines</b>	
<b>Foods and Additives</b>	<b>Responsible Chemical</b>
Beers, wines, certain liquors, cheese and cheese-food products, fresh and processed meat, seafood products, peas, pickles, olives, and sauerkraut.	Tyramine and phenylethylamine. (These chemicals tend to become more potent in foods that are stored improperly.)
Apple juice, coffee, red wine, and tea.	Tannin.
Preservatives in wines, dried fruits, and other products.	Sulfites.
A common seasoning, most notably found in food prepared by Chinese restaurants but also contained in many commercial products.	Monosodium glutamate.
Chocolate.	
Artificial sweeteners.	

## **Sleep Hygiene**

Improving sleep habits is important for everyone, and especially those with headaches. [For more details, *see Well-Connected Report #17, Insomnia.*]

## **Aerobic Exercise**

Exercise is certainly helpful for relieving stress and an analysis of several studies reported that aerobic exercise might help prevent migraines. It is important, however, to warm up gradually before beginning a session, since sudden, vigorous exercise might actually precipitate or aggravate a migraine attack.

## **Behavioral Treatments**

Behavioral techniques that reduce stress and empower the patient may help some people with migraines. These methods generally include the following:

- Biofeedback therapy.
- Cognitive-behavioral therapy.
- Relaxation techniques.

This approach may help counteract the tendency for muscle contraction and uneven blood flow associated with some headaches. They may be particularly beneficial for pregnant and nursing women, who cannot take most medications.

*Biofeedback.* Studies have demonstrated some effectiveness from biofeedback for migraine headaches. Biofeedback training teaches the patient to monitor and modify physical responses, such as muscle tension, using special instruments for feedback.

*Cognitive Behavioral Therapy.* Behavioral therapy may be useful alone but is particularly beneficial for patients who are on preventive drug treatments. It typically employs the headache diary to track activities and headaches. The patient then works with the therapist to change or add behaviors or medications that will reduce the frequency and severity of attacks.

## **Alternative Treatments**

*Non-Drug Therapies.* Alternative non-drug therapies used for headache management include hypnosis, meditation, visualization and guided imagery, acupuncture, acupressure, yoga, and other relaxation exercises. There is no clear evidence that any of these techniques have specific value for migraines. Some studies report the following:

- *Relaxation Techniques.* Muscle relaxation techniques may be helpful. One interesting 2001 study reported that relaxation treatments appeared to help adolescents with migraine but not tension headaches.
- *Electrical Stimulation.* Small studies have found that therapy with transcutaneous electrical stimulation (TENS) may reduce migraine headache episodes. The procedure involves a very mild electrical sensation across the skin. One course of TENS takes about a half hour. One report suggests that using TENS with acupuncture points, along with self-hypnosis and relaxation techniques, may be an effective management option among patients with migraine headaches, but long-term and well-conducted studies are needed to confirm this.

*Feverfew.* There is some clinical evidence that the herbal medicine feverfew helps prevent migraines and even help reduce their severity. It should be noted, however, that, like all effective headache remedies over use can cause a rebound effect. Some experts recommend purchasing feverfew in dried leaf form. It appears to be safe, but side effects can be distressing, particularly canker sores in the mouth (5% to 15% of cases) and stomach distress. This agent should not be taken during pregnancy or in women hoping to become pregnant. People with any blood clotting disorders should not take it. As with most alternative medications, herbal products are not government tested or controlled. Many brands do not have enough of the active ingredient to be effective. Be sure to let your doctor know if you are taking an herbal preparation to treat your migraines.

*Glucosamine.* Glucosamine is a natural substance being used with some success for patients with osteoarthritis. Anecdotal reports are suggesting that the use of this agent may prevent migraines. As with other natural remedies, products are not regulated by the

FDA. It is being well studied for arthritis, however, and to date has few side effects. Many available brands (e.g., CVS, Walgreens, Wal-Mart) are manufactured with appropriate ingredients.

*Coenzyme Q10.* Coenzyme Q10 is a natural substance that is important for the transport of electrons. One study reported that patients who took it experienced a significant reduction in migraine headaches after three months.

*Magnesium.* Studies have reported that some migraine patients, such as women with menstrual migraine, may have a magnesium deficiency. Intravenous magnesium sulfate has been useful for migraine relief in people with low levels of magnesium, although it does not appear to have any benefits for people with normal levels of magnesium. Over-the-counter supplements are of uneven quality and costly, and many magnesium salts are not absorbed well and may cause diarrhea. Studies are underway to determine the most effective magnesium preparation and its benefits, if any, in menstrual migraines.

## **WHERE ELSE CAN MIGRAINE SUFFERERS GET INFORMATION?**

National Headache Foundation, 428 West St. James Place, 2nd Floor, Chicago, IL 60614-2750. Call (888-NHF-5552) or (312-388-6399) or (<http://www.headaches.org> )

American Headache Society (<http://www.ahsnet.org/> ) and affiliated organization American Council for Headache Education (<http://www.achenet.org/> )  
19 Mantua Road, Mt. Royal, NJ 08061. Call (856-423-0043)

AHS Publishes the journal *Headache* (<http://ahsnet.org/journal/> )

MAGNUM (Migraine Awareness Group: A National Understanding for Migraineurs), 113 South Saint Asaph Street, Suite 300, Alexandria, VA 22314. Call (703-739-9384) or (<http://www.migraines.org> )

American Academy of Neurology, 1080 Montreal Avenue, St. Paul, Minnesota 55116. Call (651-695-1940) or (<http://www.aan.com/> )

Web site offers good information and provides names of neurologists for specific locations.

National Institute of Neurological Disorders and Stroke, Building 31, Room 8A18, 31 Center Drive, 2540, National Institutes of Health, Bethesda, MD 20892-2540. Call (301-496-5751) or (800-352-9424) or (<http://www.ninds.nih.gov/> )

American Medical Association information site for migraine (<http://www.ama-assn.org/special/migraine/> )

Upstate Medical University (State University of New York) has an excellent migraine Website, designed for doctors, but accessible to the patient, as well.

(<http://www.upstate.edu/neurology/haas/hpmirx.htm> )

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The information provided herein should not be used during any medical emergency or for the diagnosis or treatment of any medical condition. A licensed physician should be consulted for diagnosis and treatment of any and all medical conditions. Call 911 for all medical emergencies. Links to other sites are provided for information only -- they do not constitute endorsements of those other sites. Copyright 2002 A.D.A.M., Inc. Any duplication or distribution of the information contained herein is strictly prohibited.

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