HEADACHE 2010-2011

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Editor: Patricia Goldfein

This guide is the author's opinion. Medications must be individually prescribed and used only in conjunction with treatment by a physician. Side effects, as listed in the PDR, must be accepted and understood. Some medications and treatments listed do not have an official FDA indication for the condition discussed. This guide is not a prescription, and it does not represent a standard consensus of treatment.

GUIDE TO ABBREVIATIONS

BID or b.i.d.– twice a day

BMI – Body mass index

CDH – chronic daily headache

GABA - Gamma-aminobutyric acid, an amino acid in the central nervous system that is associated with the transmission of nerve impulses

GERD - Gastroesophageal reflux disease, also known as acid reflux

HTN - hypertension

IBS – irritable bowel syndrome

IM – intramuscular

IV - intravenous

MVP – mitral valve prolapse

NSAIDs – non-steroidal anti-inflammatory drugs. These may be by prescription or OTC and include aspirin, ketoprofen (Actron®), ibuprofen (Advil®, Motrin IB®) and naproxen sodium (Aleve®)

OTC or o.t.c. – "over the counter," non-prescription medicine

PO – by mouth

PRN or p.r.n.– as needed

QHS or q.h.s.– at night

TID or t.i.d. – three times a day

QID or q.i.d. – four times a day

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NEW DEVELOPMENTS IN HEADACHE DRUGS

Years of migraine drug research have finally brought new forms of treatment to the market. Recently, the FDA approved the use of a new technology with great promise for patients. Sumavel DosePro was approved by the FDA for the treatment of acute migraine, with or without aura, and for cluster headache. It is a needle-free delivery system for sumatriptan which is remarkably easy to use and non-invasive. Headache relief begins in as little as ten minutes for some patients.

Another brand-new abortive is Cambia, from Nautilus Neurosciences. This NSAID (diclofenac potassium) is a powder. In other forms, it has been extensively used for a variety of conditions. The powder is dissolved in a glass of water, making it easy to swallow and fast-acting. Diclofenac is officially FDA-indicated for the treatment of migraine. It is very useful when we need to avoid sedation or cardiac side effects.

In another significant development, MAP Pharmaceuticals is completing trials for Levadex . This is a new formulation of dihydroergotamine (DHE) that can be used at home. Previously, DHE was used intravenously in clinical settings to treat migraines. The new form is orally inhaled, non-invasive and is easier to use. Levadex has the potential to provide a fast-onset of relief, and give sustained relief for pain and other migraine symptoms, with minimal side effects. It can be used at any point in the migraine cycle.

Also in development is a new class of migraine drugs, the CGRP inhibitors. CGRP is a chemical in the brain that is involved in inflammation in the neurologic pathways. CGRP levels increase during migraines and return to normal when the pain is gone. The CGRP inhibitor drugs will be used to stop a migraine in progress; they are not used as preventives. One manufacturer, Merck, is in the final phase of testing its CGRP inhibitors. It is possible that FDA approval could be granted by the end of 2011.

TREATMENT APPROACHES FOR HEADACHE PATIENTS

THE INITIAL WORKUP

Most headache patients should undergo blood tests and routine hematologic exams, primarily to assess liver and kidney function. Patients are often taking OTC medicines that they don't remember, or don't have a sense of how many OTC's they take for pain relief. It is not unusual for headache sufferers to consume eight to ten ibuprofen or Excedrin on a daily basis, and the liver and kidneys may be affected.

With a headache that has developed suddenly, a more extensive work-up is needed. It is a case by case judgment, but new onset daily persistent headache necessitates a thorough work-up. New neurological symptoms, such as numbness, a change in mental status or visual problems, or a patient in middle or later life with new onset headaches always needs a work-up, including an MRI or CAT scan.

The patient with chronic daily headaches warrants an MRI more often than the patient with sporadic migraines. A child with migraine may not need an MRI. For instance, if a 12-year-old presents with two

migraines per month since age 6, an MRI is not absolutely necessary. However, when the kids are followed as far as college age, often there will be an incident where they will complain of a severe, prolonged headache; they usually end up having a scan at some point.

There are cultural and ethnic differences in the perception and experience of pain; being aware of this can aid treatment. There is the official definition of pain, but I like "pain is what the patient says it is, and it's as bad as the patient says it is."

A headache problem is a legitimate physical illness. Acknowledging this with statements such as, “headaches are like asthma, diabetes or hypertension: a physical medical condition,” helps to establish trust between the patient and the physician. When doctors mention that it is a medical condition, primarily inherited, and that there is too little serotonin in the brain in people with headaches, patients respond exceedingly well. Once this trust is established, the patients are much more amenable to addressing anxiety, depression, etc., with therapy or other means.

It helps to view chronic headache as a continuum or spectrum. The “in between” headaches may not fall neatly into the tension or migraine categories as currently defined. Whether these are severe tension or milder migraines, they often respond to the same medications.

We must try and achieve a balance between medication and headache; I tell patients that we are trying to improve the headaches 50% to 90%, while minimizing medications. The initial history and physical is the best time to consider a differential list of medications, because at that point we have a strong grasp of the patient’s comorbidities. If we list some alternate possibilities (in case our initial medications do not work), we do not have to reconstruct the entire patient history on later consults. In choosing preventives, comorbidities are considered, particularly anxiety, depression, insomnia, gastritis, GERD, IBS, constipation, hypertension, asthma, and sensitivities or allergies to other drugs. These often determine which way to proceed with medication. Sensitivities and allergies to medications should have a prominent place in the patient chart.

COPING

We want to seek treatments outside of the pharmacy. We need to promote active coping. We must have other modalities involved. Pharmacotherapy may be important, but certainly we want to try everything else, whether it’s physical therapy, yoga, biofeedback, etc. Biofeedback is a very useful tool. I think that the biofeedback therapists who have been trained in the last 5 or 10 years often do a better job. At-home relaxation therapies, where patients are taught by being given a booklet and tapes, can be helpful, but a seeing a good biofeedback therapist in person is much more effective. When it is done well, biofeedback promotes an internal locus of control, which helps to promote self-efficacy. Exercise and yoga can have similar effects. People need to feel that they can have a positive effect on their illness by doing things other than taking a pill.

Psychotherapy is often an important part of treatment. If it were up to me, the whole country would see a psychotherapist. However, whether it is because of money or time or preconceived ideas, most people don’t go. Cognitive-behavioral therapy is the usual approach, but with personality disorders, we take more of a dialectical tack. It is important for a doctor to identify the best therapists in the area, as the skill levels of psychotherapists vary widely. We cannot promise patients that their headaches will

improve with psychotherapy (as they often do not), but coping with headaches and the stress that headaches produce does improve with therapy.

Patients with chronic daily headache may view their situation in black and white terms; on a return visit to the doctor, they will state, "Well, I still have a daily headache." They need to accept that going from moderate or severe headaches (7 on a scale of 1-10) to mild or moderate headaches (4 on a scale of 1-10), is a greatly improved situation. It means the medications are working, and should not all be changed. If patients keep a headache chart or calendar, this helps to raise their awareness. Because headaches are not usually curable, patients must accept that treatment is limited to a substantial improvement in frequency and/or severity.

Acceptance of the pain as an illness is a very important concept. There are actually scales that measure a person's degree of acceptance. The road to acceptance of a chronic illness can be littered with many wrong turns along the way, searches for instant cures. At the end, when people have accepted that they have a chronic illness, when they know the situation is bad but they don't have to give up and suffer, they can accept that the pain is chronic; there is no cure and it needs to be managed. This relieves a lot of inner angst, where patients feel driven to find a cure. So we do promote acceptance. Acceptance does not mean resignation; people need to realize that much can be done about the headaches.

Resilience is an interesting concept. Strength of resilience is built on one's early life experiences, plus the luck of genetics. Resilience can be viewed in individuals, couples or families. In looking at resilience in individuals, the serotonin transporter gene is crucial. There are two arms on the gene, which can be either short or long. If a person has two long arms on the serotonin transporter gene, it turns out that he is going to be a lot more resilient. His childhood may be unhappy, but when the person has two long arms on the gene, he usually turns out very well. If the patient has an abusive childhood, and he has two short arms on the serotonin transporter gene, it is almost a certainty that he is going to have major problems in life, possibly borderline personality disorder, or some other major psychiatric problem. So resilience is very important in view of who can cope despite severe headaches, and who ends up disabled.

One might think that the pain level is the major predictor of disability. It has been shown, in well-done studies, that other factors are probably more important. Catastrophizing (creating a high drama out of a situation) is one of these factors, such as a patient who seems to think his headaches are a 15 on a scale of 1 to 10. Part of the doctor's job is to turn down the volume and limit the drama. We can talk to people about catastrophizing, and work on the fear that underlies it. Catastrophizing by proxy also happens, where a parent thinks his child is suffering horribly from the worst headaches on the planet. Studies of disability have shown that some of this is the result of a fear of pain. Some people have more dread at the anticipation of pain than others; as with catastrophizing, fear of pain can be worked on through therapy.

ALTERNATE THERAPIES

It can "take a village" to help a person with severe pain. Other professionals should be involved where appropriate, in disciplines such as psychotherapy, massage, physical therapy and acupuncture.

Neck and Occipital Pain. We always treat the whole person; if they have fibromyalgia or other pains, the treatment should include those conditions. Occipital pain may be derived from the cervical region, and doing blocks or injections may help. Physical therapy can be very helpful when there is associated pain in the neck and shoulders. At least half of headache patients have neck pain, particularly with their migraines. I often advocate physical therapy, and chiropractic treatment can also be very helpful. It depends, of course, on the individual practitioner; there are better medical doctors than others and there are better physical therapists than others. It is worthwhile for a doctor to establish a relationship with the best chiropractor in the area, one who is good with headaches and neck pain.

Dental Treatment, Massage, Acupuncture. Dental consultations may help when people are clenching their jaws, and certainly if they are grinding (bruxism). Massage can benefit a wide range of patients, as can acupuncture. It's been difficult to prove in studies that acupuncture is more effective than sham treatment. After examining over 500 randomized controlled trials of acupuncture for various conditions, nothing definite can be concluded as far as efficacy. I think, with many pain studies, the outcome of the study can be predicted from how robust the placebo response is. Unfortunately, in studies where sham acupuncture is performed along with real acupuncture, there is going to be a robust placebo response. It has been difficult to prove efficacy over placebo. But there are patients who do very well with acupuncture.

Pain patients are often desperate, and search the internet for a cure, or seek alternative practitioners. We should not castigate them for doing so; they are just looking for answers.

CHARACTERISTICS OF HEADACHE

The diagnosis of headache is made by patient history, not by lab tests. Headaches often fit into one of three categories: migraine, tension, or cluster (see page 33). The category is determined by the location of the pain, its duration and frequency, and qualities of sharp and stabbing or dull and throbbing. Tension and migraine headaches do share some links. The vast majority of patients with chronic daily headache (CDH) also experience migraine. Both migraine and tension headache patients respond to similar medications: antidepressants and triptans. A family history of headache is common with both. Similar serotonergic changes, essentially a dysfunction in the brain's serotonin system, are found in tension and migraine headache patients. The prevalence of epilepsy is increased in both tension and migraine. Neck pain and muscle spasm, cranial muscle tenderness and cerebral blood flow changes are common to both conditions. Clinically, it can be difficult to distinguish a mild migraine from a severe tension headache.

MIGRAINE

A typical migraineur will have one to five migraines per month, and a family history of migraine is common. The peak age of occurrence is between 20 and 35 years. About 18% of women and 7% of men will have a migraine in their lifetime; female to male ratio is 3:1

Migraine attacks can last from 4 to 72 hours. The pain is moderate, or moderate to severe, and often begins in early morning, but may begin anytime. There is often a gradual onset of pain, which peaks for

hours, then slowly declines; occasionally, the pain develops quickly. Unilateral (one-sided) pain occurs in about 50% of patients. The pain of a migraine has been described as throbbing, pounding, pulsatile, or deeply aching. Sharp “ice pick” jabs are common.

Nausea or motion sickness often accompanies migraine headaches. Photophobia (discomfort from bright light), blurred vision, phonophobia (sensitivity to sound) and dizziness are common. These can make the experience of a migraine much more debilitating than the pain alone. Many migraine patients have cold hands and feet during a headache and may have them at other times.

CHRONIC DAILY HEADACHE (CDH)

Chronic tension headaches occur more than 4 hours per day, and 15 or more days per month. Chronic daily headaches usually evolve over a period of months or years.

Transformed Migraine is headache pain for more than 4 hours per day and 15 days per month in a patient with a previous history of migraine. There is usually a slow increase in tension-type headaches, with a concomitant decrease in migraine features. It has no organic causes. Eighty percent of transformed migraine patients have been reported to overuse analgesics. The analgesic abuse may create the daily headache pattern in some of these patients.

Chronic Migraine is CDH that has migraine features (throbbing pain, one-sided, with nausea, dizziness, sensitivity to light or sound). “Chronic Migraine” is a new term for frequent or daily headaches with migraine features and is the most common reason for daily headache.

New Daily Persistent Headache is a sudden onset of chronic daily headache. It may develop in a single day, or over a week or two. Patient will have no significant migraine history, although there may be a history of episodic tension headaches.

Headache associated with cervical spine problems, particularly arthritis**,** is usually posterior occipital in location. It can be exceedingly difficult to treat.

Posttraumatic Chronic Daily Headache is a headache that begins after an accident or other trauma. It often presents with migrainous features. This can be a difficult situation to treat effectively, and often does not respond to the usual medications.

KEYS TO HEADACHE MANAGEMENT

- Watch headache triggers
- Practice good sleep habits
- Lose excess weight
- Exercise daily, and practice yoga or another relaxation technique
- Treat a migraine early in the headache
- Do not overuse pain medicine; try to limit “as needed” medications to three days a week
- If appropriate, treat with preventive medications

HEADACHE TRIGGERS

With migraine and chronic daily headache sufferers, we like to emphasize avoidance of triggers. The most common triggers are: stress, weather changes, perimenstruation, missing meals, bright lights or sunlight, undersleeping, food sensitivity, perfume, cigarette smoke, after stress is over, oversleeping, exercise, and sexual activity. In general, headache patients do better with regular schedules, eating three or more meals per day and going to bed and awaking at the same time every day. Some foods can be headache triggers, but foods tend to be overemphasized.

Managing stress with psychotherapy, exercise, yoga, etc., often will reduce the frequency of headaches. With stress, it is not so much extreme stress, but daily hassles that increase headaches. When patients are faced with overwhelming daily stress, particularly when they cannot sleep well at night, headaches can be much worse the next day.

Relaxation techniques such as biofeedback, deep breathing, and imaging can be helpful for daily headache patients, particularly where stress is a factor. Yoga may improve many elements of headache with benefits of stress management and muscle relaxation. The ideal would be to take a yoga class weekly, then do the stretches and breathing for 10 minutes a day. Patients may see some relief from associated neck or back pain. Physical therapy can also help with these. Massage may also lessen symptoms, particularly neck pain. Patients can learn relaxation techniques from books or tapes that are readily available in bookstores, so that learning does not necessarily require extended visits to a therapist. However, working with a biofeedback therapist can be very useful, if patients are willing.

Psychotherapy is extremely useful for many headache patients with regard to stress management, coping, life issues, family of origin issues, etc. Even though we may recommend psychotherapy, it is crucial to legitimize the headaches as a physical condition; they are not a “psychological” problem, but rather a physical one that stress may exacerbate.

CAFFEINE USE

Whether in coffee, caffeine pills, or combination analgesics, it is necessary to limit the total caffeine intake. The maximum amount of caffeine to take each day varies from person to person, depending upon their sleeping patterns, the presence of anxiety, and their sensitivity to possible rebound headaches.

While caffeine can help headaches, the overuse of caffeine may increase headaches because of rebound mechanisms. Some patients do not suffer rebound headaches despite the ingestion of as much as 500 mg. of caffeine per day. Others develop rebound headaches with as little as 30 mg. daily. In general, try to limit caffeine to 150 or 200 mg. a day at most.

The average 8 ounce cup of coffee has between 75 and 125 mg. of caffeine. Drip coffee is stronger than percolated, and instant coffee is the weakest form. Depending on the size of the cup and its strength, instant coffee may contain from 40 to 150 mg., but is usually closer to 40. Decaffeinated coffee contains from 2 to 5 mg. per cup, but the caffeine levels may be much higher at restaurants and coffeehouses.

These calculations all depend upon the strength of the product and the brew. Specialty coffeehouses (Starbucks, Caribou, etc.) often contain twice the usual amount of caffeine per cup.

Tea usually contains 30 to 50 mg. of caffeine per cup. Soft drinks average about 40 mg., but energy drinks may have more than 200 mg. Chocolate contains 1 to 15 mg. of caffeine per ounce, and cocoa may have up to 50 mg. for an 8 ounce serving. Caffeine is also available as tablets or capsules. Tablets such as NoDoz, Tirend, and Vivarin are available. When patients find that caffeine significantly decreases their headaches, I will occasionally utilize the pure caffeine tablets, with a dose of 50 mg. (½ of a 100 mg. pill) every 3 to 4 hours as needed. At times, it is helpful to combine the caffeine with medications that do not contain caffeine, such as Midrin (or the generic, Epidrin).

CAFFEINE SOURCES

Limit caffeine to 150 mg. per day, or, at most, 200 mg. per day

- Coffee, brewed, 8 oz. cup: 75-125 mg. Drip is the strongest form, percolated is weaker. Specialty coffee brewers such as Starbucks may be up to 50% stronger than home-brewed. A small latte has 70-90 mg.
- Instant: 40-150 mg. per cup, usually closer to 40 mg. Decaf: About 5 mg. per cup, but may be higher
- Tea, 8 ounces: 30-50 mg.
- Soft drinks: approximately 40 mg. per cup; energy drinks may have more than 200 mg. per 8 oz.
- Chocolate: 1-15 mg. per ounce
- Cocoa: 20-50 mg. per 8 ounces
- Caffeine tablets: (NoDoz, Vivarin, Tirend) contain 100 mg. of caffeine
- Caffeine is also present in many analgesic medications, such as Excedrin Migraine (65 mg.), Anacin (32 mg.) and Vanquish (33 mg.)

FOODS TO AVOID

You may not be sensitive to the foods in your diet; most people are sensitive to only two or three types. If a particular food is going to cause a headache, it will usually occur within three hours of eating. Your response to these foods may not be consistent. On one occasion, you may have a headache caused by a particular food, but, the next time you eat that same food, it is possible that a headache will not occur. Compared to other triggers such as stress, weather, hormonal changes, missing meals, bright lights, and undersleeping, food sensitivities are not that common, but some patients are sensitive to the following:

- Monosodium glutamate (MSG) – also labeled autolyzed yeast extract, hydrolyzed vegetable protein, or natural flavoring. Possible sources of MSG include broths or soup stocks, seasonings, whey protein, soy extract, malt extract, caseinate, barley extract, textured soy protein, chicken, pork or beef flavoring, meat tenderizer, smoke flavor, spices, carrageenan, seasoned salt, TV dinners, instant gravies, and some potato chips and dry-roasted nuts.
    - Alcohol. All alcohol can trigger a headache; beer and red wine are the worst offenders. White wine is not as likely to trigger a headache.

- Cheese. Ripened, aged cheeses (Colby, brick, cheddar, Roquefort, brie, gruyere, bleu, Boursault, mozzarella, parmesan, Romano) and processed cheese are the worst. Less likely to trigger a headache: cottage cheese, cream cheese, and American cheese.
- Chocolate
- Citrus fruits
- Meat that has been cured or processed, such as bacon, bologna, ham, hot dogs, pepperoni, salami, sausage; canned, aged or marinated meats.
- Nuts, peanut butter
- Yogurt, sour cream
- Large amounts of aspartame (Nutrasweet)

EXERCISE AND WEIGHT LOSS

Recent medical research has found a correlation between obesity and the prevalence of headaches. Two large population-based studies suggest that obesity is one of the risk factors for chronic migraine. The link is strongest in patients under age 55, who were found to have a nearly 40% increased risk of migraine if they were obese.

Migraine with aura appears to be a risk factor for cardiovascular events, as is obesity. A high BMI is thought to affect the frequency, severity and symptoms of a migraine. However, an important correlation is that the lifestyle that can lead to obesity can also trigger headaches.

"Several of the inflammatory mediators that are increased in obese individuals are important in migraine pathophysiology, including interleukins and calcitonin gene-related peptide (CGRP). These mediators may increase the frequency, severity, and duration of migraine attacks per se, which in turn would cause central sensitization. Repeated central sensitization may be associated with permanent neuronal damage close to the periaqueductal gray area, with poor modulation to pain. Obesity is also a state of sympathetic activation, which may contribute to increase in headache frequency. Furthermore, the levels of adiponectin are decreased in obesity. At low but not normal levels, adiponectin is nociceptive. Shared biologic predisposition may also play a major role. Orexins modulate both pain and metabolism. Dysfunction in the orexins pathways seems to be a risk factor for both conditions. Finally, conditions that are comorbid to both states (e.g., depression, sleep apnea) may also make the relationship between both diseases more complex." *From: Possible mechanisms of interaction.* Neurology 2007;68:1851-1861. *Marcelo E. Bigal, MD, PhD, Richard B. Lipton, MD, Philip R. Holland, PhD and Peter J. Goadsby, MD, PhD*

Permanent weight loss is difficult. It takes a psychological readiness, a physical commitment, and changes in lifestyle and behavior. It never comes about by just saying, "I need to lose a few pounds and exercise." It comes about via a concerted effort where exercise and weight control become a main project in your life. You need to get up every morning committed to your program, and focusing on how to get your needed exercise and arranging for healthy meals each day.

Exercising is helpful for headache patients. It is certainly crucial for weight loss. To get most of the benefits of exercise, you only need to think of exercising in small chunks of time, even 10 or 15 minutes.

Most people are able to fit exercise more easily into their lives when thinking this way. We are looking for a total of 30 daily minutes on average, but 20 minutes will do. However, for weight loss, increase exercise to 60 minutes daily. It is more important to count the minutes of exercise than to keep track of heart rate.

Some of the key steps to maintaining a long-term weight loss are:

- Exercising for 40-60 minutes daily (choose steady and low-impact activities, such as walking, biking, swimming)
- Grazing (eating small meals throughout the day while reducing portions at mealtime)
- Portion control (measure and/or weigh your food)
- Count calories or points (Weight Watchers is a good program)
- Weigh yourself often
- Eat foods that are low in fat, sugar and salt, and high in fiber
- Do NOT diet. Severely restricting food is related to the yo-yo syndrome, where weight is frequently lost but quickly regained.

Weight gain is an issue in prescribing a headache drug; although certain drugs may be more effective, using one that avoids weight gain (in those prone to it) is more likely to lead to long-term success.

COMMON MEDICAL COMORBIDITIES

The gastrointestinal (GI) system is a common site of comorbid problems in headache patients; irritable bowel syndrome (IBS) is among the problems most frequently seen. Most of our serotonin is in our gut, and certain medicines that help IBS will also increase or decrease serotonin. IBS is frequently seen in migraine patients, and often we're trying to use medicines that help the GI symptoms as well as the headache. It is easier to help patients who have diarrhea symptoms, because some medicines, such as the older tricyclics, slow the transit time through the gastrointestinal system. Constipation is tougher to help.

Hypertension (HTN). A number of the antihypertensive drugs do decrease migraine. Most beta blockers will help, as will the calcium channel blockers. More recently, the angiotensin receptor blockers (ARB's) have been utilized.

Fibromyalgia (or Chronic Widespread Pain Syndrome.) We do have a few drugs that are indicated for fibromyalgia. Many people with fibromyalgia have chronic daily headaches and insomnia. These groups overlap, not only with the physical pain, but with the psychological comorbidities as well. Fibromyalgia patients share the allodynia commonly felt by headache patients. A number of medicines, such as tricyclics and muscle relaxants, are useful for both headache and fibromyalgia. A newer drug, Savella, is FDA indicated for fibromyalgia, and may help headache as well.

Insomnia is commonly seen in migraine and chronic daily headache patients. Patients should sleep as much as they need to feel refreshed and healthy during the following day, but not in excess. Curtailing the time spent in bed seems to solidify sleep; excessively long times in bed may be related to shallow and fragmented sleep. A regular awakening time in the morning strengthens circadian cycling and, ultimately, leads to a regular time of sleep onset.

Loud noises disturb sleep even when people are not awakened by the noise and cannot remember them in the morning. Sound-attenuated bedrooms may help those who must sleep close to noise. White noise sound machines help to blunt outside sounds. Consider ear plugs (a good brand is Hearos 33db.) These are also useful when traveling.

Although an excessively warm room disturbs sleep, there is no evidence that an excessively cold room solidifies sleep. Hunger may disturb sleep; a light snack may help you sleep. Caffeine in the evening disturbs sleep, even in those who feel it does not. Alcohol helps tense people fall asleep more easily, but the ensuing sleep is then fragmented. The chronic use of tobacco disturbs sleep.

A steady daily amount of exercise should deepen sleep, but occasional exercise does not necessarily improve sleep the following night. Yoga and other breathing and relaxation techniques may be helpful. Set the alarm and get up at the same time every morning, regardless of how much you have slept during the night. This helps the body develop a constant sleep/wake rhythm. Do not nap during the day.

Go to bed only when sleepy. Use the bed for sleeping only; do not read, watch television or eat in bed. People who feel angry and frustrated because they cannot sleep should not try harder and harder to fall asleep, but should turn on the light and do something different. If unable to sleep, get up and move to another room. Stay up until you are really sleepy, then return to bed. If sleep still does not come easily, get out of bed again. The goal is to associate bed with falling asleep quickly. Repeat this step as often as necessary throughout the night.

An occasional sleeping pill may be of some benefit, but their chronic use is ineffective in most insomniacs. However, some people do well on sleeping pills for months or years. The primary sleep aids utilized have been Ambien and Ambien CR, Lunesta, and Sonata. Generic Ambien and Sonata are available. Ambien has been the most preferred, and is available in 5mg. and 10mg. tabs that may be split. Ambien CR is an excellent, longer-lasting formulation, with doses of 6.25 and 12.5 mg.; these should not be split. Lunesta has a similar mechanism of action to Ambien, primarily GABA (gamma-aminobutyric acid.) The usual dose is 2 or 3 mg. at night; some do well on ½ tablet. Side effects are similar to those of Ambien. With any sleep medicine, fatigue or cognitive effects may be seen the next day. Minimizing the dose is important. Sonata and its generic form are shorter-acting, and can be effective when taken in the middle of the night. Some patients may take Sonata at 3 A.M. and not be tired at 8 A.M. While relatively safe, any of these meds can be abused. Rozerem is a newer 'melatonin agonist,' similar to, but stronger than, the melatonin pills available over-the-counter. Melatonin is a hormone produced in the brain by the pineal gland from the amino acid tryptophan. While non-addicting and relatively safe, Rozerem is very mild in its effect. Rozerem may be used in combination with another sleep medication.

In addition to the above, the atypical antipsychotics are occasionally utilized in selected patients. These are particularly helpful in those patients with bipolar illness, or very severe anxiety. The usual medication would be Seroquel 25 mg., ½ or 1 tab, or 2, qhs**,** or Zyprexa 2.5 mg. or 5 mg. qhs**.** Risperdal, 0.25 to 0.5 mg, may also help. Fatigue may occur with both of these the next day, and weight gain is seen relatively often with Zyprexa. These atypicals do have the possibility for long term side effects, including tardive dyskinesia and diabetes, and therefore are used only in selected patients where the benefit outweighs the risk.

Certain muscle relaxants may aid sleeping. Zanaflex (tizanidine) 4 mg., ½ or 1 tab, is not addicting, and may be helpful in preventing a headache the next day. Cyclobenzaprine (Flexeril) is also sedating, not addicting, and helpful for those with neck or back pain.

Benzodiazepines are not first-line meds, but do play a role in selected patients. These are particularly useful for those with anxiety. The older antidepressants, particularly trazodone, often are useful. The trazodone dose varies from 50 mg. to 300 mg.; average is 100 mg. The tricyclics, such as amitriptyline or nortriptyline, may help with sleeping and with headaches.

MEDICATIONS FOR FATIGUE

If you ask large groups of headache or migraine patients what their biggest problem is other than headache pain, it tends to be excessive daytime sleepiness. Fatigue is such a prevalent problem that we don't want to add medicines that fatigue people even more. Unfortunately, little is understood about the cause of sleepiness. The following medications are sometimes utilized to treat fatigue:

Modafinil (Provigil or the newer form NuVigil (armodafinil)). This fairly safe medication is classified as a wakefulness promoting agent. The most common side effects with this medication are headache, nausea and anxiety. Unfortunately, Provigil may increase headaches. It is expensive, and not FDA-indicated for general fatigue.

Stimulants (dextroamphetamine, methylphenidate, Adderall). These medications may be helpful for fatigue, as well as concurrent ADD/ADHD. They may help to decrease pain or headache as well. Some of these come in both short-acting and long-acting preparations, which is helpful. The main side effects consist of decreased appetite, insomnia and dry mouth. Adderall XR is a good long-acting preparation, usually dosed once daily.

Bupropion (Wellbutrin). This medication is an antidepressant which is beneficial due to its activating nature. The doses are available as slow release tablets in 100 mg., 150 mg., and 200 mg. doses, along with a once-daily XL form, which comes in 150 mg. and 300 mg. dosage. Depending on the presence of comorbid anxiety and depression, the dose range may vary from 100 mg. up to 300 mg. per day. The advantages of Wellbutrin are that sedation, weight gain and sexual side effects are much less than with other antidepressants.

Caffeine. While caffeine may offset fatigue, it is not ideal due to its short-acting activity. Caffeine may help headache, but overuse leads to increased headaches. Usage should be limited to 200 mg. per day (at most). See section on "Caffeine Use" on page 10.

USE OF MEDICATIONS

While most patients are honest about their use of analgesics, some are reluctant to tell the doctor how much they are using. From OTC analgesics to herbal preparations, many patients are consuming larger quantities of medications than they realize.

The doctor should start with low doses of medication, particularly with antidepressants and other preventives. Headache patients tend to be fairly somatic, and there is usually no need to push medicine quickly. One exception to this is in patients with severe new-onset daily persistent headache; these patients may need quicker interventions.

Both the doctor and the patient should keep a drug medication chart. Headache patients are constantly having medications stopped and re-started. Over ten years, a patient may have been on as many as 50 different medications at various times. It may become nearly impossible to glance through the progress notes trying to determine what the next best course of action is. A drug medication flow chart from the beginning helps immensely.

Using a medication to establish a diagnosis may not be accurate. For instance, DHE or triptans, while useful for headaches, also have been effective for the pain of subarachnoid hemorrhage or tumors.

Stick with preventive medications for at least four weeks; if we abandon them too soon, we may not see the beneficial effects. However, few patients are willing to wait months for positive benefits from a medication. Patients can become frustrated by the lack of efficacy or the side effects of daily preventives. They need to know that only 50% will achieve long-term relief with preventives, and a lack of success is not their fault.

For depression to improve, it is important to control pain and, likewise, to help pain, we must treat depression. When we place patients on antidepressants, we need to make it clear that we are trying to directly help their headache by increasing serotonin, and also state that we hope this helps anxiety, depression, etc. Patients can be confused as to why they are being given an antidepressant. Make it clear that we are not trying to treat their headache by treating depression.

REBOUND OR MEDICATION OVERUSE HEADACHE

Rebound occurs when a drug is used or overused, causing a headache later in the day or the next day. Medicines that contain high amounts of caffeine are more likely to induce rebound headache. This is a murky area; some patients are told that their headaches are rebound when it is just their natural headache pattern. Some patients have rebound from a small dose of caffeine, while others have no headache despite ingesting large amounts of caffeine.

A variety of medications are linked to rebound headache, such as the NSAIDs: ibuprofen, (Advil, Motrin), naproxen (Aleve, Naprosyn). Other drugs that may induce MOH include combination pills like Excedrin (aspirin and caffeine), butalbital (Fiorinal, Esgic), opioids (Vicodin, codeine), and triptans (Imitrex, Maxalt, Zomig). If, after starting a new drug, a patient typically does not get a headache for the first day, but has a second-day headache, it may be because of medication. Another pattern to watch is this: a patient has a headache that typically lasts only two days a week. He begins a new abortive medication, and within months has daily, or nearly daily, headaches. This is when rebound headache must be considered.

We do not know the medical reasons (pathophysiology) behind rebound headache; it is likely that brainstem pathway connections are involved. Many patients diagnosed with rebound have refractory headaches. These are hard to treat; daily preventives may not help, and the patient begins dosing

himself with whatever works temporarily, whether it is triptans, Excedrin or opioids. Patients often say, "the doctor diagnosed me as being in rebound; I had the same headaches for ten years before going on that drug." We need to stop blaming the patients because our medications are not adequate.

The only practical approach to managing rebound is to withdraw the patient from daily pain medication, daily triptans and high-caffeine medications. Caffeine intake should be minimized overall, although small amounts do help headaches. A trial period of four weeks is suggested. Inevitably, the patient's response will be, "Okay, Doctor, but what do I do in the meantime to function?" We try to use a combination of preventives and minimize the abortives for the four weeks. There are various strategies for withdrawing a patient off of pain meds, but often, the result is not successful in the long term. The bottom line is that we do not know who gets rebound, or from which drugs. It is a very individualized situation.

WHEN NOTHING WORKS –THE REFRACTORY PATIENT

Kindling of the brain is important in depression, seizures, and headache. Possibly, if we treat younger patients with frequent headaches fairly aggressively, we may prevent the progression into chronic daily headache. Central sensitization is an important phenomenon that occurs in chronic headache, peripheral neuropathy, and, probably, in IBS and fibromyalgia. Once this occurs, treatment is difficult. If preventive meds are successful, they may stop the progress toward chronic central sensitization.

Before giving up on a patient with severe, refractive chronic daily headache, we consider "end of the line" strategies such as: MAOI's, daily long-acting opioids (methadone, Kadian, Oxycontin, MS-Contin, Duragesic), stimulants (dextroamphetamine, methylphenidate, phentermine), daily triptans in limited amounts, Botox injections, or a combination of approaches.

Dependency should not be confused with addiction; when treating chronic daily headache, dependency has to be accepted. However, heed red flags with patients taking opioids. Beware of prescribing opioids for a new patient. With these highly addictive medications, the doctor must be emphatic about saying NO and setting limits. Pervasive behaviors help to determine addiction, but even one red flag early in treatment should be a serious consideration. Red flags include a patient who requests specific drugs and doses, who refuses non-addictive drugs, or coaxes a prescription for higher doses. Or, after receiving a prescription for an opioid, the patient calls a few days later with a convoluted story about needing more pills.

FIRST LINE MIGRAINE ABORTIVE MEDICATIONS

TRIPTANS

Over 110 million patients worldwide have used triptans. The most effective way to use triptans is to take them early in the headache. Imitrex (sumatriptan) is an extremely effective migraine abortive medication with minimal side effects. Imitrex is effective for approximately 70% of patients and has become the gold standard in abortive headache treatment. The earlier one uses any triptan the better the effect. The usual dose is one tab every three hours as needed, but not more than twice a day.

The triptans are helpful for moderate as well as more severe migraines. Certain patients tolerate one of the triptans better than another and it is worthwhile to try several in an individual patient. Triptans are an excellent choice for migraine patients who are not at risk for coronary artery disease. Patients in their 50's or 60's can use these drugs, but they should be prescribed cautiously, and only in those patients who have been screened for CAD.

SIDE EFFECTS

Side effects are milder with the tablets than with the injections. Many people will not have any side effects with triptan tablets. With the injections, they do often sense a "rush" into their head. Feeling heat in the head or numbness in the face and hands is relatively common. Chest heaviness or pressure, or pressure in the throat, are also common. This is rarely from cardiac origin. If the chest heaviness is moderate or severe, or is associated with arm pain, the patient should not use the triptan again unless he or she is cleared by the physician. Nausea or fatigue may result, but these side effects tend to be short lasting. Most side effects resolve within 30 minutes. Occasionally patients will feel weak or dizzy. Tingling in the fingers or feet may be experienced, particularly with a high daily usage of a triptan.

As a class, the triptans have had a good record of safety over the past 18 years. The two serious side effects have been myocardial infarction and possible stroke. Stroke has occurred in a number of cases, but it is unclear whether this was due to Imitrex or was a random event. The triptans have been used to treat over 700 million migraines with a very low incidence of serious side effects.

The issue of myocardial infarction and coronary ischemia is an important consideration with the use of triptans. These effects are more marked with the injections than with the tablets. Patients at any age should be screened for coronary artery disease, by history at least, and patients over the age of 40 should have an appropriate workup. The tablets have only been associated with rare cardiac events. However, in studies investigating Imitrex tablets, patients who had coronary artery disease or ventricular arrhythmias did have some ischemia. While Imitrex has generally been a very safe medication, it is important to screen these patients. After moderate or severe chest symptoms, it is prudent to discontinue use. Patients must be informed of these possible adverse events, and be aware of their possible development.

USE WITH OTHER MEDICATIONS AND PREGNANCY/BREASTFEEDING

Pain medications and OTC's (including aspirin, Tylenol, Aleve, Vicodin, Fiorinal, etc.) may be used in the same day or even at the same time as a triptan. This may enhance efficacy in some patients. Antiemetics, such as Phenergan, Reglan, Zofran and Compazine, are safe with triptans. Triptans should not be combined with another triptan, and the overall use should be carefully limited.

Usually, triptans should not be used during pregnancy. Breastfeeding mothers, with consent, have utilized sumatriptan; the lower the dose, the better.

A SUMMARY OF THE TRIPTANS

Sumatriptan (Imitrex): The usual oral dose is one 50 mg. or 100 mg. tablet, q 2-3 hours, 200 mg. per day at most. The SQ Imitrex (4 or 6 mg.) is the most effective migraine abortive for severe, faster onset

migraines. It is also available as a nasal spray. Over 100 million people have used Imitrex, and it has been utilized for nearly 20 years. The addition of an NSAID to a triptan may enhance efficacy and prevent recurrence.

Treximet (sumatriptan plus naproxen) is an excellent combination drug that helps to prevent recurrence of the headache. The usual dose is one every three to four hours, two in a day at most. The addition of naproxen may cause stomach pain or nausea.

Sumatriptan Injections (Sumavel DosePro, Imitrex STATdose). Sumatriptan injections are available in the Imitrex STATdose injector form, and also the new needle-free Sumavel DosePro. Sumavel DosePro has been available since January, 2010. It is a selective 5-HT1B/1D receptor agonist for the treatment of migraine attacks, with or without aura, and the treatment of cluster headache episodes. The needle-free Sumavel is an excellent new product which is easier to use than STATdose. While the usual dose had been 6 mg., the 4 mg. STATdose is often effective. The injections are dosed at one every three to four hours as needed, but limited to two per day.

The tablets are usually limited to ten tablets per week, and the injections to four per week. The vials of sumatriptan, 6 mg per 0.5 cc, are also available. The patient draws up 0.25 cc (3 mg. Imitrex) or 0.5 cc (6 mg.) into an insulin syringe.

Rizatriptan (Maxalt) is very similar to Imitrex. Maxalt is very effective for migraine. The usual dose is one standard 10 mg. tablet, or the 10 mg. Maxalt MLT (rapidly disintegrating tablets) which are placed on the tongue. These rapidly disintegrating tablets have a pleasant taste and may be taken without water. Side effects are similar to those of Imitrex. Maxalt is very well tolerated.

Eletriptan (Relpax) is an effective and well-tolerated triptan. It is available in 20 and 40 mg. strengths; 40 mg. is the usual dose. The side effects, in general, have been found to be fairly minimal. They include possible nausea, pressure in the throat, dizziness and tiredness or weakness.

Zolmitriptan (Zomig), in 2.5 mg. or 5 mg. tablets, is another very effective abortive. The usual dose is 5 mg. every three to four hours, as needed, two per day at most. Zomig ZMT, 5 mg., is a pleasant-tasting, dissolvable tablet. Like Maxalt MLT, it provides an alternative to the oral tablets.

Frovatriptan (Frova) is well tolerated. The long (26 hours) half-life is advantageous for those with prolonged migraines. Mean maximal blood concentrations are seen approximately 2 to 4 hours after a dose of Frova. Frova has been particularly useful for those with slower-onset moderate or moderate to severe migraines. Frova is available in 2.5 mg tablets. Frova has been effective for preventing menstrual migraines.

Almotriptan (Axert) is very similar to the other triptans, and effective for migraine headache. The usual dose is one 12.5 mg. tablet, every 3 to 4 hours, limit of two per day. Side effects are similar to those of the other triptans. Axert combines good efficacy with excellent tolerability. In 2009, Axert gained an official FDA-indication for use in adolescents with migraine.

Naratriptan (Amerge) is a milder, longer-acting triptan. A generic form is now available. The usual dose is every three to four hours as needed, but limited to two per day at most.

NON-TRIPTAN FIRST LINE ABORTIVES FOR MIGRAINE

Cambia (diclofenac potassium). New in the USA in 2010, Cambia is an excellent new migraine abortive. It is useful in younger patients, or older ones who can tolerate NSAIDs. It is a 50 mg. diclofenac packet to be mixed with water; it is available in boxes of three or nine packets. The usual dose is one packet, which may be repeated every two to four hours, with a limit of three packets in a day at most. Typical side effects of NSAIDs, primarily GI, may occur. Cambia may be combined with triptans. Caffeine may be added to increase efficacy.

Excedrin (or Excedrin Migraine). Useful as an over-the-counter preparation, it contains 250 mg. aspirin, 65 mg. caffeine, and 250 mg. acetaminophen. Anxiety from the caffeine or nausea from the aspirin is common. One or two tablets every three hours is an effective dose for patients with mild or moderate migraines. Tension Excedrin is also available, but is less effective. It contains acetaminophen plus caffeine. Rebound headache may occur with overuse; four per day (but not on a daily basis) should be the maximum.

Naproxen (Anaprox, Aleve).Useful in younger patients, naproxen is occasionally helpful for menstrual migraine. It is non-sedating, but patients report very frequent GI upset. The usual dose is 500 mg. with food or a Tums to start; it may be repeated in one hour if no severe nausea is present, and again in three or four hours. Limit to three per day at most. Available over-the-counter as Aleve, 220 mg., or generic. Adding caffeine increases efficacy. Naproxen may be used at the same time as a triptan.

Ibuprofen (Advil, Motrin). Available over-the-counter, and approved for children. Liquid Advil is also available. Occasionally useful in treating menstrual migraine; GI side effects are common. The usual dose is 400 to 800 mg., every three hours, limiting the total dose to 2,400 mg. per day. Combining ibuprofen with caffeine may be helpful. The short half-life is a drawback. May be used with triptans, even at the same time.

MigraTen (similar to Epidrin, though Epidrin has an added sedative and does not contain caffeine; Epidrin is more readily available). MigraTen capsules are a combination of 100 mg. caffeine, 65 mg. isometheptene, and 325 mg. acetaminophen. Isometheptene is a mild vasoconstrictor. The usual dose is one capsule every two to three hours as needed. Due to the caffeine, limit these to two or three a day, with some exceptions. MigraTen is non-sedating and non-addictive. The caffeine may cause nervousness or a faster heartbeat. Patients with insomnia should not use it after 3 P.M. or so. Patients with high blood pressure should use MigraTen with caution, and only if the blood pressure is controlled. MigraTen is helpful for migraines as well as less severe headaches. It fits the need for a non-addicting medication that does not cause drowsiness. The availability of MigraTen varies. If it is not available, Epidrin is usually used, along with additional caffeine.

TREATMENT OF MENSTRUAL MIGRAINE

Menstrual headaches are often severe, prolonged and debilitating. The severe intensity of menstrual migraines often dictates stronger abortive measures. Therapy for them follows the general abortive therapy for migraine; triptans are particularly useful for menstrual migraine. In addition to the usual abortives, cortisone (prednisone, dexamethasone) is effective for many women; it is utilized in very

limited amounts. We use 10 or 20 mg. prednisone or 2 to 4 mg. dexamethasone every 8 to 12 hours, with a limit of three tabs per month. Many women with severe menstrual migraines require a combination of triptans, low dose cortisone, analgesics, and antiemetics.

The timing of preventive therapy is difficult for most women; either their menstrual periods are irregular, or the headaches occur at different times in the cycle. However, for some the following are helpful:

NSAIDs (Naproxen, etc.): Effective for many women and usually well tolerated. These are started one day prior to the expected onset of the headache. Many NSAIDs have been utilized, including naproxen, ibuprofen, flurbiprofen, meclofenamate sodium, etc. GI upset is common.

Triptans. Frova (frovatriptan) is a long-acting and well-tolerated triptan. Its utility in menstrual migraine has been established. One method of dosing is 2.5 mg., once or twice a day for three to five days around the time that the menstrual migraine would typically occur. Although not as well-studied, the other triptans may also be helpful as menstrual migraine preventives. They are started the day prior to headache onset.

Hormonal approaches. Estrogen prior to menses has been used, but is questionable in its effectiveness. Occasionally, the birth control pill, used on a cyclic basis, will reduce headaches. When used continuously (no break), it may provide better relief. The most commonly utilized hormonal approach is the continuous birth control pill, with a menstrual period every 4 months. However, the birth control pill can increase migraines. As with other preventives, hormonal approaches often are disappointing, or they may initially provide relief and then decline in efficacy over the following months.

SECOND LINE ABORTIVE MEDICATIONS FOR MIGRAINE AND CDH

Ketorolac (Toradol; generic is available). The injections are much more effective than the tablets. Patients may use the injections at home, 60 mg. per 2 cc. The usual dose is 60 mg., which may be repeated in one hour if necessary. Nausea or GI pain may occur. Ketorolac is nonaddicting and does not usually cause sedation. Limit to three per week due to possible nephrotoxicity. IV Ketorolac is very effective.

DHE. (Migranal is the brand name of DHE Nasal Spray. Inhaled form (Levadex) is awaiting FDA approval). Effective as an IV or IM injection, and occasionally as a nasal spray. A new, inhaled form, Levadex, is pending FDA approval, and indications are that it may be an excellent abortive. All forms of DHE are safe and well tolerated. Nausea, leg cramps, and burning at the injection side are common. IV DHE is very effective in the office or emergency room. One mg., IM or IV, is the usual dose, but this may be titrated up or down. If it is the first time a patient has used DHE, start with 1/3 or 1/2 cc only.

Butalbital. (Fiorinal, Fioricet, Esgic, Phrenilin) Fiorinal contains ASA, butalbital, and caffeine; Fioricet, Phrenilin and Esgic replace the ASA with acetaminophen. Generics of these compounds may not work as well. These medications are addicting, but very effective for many patients. Dosage is one or two tablets or capsules every three hours, with a limit of 30 or 40 pills per month at most. Fiorinal #3, or

Fioricet with codeine, adds 30 mg. of codeine and is more effective than plain Fiorinal or Fioricet. Esgic Plus adds additional acetaminophen to Esgic. Phrenilin contains no aspirin or caffeine, and is very useful at night, or in those with GI upset. Short-lasting tiredness and spacey or euphoric feelings are common side effects. Butalbital must be used sparingly in younger people.

Opioids. (Fiorinal with codeine, Vicoprofen, Vicodin, oxycodone, meperidine, etc.) PO or IM, these are often the best of the 'last resort' approaches. When given IM, they are usually combined with an antiemetic. While addiction is a potential problem, the difference between dependency and addiction is crucial to understand. Ultram (tramadol is the generic) is milder, with relatively few side effects. Vicoprofen combines 7.5 mg. of hydrocodone with 200 mg. ibuprofen; generic is available. It is more effective than the other hydrocodone preparations because of the addition of ibuprofen, and generally is well tolerated. Actiq (Fentanyl oral) has been used in several small studies, but is not indicated for this use. Opioids should be used sparingly in younger patients.

Corticosteroids. Cortisone is often the most effective therapy for severe, prolonged migraine. Dexamethasone (Decadron) or Prednisone are the usual oral forms, and are dosed at 4 mg. of Decadron or 20 mg. of Prednisone, 1/2 or 1 every 8 to 12 hours, as needed. Smaller doses may also be effective. Three tablets a month is the usual maximum. These are very helpful for menstrual migraine. The small doses limit side effects, but nausea, anxiety, a "wired" feeling and insomnia are seen. IV or IM steroids are very effective as well. Patients need to be informed of, and accept, the possible adverse events.

Ergots. These older vasoconstrictors have many side effects, but are often effective. At most, use on only two days out of seven. Nausea and anxiety are common with ergotamine compounds. Cafergot adds caffeine to the ergotamine. Only compounded Cafergot PB is available. The suppositories are more effective than the tablets. Rebound headaches are common with overuse of ergots. Use with caution after age 40, particularly with cardiac risk factors. Ergomar SL tabs are back on the market. Ergomar is an excellent brand, pure ergot with no caffeine. The Ergomar dose is 1/2 or 1 tab once or twice a day PRN.

Miscellaneous Approaches. Muscle relaxants (Soma, Valium) or tranquilizers (Klonopin, Xanax) are occasionally useful, primarily to aid in sleeping. IV Depacon (sodium valproate) is safe and can be effective. The "atypical antipsychotics," such as Zyprexa or Seroquel, may be occasionally useful on an as-needed basis. In the ER, IV Compazine or Reglan may be useful. Certain preventive medications (Depakote, Topamax, amitriptyline) may be useful on an "as-needed" basis, utilizing low doses every 4 to 6 hours PRN. The antihistamine Benadryl is occasionally useful IM.

This guide is the author's opinion. Medications must be individually prescribed and used only in conjunction with treatment by a physician. Side effects, as listed in the PDR, must be accepted and understood. Some medications and treatments listed do not have an official FDA indication for the condition discussed. This guide is not a prescription, and it does not represent a standard consensus of treatment.

ANTIEMETIC MEDICATIONS

These are commonly prescribed for nausea and other GI symptoms.

Promethazine (Phenergan): Mild but effective for most patients. Very sedating, but with a low incidence of serious side effects. Available as tablets, suppositories and oral lozenges (which are formulated by compounding pharmacists). Used for children and adults.

Prochlorperazine (Compazine): Very effective but there is a high incidence of extrapyramidal side effects. Anxiety, sedation and agitation are common. Given intravenously, it may stop the migraine pain as well as the nausea. Tablets, long-acting spansules, and suppositories are available.

Metoclopramide (Reglan): Mild, but well tolerated; commonly used prior to IV DHE. Fatigue or anxiety do occur, but usually are not severe. Five to 10 mg. are given PO, IM or IV. It is in Pregnancy Category B (relatively safe).

Trimethobenzamide (Tigan): Well tolerated, useful in children and adults. Tablets, suppositories or oral lozenges may be used; lozenges are formulated by compounding pharmacists.

Ondansetron (Zofran; generic is available) Dose is 4 or 8 mg. PO. A very effective antiemetic with few side effects, but very expensive. It is not sedating. Zofran is extremely useful for patients who need to keep functioning and not be sedated with an antiemetic. Available as oral tablets or as Zofran ODT (orally disintegrating tablets). It is in Pregnancy Category B (relatively safe).

PREVENTIVE MEDICATIONS

WHAT PATIENTS NEED TO KNOW PRIOR TO STARTING A PREVENTIVE

In using medication, a realistic goal is to decrease the tension headache severity by 70%, not to completely eliminate the headaches. It is wonderful when the headaches are 90% improved, but the idea is to minimize medication. Most patients need to be willing to settle for moderate improvement.

Patients with more than three migraines per month that are not well-controlled may be candidates for preventives. Those with chronic daily headache are more likely to need preventives. A preventive is chosen with regard to the type of headache and comorbidities, such as anxiety, depression, GI upset, etc. Preventives may take 3 to 6 weeks to work, and there may be only a 50% improvement. The patient must accept this, and be willing to tolerate the possible side effects.

Patients must be willing to change medications when necessary. They need to be aware that what is effective for someone else may not work for them. Trial and error is often used to find the best preventive approach for a person. Preventive medications may take weeks to become effective. The doses often need to be adjusted, and thus patience is necessary with these medications. The physician needs to be available for phone consultations pertaining to the headaches and medicine. In the long run, preventive medications are effective for approximately 50% of patients.

Preventive medications are individualized toward the patient's needs. We use a particular preventive depending upon the person's comorbidities, GI system, medication sensitivities, etc. Fatigue is another major reason for patients abandoning a preventive medication. Headache patients commonly complain of fatigue, and tend to give up on medications that increase tiredness.

Side effects are possible with any medication; a patient has to be prepared to endure mild side effects in order to achieve results. We cannot stop one medication and switch to another because of very mild side effects. Most patients are willing to put up with mildly annoying side effects. Most preventive medications are utilized in medicine for another purpose. Patients should be informed that Elavil, for instance, is also used for depression, usually in much higher doses. Patients using Elavil should be told why, and be reassured that it is not because they are depressed.

NATURAL SUPPLEMENTS AND HERBS FOR HEADACHE

Feverfew, Petadolex (butterbur), and magnesium oxide have all proven effective in double-blind studies as migraine preventives. Of these, Petadolex has been the most effective. Omega-3 fatty acids may help headaches, and are an excellent supplement for general good health.

Petadolex is commonly used in Europe, and this herbal preparation has been successful in preventing migraines in several well-designed blind studies. The usual dose is 50 mg., twice a day. Earlier concerns about carcinogenesis with this family of herbs have decreased with Petadolex, which is a purified form of the herb butterbur. Patients have occasionally experienced GI upset or a bad taste in the mouth, but Petadolex is usually well tolerated. It is prudent to stop it every three months or so. Available by calling 1-888-301-1084 or through www.petadolex.com.

Magnesium is a naturally occurring mineral which helps many systems in the body to function, especially the muscles and nerves. It has been shown that magnesium levels in the brain of migraine patients tend to be lower than normal. Magnesium oxide is used as a supplement to maintain adequate magnesium in the body. A dose of 400 or 500 mg. per day can be used as a preventive; tablets are found in most pharmacies. However, mild GI side effects may limit use. There are also complications from drug interactions, and kidney and other diseases.

Feverfew has been demonstrated to be mildly effective in some patients for prevention of migraine headache. Feverfew can cause a mild increased tendency toward bleeding, and should be discontinued two weeks prior to any surgery. The problem with many herbal supplements is quality control. The amount of parthenolide (the active ingredient in feverfew) varies widely from farm to farm; certain farms consistently have better quality than others. Eclectic Institute uses a process that freeze-dries the herbs, making the product highly reliable. It is available in health food stores and at Whole Foods. The usual dose is 2 capsules each morning. Patients occasionally will be allergic to feverfew, and it should not be used during pregnancy.

Long Chain Fatty Acids (Omega-3 fatty acids) may play a role in headache prevention, and possibly be useful against anxiety, hypertension, arthritis, high lipids, depression and heart disease. We usually recommend fish oil or flaxseed oil, 1000 mg. capsules, two to four per day. (In studies on depression, as many as eight per day have been utilized). Fish oil capsules may be more effective than flaxseed oil.

Fatty fishes such as salmon and tuna contain more oil than others. Look for the brands with the highest amounts of EPA/DHA listed on the label.

FIRST LINE PREVENTIVE MEDICATIONS FOR MIGRAINE

Topamax (topiramate). Topamax is FDA approved as a migraine preventive. A generic is available, but is not always as effective. This anti-seizure medication is utilized for migraine, CDH, and cluster headache. It does not irritate the liver. Sedation and cognitive side effects (such as confusion or memory problems) may limit its use. Topamax often decreases appetite, which leads to weight loss; this is unusual among headache preventives. The starting dose is 25 mg. once or twice daily; this may be pushed to 100 mg. once or twice per day. 100 mg. daily is the usual dose. It is usually well-tolerated in lower doses; may be effective as a mood stabilizer for some milder bipolar patients. GI upset may occur. Acute glaucoma has been a rare side effect. The risk of forming kidney stones is increased by the use of Topamax. Bicarbonate levels should be monitored, as Topamax may cause a dose-related metabolic acidosis.

Valproate (Depakote).This seizure medication is a long time staple, popular for migraine prevention. It is usually well tolerated in the lower doses utilized for headaches. The generic may not be as effective. Liver functions need to be monitored in the beginning of treatment. Side effects include lethargy, GI upset, depression, memory difficulties, weight gain and alopecia. Dosage ranges from 250 to 1500 mg. per day, in divided doses. The average dose is 500 to 1000 mg. per day. Levels need to be checked for toxicity on the higher doses. Depakote is also one of the primary "mood stabilizers" for bipolar. Available in 125, 250 and 500 mg. tablets. Depakote ER, 500 mg., is an excellent long-acting tablet that may be dosed at once daily; Depakote 250 ER is also available. As with most preventives, Depakote needs four to six weeks to become effective. It is FDA-approved for migraine prevention. Depakote should not be used during pregnancy.

Beta Blockers. Effective for migraine. Long-acting (LA) Inderal capsules may be dosed once per day. Occasionally effective as a preventive for daily headaches. Sedation, diarrhea, lower GI upset and weight gain are common. Very useful in combination with amitriptyline. Dosage begins with the long-acting at 60 mg., and is usually kept between 60 and 160 mg. per day. Lower doses are sometimes effective, such as 20 mg. BID of propranolol. Other beta-blockers are also effective, such as metoprolol (Toprol XL) and atenolol. Some of these are easier to work with than propranolol because they are scored tablets, and metoprolol and atenolol have fewer respiratory effects. Depression may occur. Beta blockers are useful for those with concurrent hypertension, tachycardia, panic, anxiety, and MVP. A new beta blocker, nebivolol (Bystolic), may be helpful, and has fewer side effects.

Amitriptyline (Elavil and other tricyclics). Effective, inexpensive and also useful for daily headaches and insomnia. Use in low doses, at night. Sedation, weight gain, dry mouth and constipation are common. Starting dose is 10 mg., working up to 25 or 50 mg.; can be pushed up to 150 mg., or decreased to 5 mg. Other tricyclic antidepressants such as doxepin and protriptyline can be effective for migraine. Nortriptyline is similar to amitriptyline, with somewhat fewer side effects. These are also used for daily tension-type headaches. Protriptyline is one of the few older antidepressants that does not cause weight gain. However, anticholinergic side effects are increased with protriptyline. While the

SSRI's are utilized, they are more effective for anxiety and depression than for migraine. Tricyclics are more effective for pain than are the SSRI's.

Naproxen (Naprosyn, Naprelan, Anaprox, Aleve, and other NSAIDs). Useful in younger patients, once a day dosing. Sometimes helpful for daily headaches, but particularly useful for menstrual migraine. Nonsedating, but frequently causes GI upset. Effective as an abortive, and may be combined with other first line preventive medications. The usual dose is 500 or 550 mg. once a day, but this may be pushed to twice a day. Other anti-inflammatories can be utilized for prevention of migraine. As with all anti-inflammatories, GI side effects increase as people age, and so these are used much more in the younger population. With daily NSAIDs, blood tests are needed to monitor liver and kidney function.

Verapamil. Reasonably effective for migraine; once a day dosing with the slow release (ER) tablets. Usually nonsedating, and weight gain is uncommon. Occasionally helpful for daily headaches. May be combined with other first line medications, particularly amitriptyline or naproxen. Constipation is common. Starting dose is 1/2 of a 240 mg. ER tablet, increasing quickly to one 240 mg. tablet per day. May be pushed to 240 mg. twice a day, or decreased to 120mg. or 180 mg. per day. With doses higher than 240 mg. daily, an EKG needs to be done.

Natural Supplements and Herbs. Many patients prefer to start with the natural preventives. Petadolex, a safer form of the herb butterbur, has been the most effective natural preventive. It has held up well in multiple trials. It is widely used in our office, and effective for all ages. See "Natural Supplements and Herbs for Headache," page 24.

SECOND LINE MIGRAINE PREVENTIVE THERAPY

Botulinum Toxin Injections. Botulinum Toxin A (Botox, Dysport) has been studied extensively in migraineurs. Approximately 50 to 60% of patients have significant relief after botulinum injections. Low doses are usually used (50 to 100 units total per patient, in 8 to 12 injections) primarily in the frontal and temporal areas. While it is expensive, Botox is relatively safe and only takes a few minutes to inject. One set of injections can decrease the headaches for 1 to 3 months. Posterior (occipital) or upper cervical injections are starting to be investigated, and appear to have some utility. Botulinum toxin may be safer than many of the medications that are utilized for headache.

Gabapentin (Neurontin; generic available). Neurontin is an anti-seizure medication that has been demonstrated to be useful in migraine and tension headache prophylaxis. Tablets are available in 100, 300, 400, 600 and 800 mg. sizes. The usual dose for headache prevention is 600 to 2400 mg. per day. In a large study on migraine, doses averaged around 2,300 mg. per day, but lower doses are usually prescribed. Some patients do well with very low doses (200 or 300 mg. per day). Sedation and dizziness may be a problem; however, Neurontin does not appear to cause end-organ damage, and weight gain is relatively minimal. Neurontin can be used as an adjunct to other first line preventive medications. The generic, gabapentin, is now widely in use. A newer drug, Lyrica (pregabalin), has a similar mechanism of action to gabapentin. Lyrica is an anti-seizure drug, useful also for preventing pain. Side effects are similar to those of gabapentin. The dose of Lyrica varies from 25 mg BID to 150 mg TID.

Polypharmacy. Two first line medications are used together. The combination of two preventives is more effective than one drug alone. Depakote is often combined with an antidepressant. Amitriptyline

may be combined with propranolol, particularly if the tachycardia of the amitriptyline needs to be offset by a beta-blocker; this combination is commonly used for "mixed" headaches (migraine plus chronic daily headache.)

The NSAIDs may be combined with most of the other first line preventive medications. Thus, naproxen is often given with amitriptyline, propranolol or verapamil. Naproxen is employed simultaneously as preventive and abortive medication. Polypharmacy is commonly employed when significant comorbidities (anxiety, depression, hypertension, etc.) are present.

Tizanidine and Cyclobenzaprine. A safe, non-addicting muscle relaxant, tizanidine is useful for migraine and CDH. The usual dose is one or two 4 mg. tablets qhs; the 4 mg. tablets are double-scored, so that patients may begin with 1/4 or 1/2 tablet. Sedation and dry mouth are common. Tizanidine may be used on a PRN basis for milder headaches, or for neck or back pain. A 2 mg. tablet is also available. Cyclobenzaprine (10mg) is helpful for sleeping, and helps some with migraine and CDH. A half- tablet may be used. Sedation is a common side effect.

Ace inhibitors and ARB's. There have been a number of studies on this category of blood pressure meds; ARB's are preferred due to the minimal side effects. Examples include Cozaar,***(losarton??)*** Benicar, and Atacand. For the patient with HTN and migraine, these may be useful. Side effects include dizziness, among others, but they are usually well tolerated, with no sedation/weight gain.

Antidepressants (Effexor XR, Cymbalta, Pristiq) Effexor XR is an excellent antidepressant; used primarily as a SSRI at lower doses, and at 100 to 150 mg., norepinephrine is also increased. The generic form of Effexor may not be as effective. The antidepressants with dual mechanisms (serotonin and norepinephrine are more effective for pain and headache. Doses vary from 75mg to 225mg, and Effexor XR is particularly useful for anxiety with depression. Pristiq is an excellent newer version of Effexor. Duloxetine (Cymbalta) also has a dual mechanism of action, and has been useful for pain.

WHEN TO PROCEED QUICKLY WITH TWO PREVENTIVES AT A TIME

With most patients, we utilize one preventive medication at a time, beginning with low doses and slowly raising the dose as needed. Most patients appreciate the approach, and are willing to wait for the medication to work.

At times, patients can become extremely frustrated with their headaches, and desire quick results. When these patients suffer from moderate or severe chronic daily headache, or with severe migraines, pushing ahead at a faster rate with a preventive approach is justified. For instance, amitriptyline and verapamil, or amitriptyline and propranolol may be initiated at the same time. Alternatively, doses of a single medication may be increased rapidly. The initial amount of preventive medication utilized for a patient depends upon the severity of the headaches and the frustration level of the patient.

Patients with new onset of severe headaches, typically daily headaches plus migraine, are often extremely upset and frustrated with the pain. In this situation, pushing preventive medication at a faster pace is justified. Of course, patients need to be willing to put up with certain side effects.

THIRD LINE MIGRAINE PREVENTION (For Refractory Patients)

More information is available in the extensive article "Refractory Chronic Migraine" on our website, www.headachedrugs.com

LONG-ACTING OPIOIDS

(METHADONE, OXYCONTIN, KADIAN, MS-CONTIN, AVINZA, DURAGESIC)

In my practice, long-acting opioids are the most commonly utilized approach for refractory chronic migraine. In a small, select group of severe headache patients, particularly those with severe, chronic daily headaches and migraines, long-acting opioids have some demonstrated utility. The best candidate for long-acting opioids (LAO's) is the person who has done well on short-acting opioids (SAO's) and who does not have characteristics of a personality disorder and has not been addicted in the past.

The advantages of long-acting opioids include:

- avoidance of mini-withdrawals throughout the day and the "end-of-the-dose" phenomenon
- consistent dosing of one or two times daily decreases the obsession with the next dose
- maintenance of stable blood levels
- avoidance of the acetaminophen, aspirin and NSAIDs that are components of many short-acting preparations
- probable diminished risk of significant abuse
- better compliance, with less psychological dependency on the drug

Disadvantages of the long-acting opioids include:

- social stigma
- fatigue and constipation
- difficulty in obtaining scripts, with no refills available
- need for frequent office visits and monitoring
- risk of opioid-induced hyperalgesia
- risk of abuse, although probably less than the SAO's
- interactions with other sedating drugs and alcohol
- risk of overdose

Using higher doses of the opioid rarely works in the long term, in my experience. It places the patient at increased risk of addiction and abuse, and complicates withdrawal. Given the great variation in individual responses, it may be thought that the opioid should be increased or "pushed" to whatever level is beneficial to the patient. However, medical and regulatory considerations should be limiting factors in keeping the opioid dose at a low level. The choice of opioid may be a key factor; some have been shown to have less abuse potential. The long-acting fentanyl patch is subject to less abuse than oxycodone CR. Taken once or twice daily, the long-acting morphine preparations such as Kadian, Embedda or MS Contin have not been subjected to widespread abuse. Methadone may be more effective than some of the other medications, but has a litany of problems associated with it. Besides the social stigma, high protein binding is a risk, which may lead to irregular drug levels, difficulty with withdrawal, and an increased risk for sudden death. If methadone is used, it should be started at a very

low dose of no more than 5-10 mg. a day and titrated slowly. Patients placed on methadone require close monitoring, and other sedatives must be reduced or discontinued.

The usual dosing range in my practice is: methadone, 5 to 40 mg. per day; morphine, 20 to 90 mg. per day; oxycodone, 20 to 60 mg. per day; fentanyl patch, 12.5 to 50 mcg. per day. Opioids may be combined in low doses with stimulants. Stimulants may help the pain, and also offset fatigue. Patients must be aware of, and accept the risks of these medications.

DAILY OR FREQUENT TRIPTANS

Some patients respond only to triptan medications (sumatriptan, naratriptan, rizatriptan, almotriptan, zolmitriptan, frovatriptan, eletriptan). Short-lasting adverse events are often encountered with triptan use. These include paresthesias, fatigue, chest heaviness, jaw or neck discomfort, etc. Chest symptoms are, with rare exceptions, not of cardiovascular origin. Cardiac ischemia due to triptan use is rare. Triptans do constrict coronary vessels, but it is a mild and short-lived effect. Despite widespread triptan use, the number of adverse cardiac events has been limited. Echocardiography and electrocardiography generally are normal after triptan use, even in the presence of chest symptoms.

The primary issue with frequent triptan use, assuming rebound headache is not present, is long-term adverse events. The cardiovascular system would be the most likely for possible long-term sequelae. Chronic ischemic changes, valvular abnormalities, or fibrosis are theoretical considerations. To date, there is no evidence of long-term triptan use producing any of these adverse events. This has not been systematically studied, however. The number of patients throughout the world who have utilized triptans on a near-daily basis is unknown. Until these patients have been studied, it is reasonable and prudent to do cardiac monitoring, as well as hematologic tests.

STIMULANTS

When prescribed for headache patients, stimulants (dextroamphetamine, methylphenidate, phentermine, Adderall, Vyvanse) may be beneficial for various comorbidities, such as attention deficit hyperactivity disorder (ADHD), depression, and fatigue. In addition, stimulants do not cause the weight gain that is seen with a number of other current headache preventives. Amphetamines have been shown to possess intrinsic analgesic properties, primarily through brain catecholamine activity. They also intensify the analgesic effects of certain opioids. Stimulants have been utilized to counteract the sedation encountered by opioids. An excellent review article on stimulants as adjuncts for opioids concluded that, “The evidence suggests that amphetamine drugs may enhance the effect of opioids and, at the same time, decrease somnolence and increase cognitive performance.”

Advantages of stimulants include enhanced cognition and alertness, with no weight gain. Disadvantages primarily revolve around the side effects, such as anxiety or insomnia. Abuse may certainly occur, but it is uncommon in adults. Stimulants should be considered in patients with certain comorbidities. The few studies to date have indicated a positive role for stimulants, but further studies on stimulants for headache would help to clarify that role.

MONOAMINE OXIDASE INHIBITORS (MAOI'S)

For those with refractory chronic migraine and unipolar depression, MAOI's may be of help. MAOI's are sometimes effective for treatment-resistant depression. They are also effective for alleviating anxiety. MAOI's were commonly prescribed in the 1980's, but with the advent of SSRI's and triptans, they fell out of favor. Careful patient selection is crucial when using the MAOI's. Patients need to strictly observe the restrictions on diet and medications. I usually prescribe low doses of phenelzine (Nardil) 15 mg. tablets, and start with one tablet at night, increasing after a week to two tablets at night. If no response is noted after three to four weeks, I usually push the dose to three tablets. Five tablets a day (75 mg.) is the usual maximum. By always using the MAOI at night, the patient is less likely to encounter a food interaction. Side effects include insomnia, weight gain, sedation, and orthostatic hypotension.

The MAOI's have a reputation as being somewhat dangerous and difficult to use. Despite this reputation, MAOI's are usually well-tolerated. The hypertensive crisis that may occur with a food interaction is due to a number of factors, primarily the amount of tyramine, an amino acid, absorbed into the bloodstream. The tyramine content of food has been difficult to accurately establish, but there are lists of tyramine-rich foods to avoid. Look online or ask a dietician for the "MAOI diet." When patients consume the phenelzine at night, in low doses, while avoiding the major tyramine-rich foods, interactions are less likely.

REPETITIVE IV DHE THERAPY

Treatment with intravenous dihydroergotamine (IV DHE) is helpful for patients with frequent migraine, severe daily headache, and status migraine. DHE has a long track record with a good safety profile. Weeks of headache improvement are often seen. IV DHE is useful in patients who are withdrawing from analgesics. The protocol can be done in the office or hospital. In the office, the first dose of 1/3 mg. is given, and if it is well tolerated, the subsequent doses are 1/2 or 1 mg. Oral Reglan is usually given prior to the DHE to combat nausea. Three or four doses are given over two days in the office, and up to nine may be given in the hospital. The IV DHE is usually well tolerated and effective. Side effects include nausea, heat flashes, muscle contraction headache, leg cramps, diarrhea, and GI pain. After the DHE, patients are continued on prevention medication. Occasionally, Migranal (DHE) nasal spray, used daily for several weeks, is effective.

Levadex, the newer form of inhaled DHE, is awaiting approval by the FDA. In recent trials, patients with allodynia, menstrual migraine, migraine with nausea and vomiting, severe migraine and those treating late in their migraine cycle responded well to Levadex.

This guide is the author's opinion. Medications must be individually prescribed and used only in conjunction with treatment by a physician. Side effects, as listed in the PDR, must be accepted and understood. Some of the medications and treatments listed do not have an official FDA indication for the condition discussed. This guide is not a prescription, and does not represent a standard consensus of treatment.

FIRST LINE ABORTIVE MEDICATIONS FOR TENSION HEADACHE

Acetaminophen, Aspirin. These are the staple of OTC pain relief; acetaminophen is less effective for headache, but better tolerated. These need to be limited, so as to avoid a rebound situation; limit to no more than two per day, on average.

Ibuprofen (Motrin, Advil, Nuprin). Helpful for migraine and tension headache. Useful in children; liquid form is available. GI upset is relatively common, but ibuprofen is more effective for headache than acetaminophen. Adding caffeine can increase efficacy.

Caffeine. Caffeine beverages or tablets (100 mg.) are helpful for migraine and tension headache, either alone or as an adjunct to analgesics. Caffeine added to other abortives enhances their effectiveness and decreases drowsiness. For example, Midrin plus caffeine is an effective combination. Caffeine must be limited so as to avoid "rebound" headaches. The usual limit should be 150 to 200 mg., at most in one day. See sections on Caffeine Sources, page 11, and Medication Overuse Headache, page 32.

Caffeine-aspirin combinations. Excedrin Migraine has 65 mg. caffeine, 250 mg. of aspirin, and 250 mg. of acetaminophen; this is a very effective OTC preparation, but overuse leads to rebound headaches. Anacin contains half the caffeine but more aspirin. Excedrin Tension Headache is a very useful combination of acetaminophen and caffeine. Norgesic Forte is a useful combination of aspirin, caffeine, and orphenadrine, a non-addicting muscle relaxant; only generic is available.

Naproxen (Aleve (OTC), Anaprox, Naprelan(prescription)). Useful in younger patients and non-sedating, but it does frequently cause GI upset. The usual dose is one 500 mg. tablet with food; this may be repeated up to a maximum of three per day. If used on a daily basis, two per day should be the limit. Adding caffeine can increase efficacy. Naprelan is an excellent long-acting form of naproxen, available in 375 mg. and 500 mg. One Aleve equals 220 mg. Generic naproxen is also available OTC. Other NSAIDs, such as diclofenac, may be useful.

MigraTen. MigraTen caps are a combination of 100 mg. of caffeine, 65 mg. isometheptene, and 325 mg. acetaminophen. The usual dose is one capsule every two to three hours as needed. I usually limit these to two or three a day because of the caffeine. MigraTen is non-sedating and not addictive. The caffeine may cause nervousness or faster heartbeat. Patients with insomnia should not use it after 3 P.M. In patients with high blood pressure, MigraTen should be used with caution, and only if the blood pressure is controlled. MigraTen is helpful for the smaller headaches, as well as for migraines; it fits the need for a non-addicting medication that does not cause drowsiness. If used daily, limit to two per day. It is not always available; if not, caffeine may be added to Epidrin.

Tramadol (Ultram; generic available in all forms). Comes in 50 mg. tablets, 1 or 2 taken every four hours; usual dose is 100 to 200 mg. a day. Need to limit to 4 per day and 10 per week. It is generally well tolerated and has relatively few side effects but sedation, nausea, and dizziness may occur. Addiction is uncommon but is occasionally seen. Overuse may lead to seizures. Ultram is an opioid-like medication that is milder than codeine or hydrocodone. There is a long-acting form, Ultram ER (100 or 200 mg.) Generic Ultram ER is not always as effective. Ultracet is a combination of 37.5 mg. tramadol and 325 mg. acetaminophen.

SECOND LINE ABORTIVE MEDICATIONS FOR TENSION HEADACHE

Sedatives. Most are benzodiazepines, such as diazepam (Valium) and clonazepam (Klonopin). Sedation is common; because of this they are helpful for insomnia and anxiety. These drugs are habit-forming and need to be monitored with a monthly limit. They are a last resort, not a first choice. Addiction is always the major drawback.

Muscle Relaxants. These are occasionally useful on a "PRN" basis; the nonaddicting ones are preferred. These include orphenadrine (Norflex), tizanidine (Zanaflex), cyclobenzaprine (Flexeril), and Skelaxin. These may be combined with caffeine or NSAIDs. Sedation may be a problem. Zanaflex is particularly useful; doses range from ¼ to 1 of the 4 mg. tablets. Skelaxin is mild but non-sedating. Generic is available for all of these, except Skelaxin.

See Migraine Abortive section, pages 18-22, for other options. In patients with CDH and migraine, the migraine abortives often work well for regular daily headaches, but these also need to be limited.

FIRST LINE CHRONIC DAILY HEADACHE PREVENTIVE MEDICATIONS

Valproate (Depakote). See "First Line Preventive Medications for Migraine," pages 25-26.

Amitriptyline (Elavil). See "First Line Preventive Medications for Migraine," pages 25-26.

Topamax. See "First Line Preventive Medications for Migraine," pages 25-26.

SSRI's, Cymbalta, Pristiq and Effexor. Fewer side effects than amitriptyline, but are not as effective. More effective for anxiety and depression than for headache. Nausea, anxiety, sexual dysfunction, fatigue, and insomnia are common; weight gain is relatively common. Helpful for migraine in some patients. Begin with low doses. All of the SSRI's have been somewhat useful for preventing chronic daily headache, and for migraine, to a lesser extent. The dose for headache is usually lower than that for depression. Considering tolerability, these are often the best choice for chronic daily headache. Any of these may also exacerbate headaches. See section on SSRI's, pages 42-44; for Cymbalta, Pristiq and Effexor, see the section on antidepressants under Second Line Migraine Prevention, page 27.

Protriptyline (Vivactil). Effective and nonsedating. While weight gain does not occur, dry mouth, constipation, and dizziness are common. Commonly used in the morning, as insomnia may be a side effect. May be used in the morning with a sedating tricyclic used at night. Usual dose is 5 to 15 mg. per day (lower than the dose for depression). This is the only tricyclic that tends not to cause weight gain. It increases norepinephrine, not serotonin.

Nortriptyline (Pamelor). A metabolite of amitriptyline, nortriptyline is better tolerated than amitriptyline, but less effective. Side effects are similar to amitriptyline, but less severe. Useful in children, adolescents and the elderly. Occasionally helpful in migraine. Usual dose is 25 to 75 mg. per day; some patients do well on one 10 mg. capsule daily.

Doxepin (Sinequan). Very similar to amitriptyline. Begin with very low doses (10 mg. each night), as many patients cannot tolerate more than this amount. Usual dose is 25 to 75 mg. per day. Same side effects as amitriptyline, but generally better tolerated. It primarily increases norepinephrine.

NSAID's. These are not as effective as the antidepressants for chronic daily headache, but do not have the cognitive side effects. GI side effects are common, however. Hepatic and renal blood tests need to be monitored. NSAID's are used more frequently in younger patients. Ibuprofen is available over the counter, but is short-acting. Naproxen (Naprosyn, Naprelan, Aleve, Anaprox) is more effective than ibuprofen. Flurbiprofen (Ansaid) and diclofenac sodium (Voltaren) are also utilized. As always, we attempt to use the minimum effective dose.

Gabapentin (Neurontin). See "Second Line Preventive Medications for Migraine," on page 27. The newer Lyrica (pregabalin) may also be effective.

Tizanidine (Zanaflex) and cyclobenzaprine. These are muscle relaxants. See "Second Line Migraine Preventive Therapy," page 27.

Second and Third Line CDH Prevention Medication: See the Migraine Prevention section and the article, "Refractory Chronic Migraine" at www.headachedrugs.com

CLUSTER HEADACHE

Cluster headache is among the most severe pains known to mankind. It is characterized by excruciating, debilitating pain lasting from 15 minutes to three hours, and occasionally longer. The pain is usually located around or through one eye, or on the temple. The series of cluster headaches lasts several weeks to several months, once or twice per year. Clusters may occur every other year, or even less frequently. Several of the following are usually present: lacrimation, nasal congestion, rhinorrhea, conjunctival injection, ptosis, miosis of the pupil, or forehead and facial sweating. Nausea, bradycardia, and general perspiration also occur in many patients. Attacks usually recur on the same side of the head. Cluster headaches tend to occur more in spring and fall. There is usually no family history of cluster headache.

CHARACTERISTICS

Males are predominantly afflicted, in a 4:1 ratio to females. The onset of the clusters is usually between age 20 and 45, but there are cases of cluster headaches in teenagers, and occasionally clusters begin after age 50, though rarely after 70. Approximately one out of 250 men has cluster headaches. Women tend to have an older age of onset for their clusters than men.

The pain of the cluster attack is extreme and starts very quickly, usually without an aura or a warning. Within minutes, it becomes very severe. Although the pain is usually located about the eye or temple, it may be more intense in the neck or facial areas. Usually unilateral, the pain does change sides in 10% to 15% of patients, either during a cluster cycle, or at the next cycle. The pain itself is excruciating, described as sharp, stabbing, and even "like my eye is being pulled out."

The length of attacks varies, but 45 minutes is the average. Cluster patients usually experience one or two headaches per day, but this may increase to as many as seven in 24 hours, or decrease to as little as one or two per week. They usually occur around the same time each day, with the time period of 9 P.M. to 10 A.M. being most frequent. Approximately half of patients awaken from sleep with the headaches.

Cluster cycles, except in the chronic variety, usually last three to eight weeks, and then stop until the next bout. The cluster series can last as little as a few days, or as long as five months, at which time we begin to think that they may have converted to the chronic cluster type. Ten percent of cluster patients have chronic clusters, where there is no break of at least six months between attacks. One to two bouts of the clusters per year is average for most patients. They may increase in frequency, with only several months in between bouts, or several years may elapse between attacks. When periodic clusters begin at older ages, the chance of conversion to chronic cluster becomes greater. The natural history of clusters is not known, but the tendency is for the cluster series to stop at a certain age. Many patients "lose" their clusters in their late thirties or forties, particularly if they have had them for many years.

During the cluster series, the majority of patients are very sensitive to alcohol, and most patients will have an attack triggered by ingestion of alcohol. The other headache-provoking foods are less important, but avoiding MSG, aged cheeses and meats, and chocolate is prudent during a cluster series. MSG, in particular, seems to trigger a more severe headache in some patients. Cluster patients may experience their clusters after a stressful event ends, and occasionally excessive cold, heat, or bright light have been associated with the precipitation of a cluster. However, most cluster patients have very little control over their headaches, except with medication.

The typical episodic cluster series builds over one to two weeks and peaks for one to three weeks, then decreases. In the 10% of cluster patients with chronic clusters, periods of peaks and valleys with the headaches also occur, but the extended break without any clusters is not present. Chronic clusters are not usually consistent throughout the year, but tend to increase in certain seasons. In managing the clusters, we keep in mind the fact that the clusters build and then peak, and I often treat them with somewhat less medication, particularly corticosteroids, in the beginning of a cluster period. The natural history of cluster is unknown; however, it appears as if the longer people have had them, the more likely they are to abate.

NON-MEDICATION TREATMENT OF CLUSTER HEADACHE

Other than medication, very little is available for sufferers of cluster headache. The pain is too severe for relaxation techniques, and some patients have stated that biofeedback or relaxation exercises can precipitate or increase a cluster. However, simple deep breathing techniques or relaxation methods do aid some patients in helping to curb the anticipation of the cluster attacks. Much anxiety is generated during the day when the patient knows that nighttime will bring intense, excruciating pain.

Ice to the area of the pain may help, although sometimes heat will be more effective. Some patients let hot water from the shower run over their cervical area, or they use a water massage apparatus to direct the hot water over their cervical or frontal area. Applying moderate pressure to the temporal area is occasionally helpful. Cluster patients usually feel better when moving about during an attack. They tend to pace or otherwise be active, as opposed to the quiet sought by migraineurs.

Oxygen, a very effective treatment with no side effects, may be combined with abortive medications. Oxygen is worth trying for all patients. The success rate is about 60%. It is necessary to rent the tanks of oxygen. The usual dose is 12 liters/min, for 10-20 minutes; this may be pushed to 13 liters/min. The patient uses a mask while sitting up and leaning slightly forward.

ABORTIVE MEDICATIONS FOR CLUSTER HEADACHE

Sumatriptan Injections. The most effective cluster headache abortive medication is sumatriptan. The injections often work within minutes, and cluster patients often prefer this route of administration. At times, patients may require two or three injections in a day. Chest heaviness or pressure, tingling or a hot sensation, nausea and fatigue may occur. The STAT dose is available in 4 or 6 mg; the 4 mg. dose is usually effective. Many cluster patients do well with 3 mg. subcutaneous injections (half doses of the 6 mg.)for these, the individual vials are ordered with insulin syringes. Sumavel DosePro is a new, needle-free system in 6 mg. doses; see page 5.

Sumatriptan Nasal Spray (Imitrex or Zomig Nasal Spray). The 20 mg. nasal spray is convenient and easy to use. Although not as fast-acting or effective as injections, many patients prefer this route. Side effects tend to be minimal, but an unpleasant taste in the mouth is common. Cluster patients often require two or three nasal sprays in a day. Many patients use nasal sprays at times, and injections at other times, or, occasionally, the tablet form. Zomig NS is an effective form that is stronger than Imitrex nasal spray.

Oral triptans. Most tablets have been used for cluster headaches; these are more helpful for longer attacks, or clusters that are moderate in intensity. See the section on Migraine Abortive Medications, pages 17-19. Many patients prefer these to the injections, despite the longer onset of action.

PREVENTIVE MEDICATIONS FOR CLUSTER HEADACHE

Cortisone. Very effective for cluster headache, cortisone is used primarily for episodic clusters. It is given for one to two weeks during the peak of the cluster series. Prednisone, Decadron, or injectable forms may be utilized. When used for short periods of time, side effects are minimal. A typical regimen is to take prednisone (20 mg.) or Decadron (4 mg.) once a day for three days, then one-half tablet per day for ten days, then stopping. Additional cortisone may be given later in the cycle when the clusters increase. Higher doses may be needed when the cluster cycle is peaking in intensity. Due to adverse side effects, it is very important to minimize the use of cortisone.

Verapamil. A well-tolerated calcium channel blocker, verapamil is effective in episodic and chronic cluster. One 240 mg. ER tablet is taken once or twice a day. This is often initiated at the onset of the headaches, in conjunction with cortisone. Verapamil is then continued while the cortisone is stopped. Constipation is a common side effect. An EKG should be performed because of the possibility of cardiac abnormalities with higher doses of verapamil. Because of its efficacy and minimal side effects, verapamil is a mainstay of cluster prevention.

Lithium. Helpful for chronic cluster, and to a lesser degree, episodic cluster, lithium is utilized in small doses of 300 mg., one to three times per day. It may be combined with verapamil and/or cortisone. Lithium is usually well-tolerated in low doses; drowsiness, mood swings, nausea, tremor and diarrhea may occur. Blood tests need to be done to assess kidney and thyroid function.

Indomethacin. This powerful NSAID is helpful for some cluster patients; GI side effects may limit its use. The dose varies from 25 mg., once or twice daily, up to as much as 75 mg., two or three times a day.

HEADACHE IN CHILDREN AND ADOLESCENTS

Headache is a common complaint among children and adolescents. The prevalence of migraine in those with headache varies by age and gender throughout childhood. Migraine begins earlier in boys than in girls, and until the age of seven, migraine occurs slightly more often among boys**.** By menarche, the prevalence of migraine in boys and girls is roughly equal. However, after menarche, migraine begins to predominate among females, and this gender separation increases even further in late adolescence.

Headaches, especially migraines, have a significant impact on the lives of young people. Approximately 65-80% of children with migraine headaches will experience disruption of their normal daily activities at home, in school and other social settings. The burden of migraine may also result in the development or worsening of anxiety or depression. Because of quality of life issues, early recognition and management of headaches in children and adolescents is crucial.

Headache disorders can be categorized as either primary or secondary. As with adults, the vast majority of headaches in children and adolescents are primary headache disorders: migraine (with or without aura), tension-type headache, and chronic daily headache. Secondary headache disorders, although much less common, may be due to various organic etiologies which can range from the relatively benign to the serious. Such underlying organic conditions include infections, tumors, etc.

DIAGNOSTIC APPROACH

Although headache can be a presenting symptom of underlying organic pathology, accurate information from the patient and family is often enough to identify or rule out the most serious etiologies. The overwhelming majority of headache disorders are diagnosed by a thorough history and physical examination. A complete medical and psychiatric history, family history, medication history (including prescription, OTC, and vitamins or herbs), allergy history, and social history should also be obtained.

Migraine tends to be underdiagnosed**;** patients and their parents often attribute headaches and nausea to “the flu” or dismiss them as “sinus headaches.” Careful attention must be paid to the patient’s description of headache onset: its timing, frequency and duration; the severity, quality and location of pain, and any triggers, aggravating or alleviating factors. Associated symptoms, especially nausea, vomiting, photophobia and phonophobia, are often the key to an accurate diagnosis of migraine.

Potential indicators of organic pathology can include severe vomiting, a headache which awakens a child from sleep, and the absence of a family history of migraine. Also, progressive, unremitting daily

pain, neurologic symptoms and fevers are important. If any of these red flags are present, the appropriate laboratory and imaging investigations should be performed.

In a patient with an unremarkable history, where a primary headache disorder is suspected, laboratory investigation is usually not warranted beyond baseline labs. These usually include, but are not limited to, a complete blood count and metabolic panel.

Neuroimaging studies are usually not indicated in children with a normal neurologic examination and a history consistent with a primary headache disorder, especially migraine or tension-type headache. These children will not usually have significantly abnormal findings on head CT scans or intracranial MRIs. A small percentage may have incidental and/or unrelated findings, but routine neuroimaging is not absolutely indicated in children with typical primary headaches.

Usually, electroencephalography (EEG) is not helpful in the routine diagnostic assessment of pediatric headache patients. An EEG should be performed on patients with an atypical migraine aura, episodic loss of consciousness, or symptoms suggestive of a seizure disorder. Background slowing may be seen during some migraine attacks, but the EEG results are usually normal.

Lumbar puncture (LP) is indicated if meningitis, encephalitis, subarachnoid hemorrhage, or high-low pressure syndromes are suspected. Cerebrospinal fluid and pressure measurement should also be performed. In those patients where increased intracranial pressure is suspected, or in those with focal neurologic deficits, a head CT scan or similar neurologic imaging modality should be performed prior to a lumbar puncture. We attempt to avoid the LP unless absolutely indicated. However, if meningitis or encephalitis is suspected in a toxic-appearing patient, treatment should not be delayed in order to perform the head CT scan first.

THE BIOPSYCHOSOCIAL APPROACH TO MANAGEMENT

For those with more severe or frequent headaches, a comprehensive biopsychosocial approach is needed. This approach requires the collaboration of medical and behavioral specialists working together to improve a patient's overall functioning and quality of life. The combination of both pharmacologic and nonpharmacologic treatments is ideal for those with frequent headaches. Nonpharmacologic treatments are particularly important as they are typically more effective in children, and help to minimize medications and side effects.

Nonpharmacologic modalities consist of patient education, lifestyle strategies, behavioral interventions, physical therapy, etc. Patient education should be the first step taken. Legitimizing the headache as a physiological disorder is of primary importance. It helps to state, "…migraines are a genetic medical condition, like asthma or diabetes…"

Children and their parents usually want to hear three things from the physician: (1) the cause of the headache, including triggers, (2) the treatment and prognosis, and (3) reassurance that a primary headache disorder is not serious. It is important that realistic goals and expectations are set. Children and their parents should understand that there are no miracle cures for headaches.

It is usually helpful to use a headache diary as a means to identify specific triggers. Of course, some triggers (e.g. weather changes, stress, hormonal influences) cannot be avoided, but certainly many can be managed, such as missing meals, bright lights/sunlight, undersleeping/oversleeping, foods, perfume,

cigarette smoke and certain types of physical exertion. Headache diaries should record the frequency and severity of headaches as well as document the efficacy and side effects of treatments. Using a diary will improve the patient's or parents' recall of the headaches and make office visits more productive. They can also help persuade children and adolescents of the need for lifestyle changes.

Lifestyle strategies should include an emphasis on proper diet, exercise, and sleep habits. Headache patients do better with regular schedules, eating three or more meals per day, and going to bed and rising at the same time every day, including weekends. Daily exercise can be particularly helpful; young patients should strive for a minimum of at least 30 minutes of exercise per day. Generally, headache patients do better with low impact exercise such as swimming, walking, biking, and yoga.

Relaxation techniques such as biofeedback, deep breathing, and imaging should be encouraged. Most adolescents can learn relaxation techniques from books or audiovisual aids that are readily available. However, seeing a therapist who teaches biofeedback is much more effective. Most children under 10 can't learn biofeedback, but some as young as 7 can learn simple breathing and imaging techniques.

Behavioral interventions such as psychotherapy, counseling and relaxation techniques may be helpful for many adolescents who experience significant stress in their lives. Overscheduling adds to the usual adolescent stressors. Hard-driving, perfectionistic behavior and depression are increased in adolescents with severe headache. Children and adolescents who miss substantial blocks of time in school or social activities need to be assessed for depression, school phobia, and secondary gains. Counseling for the patient, as well as family centered therapy for children and parents, is helpful in promoting active coping.

PHARMACOLOGIC TREATMENT

There are two types of pharmacologic treatment for headaches: abortive and preventive. Decisions on medication will depend upon the frequency and severity of the headaches, and how much they bother the patient. Some children are not overly bothered by their daily headaches and tend to ignore them. Others may be incapacitated and miss an entire year of school.

As with adult headaches, abortive medication is used in the overwhelming majority of cases, without daily preventive medication. Patients should be encouraged to use their abortive medication early, while their headaches are mild. Early intervention is a key step in successful use of migraine abortives. See the list of first line abortive medications on page 37.

It is always reasonable to try biofeedback as the first step, with simple abortive medications, and attempt to avoid daily preventive medication if possible. However, with frequent migraines, or for moderate to severe daily headaches, daily preventive medication may be necessary. In order to minimize medications, start at a low dose of a daily preventive and slowly titrate up to reasonable efficacy. A more complete list of criteria for the use of preventive medication is on page 38.

Realistic goals and expectations for medications need to be discussed. The goal for abortive medications is to achieve significant relief, a 70% improvement, as quickly as possible. When preventive medications are used, the goal is to reduce headache frequency and severity by 30% or more, and to improve functioning. For some patients, the efficacy of their abortive medications improves with the use of a daily preventive.

When preventive medications are used in young people, it is wise to periodically attempt to discontinue the daily preventive, in an effort to minimize medications. As with adults, the idea is to see if the patient may return to simply using abortive medication. However, if an adolescent has had headaches for years, and has found a preventive that works, the usual practice is to continue to use it long-term.

Many children and adolescents have episodic migraines that respond easily to abortive medications. The challenge is in dealing with those who have frequent and debilitating headaches. A multidisciplinary approach is the most helpful for patients with severe headaches: a balance of medication with therapy and lifestyle changes. Management of headache disorders is a trial and error process; there is no "cookie cutter" approach. Although decreasing the frequency and severity of headaches is important, success is ultimately measured by how much we help the child return to normal functioning in home, school and social life.

ABORTIVE MEDICATIONS FOR MIGRAINE AND TENSION HEADACHES IN CHILDREN AND ADOLESCENTS

The following gives a practical guide to drug therapy in young people. Many drugs that are helpful for headache have not yet received an FDA indication for this use, and often have not been approved for children. The risks, side effects and problems associated with medications, as listed in references like the PDR, need to be fully explained to the family. Only when the family understands the risks and side effects, and accepts the potential problems, is a medication given to a child.

UNDER 12 YEARS OF AGE:

Ibuprofen. Effective, and available as a liquid, but GI upset is relatively common.

Acetaminophen. Well tolerated, safe, but not as effective as ibuprofen. Chewable tablets and liquid are available. Due to its relative safety, acetaminophen is the usual primary abortive used in children.

Naproxen (Naprosyn, Aleve) Effective abortive that is non-sedating and is available as a liquid. However, GI side effects are common. (Aleve = OTC = 220 mg.)

Midrin Capsules (Epidrin) (acetaminophen 325 mg/dichloralphenazone 100 mg/isometheptene 65 mg): ½ or 1 capsules in 4 hours PRN. Limit to two a day at most. These are very large capsules, but may be taken apart and sprinkled into apple sauce or juice. Sedation and lightheadedness are common; GI upset occurs at times.

Caffeine. Either used by itself, or with an analgesic, caffeine is useful for tension and migraine headache. In children, soft drinks containing caffeine are helpful. Side effects are minimal when caffeine is used in very limited amounts.

Triptans are off-label, but occasionally used in low doses at ages 10-11.

OVER 12 YEARS OF AGE (includes the previous list plus the following):

Triptans. Almotriptan tablets (Axert) is the only triptan that is FDA-indicated in adolescents. Triptans are generally more effective than analgesics. They are contraindicated in complicated migraine and in those with cardiovascular risk factors. Potential side effects include flushing, chest tightness,

paresthesias, nausea, and somnolence. More effective when taken early. May be combined with NSAIDs (ibuprofen, naproxen). See section on migraine abortives for adults, page 18.

MigraTen (generic available). A combination of acetaminophen, isometheptene and caffeine, this is similar to Midrin (Epidrin), but non-sedating. Availability varies; if not available, we use Midrin and add caffeine.

CRITERIA FOR THE USE OF PREVENTION MEDICATION

- The headaches interfere significantly with the child's functioning socially or at school. The extent to which the headaches bother the child is a major consideration.
- Failure of nonpharmacological approaches (watching triggers, biofeedback, etc.)
- The child's and parent's willingness to utilize daily medication with possible side effects.
- Willingness of the child and parents to change medication, if necessary.
- Failure of abortive medication to effectively treat the headaches; continued frequency of headaches, daily or near-daily.

PREVENTIVE MEDICATIONS FOR MIGRAINE, TENSION, AND CHRONIC DAILY HEADACHES IN CHILDREN AND ADOLESCENTS

UNDER 12 YEARS OF AGE:

Cyproheptadine. Safe, but efficacy is questionable. It is usually well tolerated but fatigue and weight gain may be problems. Not as useful in children over the age of 11. It may be dosed once a day and is available in liquid form.

NSAIDs (ibuprofen, naproxen). Ibuprofen and naproxen may be utilized as daily preventives or as abortive for both tension and migraine headaches. The lack of sedation renders these very helpful for daily use. GI side effects are relatively common, and when these are used on a long term basis, regular blood tests for hepatic enzymes and renal function need to be done.

Petadolex (age 9 and older). A form of the herb butterbur, with good evidence for efficacy in migraine. Widely used in Europe; available for over 35 years and regarded as safe. One tablet (50 mg.) daily, may be increased to two. Occasional mild GI upset. May be ordered on www.petadolex.com, 888-301-1084.

Magnesium oxide. Available OTC as "Kid Calm." Mild, but effective for some. Safe in this age range. Usual dose is 100 – 200 mg. a day.

OVER 12 YEARS OF AGE:

Also see previous sections on preventives for adults

Petadolex. (see above)

Topiramate. Useful for both migraine and CDH, lower doses (25-50 mg.) are often effective; may be pushed to 100-150 mg. daily. Potential side effects include cognitive slowing, paresthesias, decreased appetite, weight loss, and, rarely, acute glaucoma, renal stones, and acidosis. Cognitive side effects often limit use.

Divalproex. Useful for both migraine and chronic daily headache (CDH), lower doses (e.g. 250 mg.) are usually used with some efficacy. May be pushed to 750-1000 mg. daily. Potential side effects include GI upset, sedation, weight gain, tremor, dizziness, and alopecia. Blood tests should be performed periodically for hepatic enzymes.

Gabapentin. Useful for both migraine and CDH, lower doses (e.g. 100-300 mg. BID to TID) are often effective. Potential side effects include dizziness and weight gain, although it is usually very well tolerated by most people, especially at the lower doses recommended.

Tricyclic Antidepressants. Effective for migraine and CDH.

Nortriptyline and **amitriptyline** are commonly used. Usually well tolerated in low doses and safe for long term use. Cognitive side effects, dry mouth, drowsiness, dizziness, and weight gain are common. Usual dose of amitriptyline is 10-50 mg daily.

Protriptyline does not cause weight gain, but is somewhat less effective. Blood tests should be performed periodically for hepatic enzymes and renal function.

Propranolol. Generally well tolerated. Fatigue, weight gain and decreased exercise tolerance may be a problem. Usual dose is 20-80 mg daily. With doses less than 60 mg. a day, BID dosing is required which is inconvenient for children. Other beta blockers may be used, including atenolol, metoprolol or nadolol.

Verapamil. A calcium channel blocker which is effective for migraine and occasionally CDH, it is generally well tolerated, with constipation a common side effect. Convenient once-a-day dosing with the sustained release formulations. Usual dose ranges from 80 mg. once a day up to 240 mg. ER a day.

PSYCHOLOGICAL FACTORS ACCOMPANYING HEADACHE

ATTENTION DEFICIT DISORDER (ADD)

Studies indicate that 4.7% of adults have ADD. It tends to be underdiagnosed, and is one of the more undertreated conditions in the country. ADHD includes the "H" for hyperactivity, but most people lose the hyperactive, fidgety portion by age 20. ADD is the most genetic of all psychiatric conditions. We usually screen family members for ADD. It is not uncommon for a parent to say, "my child was diagnosed with ADD and I think that I have it, too." To have ADD as an adult, you must have had the condition as a child or adolescent. If you did not, the attention problem as an adult is not ADD, but more likely a combination of stress, insomnia, medication, or other factors. It is an attentional problem, but not true ADD. The cost of untreated ADD is enormous; it can be linked to substantial increases in legal trouble, substance abuse, auto accidents, and broken or unfulfilled lives. Many people do compensate for their ADD and are able to achieve a great deal, but they usually do better when they are treated.

Adults with ADD will remember that they had difficulties with completing homework, with boring projects or reading assignments, and poor attention in many areas. They often remember working twice as much as others to achieve half the amount. While people do learn to compensate for the attentional problems, ADD still takes a great toll on quality of life, for both the patient and the family.

The characteristics of ADD include difficulty with tedious work, careless mistakes, inability to start projects or assignments, difficulty finishing assignments, irritability and impulsivity. An external clue may be unfinished piles of materials laying about the house. In addition there may be a tendency to misplace things, be easily distracted, have poor attention, and difficulty remembering appointments. ADD often has coexisting psychological conditions such as anxiety and depression. ADD itself creates stress, and the attention problem interferes with life's functioning, which can spiral into more anxiety and depression.

We utilize the Adult Self Report Scale (ASRS) as a screening test for ADD in adults. The scale should be answered as follows: **0=Never 1= Rarely 2=Sometimes 3=Often 4=Very Often**

1. How often do you make careless mistakes when you have to work on a boring or difficult project?
2. How often do you have difficulty keeping your attention when you are doing boring or repetitive work?
3. How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?
4. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?
5. How often do you have difficulty getting things in order when you have to do a task that requires organization?
6. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?
7. How often do you misplace or have difficulty finding things at home or at work?
8. How often are you distracted by activity or noise around you?
9. How often do you have problems remembering appointments or obligations?

Add up your score. The scale is:

0-16: Unlikely to have ADD **17-23:** Likely to have ADD **24 or higher:** Highly likely to have ADD

There are a number of good books in the bookstores on ADD. Some are general books that encompass child and adult problems, and others are books that focus on adult ADD. Outside of medication, behavioral treatments and therapies have been somewhat disappointing. Life coaches or therapists may be helpful, particularly with coexisting anxiety or depression. The primary mode of treatment' has been medication, as these have been the most successful of all of the therapies. If you feel that you may have ADD, it is important to work with a doctor who is trained in dealing with adult ADD patients.

The "first-line" medications for ADD are the amphetamines (Adderall, Adderall XR, Vyvanse) and methylphenidates (Ritalin, Ritalin LA, Focalin, Focalin XR, Concerta). Adderall XR is a longer-acting, once-daily form; Ritalin LA, Focalin XR, and Concerta are also longer-acting. Side effects of these include, among others, anxiety, faster heart rate, and insomnia. These medications do, at times, help headaches and fatigue.

If Adderall or Ritalin-type medications are ineffective, or can't be used, the second-line drugs include atomoxetine (Strattera), bupropion (Wellbutrin), nortriptyline, or desipramine. Other antidepressants have also been used. As usual, the idea with medication is to find an effective dose, but minimize medication. Modafinil (Provigil) is not FDA-indicated for ADD but is utilized as a second-line ADD drug. A new medication, Intuniv, is indicated for ADD, and may help certain behavioral disorders as well.

DEPRESSION

Depression profoundly affects feelings and moods, as well as productivity and behavior. In addition, depression often causes physical problems. Depression is a medical illness of a physiological nature; there is a strong genetic component, although not everyone will have a family history of depression. Depression is common in every socioeconomic group. It may occur once in a lifetime, or may be ongoing and chronic.

The symptoms of depression vary widely. There is typically a depressed mood with feelings of helplessness, sadness and hopelessness. Fatigue, decreased motivation and loss of interest in pleasurable activities are common indicators. There may be sleep disturbances, either sleeping too much or not enough. Easy awakening or difficulty going to sleep are common symptoms; so are concentration problems and difficulty in making decisions. They may have no interest in sex. Often, there is agitation and irritability.

Along with behavioral changes, physical changes often accompany depression. These may be seen in the GI system (stomach cramps, diarrhea or constipation) or in manifestations of pain, such as backaches, headaches or other syndromes. Weight may increase or decrease due to appetite changes.

Depression takes its toll on self-esteem, and patients may feel that they are worthless. The most serious side effect of depression is, of course, suicidal thoughts and the risk of suicide. While depression can affect any age group, in does appear somewhat differently in the various age ranges.

Some people have major depression, a bout lasting two weeks or more, while others have mild, ongoing depression. There is also bipolar depression, an important category (see page 46). Depression may worsen in certain seasons; it is called Seasonal Affective Disorder (SAD) when it is primarily related to the decreased sunlight of late fall and winter. Light boxes have been very effective in treating SAD.

Stressful events may trigger depression, or it may cycle in and out of people's lives, regardless of stress. Chronic medical illness or family illness may trigger depression, as can financial problems. Hormonal changes are known to play a role in postpartum depression; it is crucial to recognize and treat depressive symptoms in new mothers. The primary treatments for depression are medications and psychotherapy. The combination of the two is ideal. Exercise may also help.

ANXIETY

Everyone feels anxious or worried at times, especially around stressful events. Feeling very anxious or constantly worried without stress may be Generalized Anxiety Disorder (GAD). With GAD, there is usually unrealistic worrying and anxiety. Symptoms include irritability, trouble with concentration,

restlessness, a constant feeling of being keyed-up, loss of patience, feeling short of breath, overall muscle tension, increased sweating, difficulty sleeping, trouble swallowing, or a lump-in-the-throat feeling, heartburn, acid reflux or diarrhea. GAD is often accompanied by Irritable Bowel Syndrome (IBS) and headaches.

GAD may cycle throughout people's lives, and is certainly worse with stress. There is almost always a family history of anxiety, and the anxiety usually begins in childhood. Other anxiety disorders that may occur in children or adolescents are obsessive compulsive disorder, separation anxiety and panic disorder. As with depression, there are differences in the brain and nervous system of people with anxiety. Certain neurochemicals or transmitters show changes. Genetics has a major role in these disorders, which have as much of a physical component as asthma, headaches or diabetes. The amygdala, a small, walnut-shaped portion of the limbic system, is larger in those with anxiety. Certainly, stressful events can trigger anxiety, but most people with GAD have inherited physical and chemical differences in their brains.

Anxiety is eminently treatable with exercise, relaxation techniques, psychotherapy and medication. The medications involved are primarily the antidepressants, or the pure anti-anxiety drugs, the benzodiazepines (Xanax, Ativan, etc.) Examples of antidepressants are the SSRI's (Zoloft, Prozac, etc.) While it is inconvenient and expensive to go to a psychotherapist on a regular basis, it is very helpful in treating anxiety over the long run.

SSRI'S (SELECTIVE SEROTONIN REUPTAKE INHIBITORS)

Chronic anxiety is a problem in approximately 35% of migraine patients. Dysthymia or major depression is seen in 17% of migraineurs. Migraineurs are 12 times more likely to have panic disorder than those without migraine. The chronic anxiety or depression leads to a decreased quality of life in migraine patients. These comorbidities of anxiety or depression are a physical, genetic problem, just like migraines. The selective serotonin reuptake inhibitors (SSRI's) have been very effective in combating anxiety and depression. They also are somewhat helpful in preventing migraine or tension headache. Large-scale studies have not revealed SSRI's to be more than mildly helpful for preventing headaches. However, they continue to be widely used throughout the United States for headache patients because of the positive effect on anxiety and depression. The low incidence of adverse reactions is another factor in the widespread use of SSRI's.

The safety and efficacy of the major SSRI's (Prozac/Zoloft/Paxil/Celexa/Lexapro) in treating anxiety or depression is well established. Although SSRI's are not as effective as tricyclics (amitriptyline, nortriptyline, etc.) for pain, they have a very favorable side effect profile. The SSRI's have less of the dry mouth, constipation, weight gain and sedation seen with the tricyclics. SSRI's are also a safer choice in the elderly, primarily due to tolerability and the lack of cardiac side effects.

The major SSRI's differ somewhat in their side effect profile. Some patients do extremely well with one SSRI, but not with another. The most common side effects are nausea, spaciness, drowsiness or fatigue, dry mouth, anxiety, insomnia, decreased libido, impotence, asthenia, sweating, constipation, tremor, diarrhea and anorexia. Weight gain may be a major problem. These can decrease motivation. Many of the side effects are dose related. Minimizing the dose can, for instance, decrease the sedation or sexual

side effects. One key to minimizing side effects is to begin with low doses. Compliance is enhanced when the SSRI's are slowly titrated. The initial anxiety seen with SSRI's often abates if low enough doses are utilized. Since any antidepressant can trigger hypomania or mania in bipolar patients, it is prudent to "start low and go slow." Weight gain and sexual side effects are the most common reasons for discontinuation.

KEYS TO USING SSRI'S IN HEADACHE PATIENTS

- Start with very low doses. This minimizes sedation and anxiety and increases compliance. If the patient is bipolar, SSRI's are best avoided.
- If patients are warned about the initial anxiety that may occur with SSRI's, they are more likely to be compliant and stay on the medication.
- For most headache patients, lower doses are utilized than for severe depression.
- If one SSRI does not help or causes side effects, it is very often worthwhile to try another. Patients have widely differing responses to these medications.
- Slowly withdraw patients in order to avoid the withdrawal syndrome.
- If the headaches are exacerbated, discontinue the SSRI.
- Paroxetine (Paxil), fluoxetine (Prozac), and duloxetine (Cymbalta) have more drug interactions than the others. These are all 2D6 inhibitors.

THE MAJOR SSRI'S

These are more effective for moods than for headaches.

Fluoxetine (Prozac). Prozac is available in 10 mg., 20 mg., 40 mg. pulvules, 10 mg. scored tablets, or liquid(20 mg./5 ml.) Prozac Weekly is a once a week capsule, equal to 20 mg. daily. A generic form of Prozac is available. Prozac is the prototype SSRI, having been used in tens of millions of people. Prozac is a long-acting SSRI with a well- established track record Its elimination half-life is 4 to 6 days, but the active metabolite, norfluoxetine, has an elimination half-life of 4 to 16 days. The long half-life is generally an advantage in avoiding the SSRI withdrawal syndrome. It is important to start with low doses of SSRI's; 5 or 10 mg. of Prozac is a good starting point. Many patients report initial anxiety (or even panic) from SSRI's, and if they are on a low enough dose, they are less likely to discontinue the medication. Patients can begin with 1/2 tablet of 10 mg. Prozac. Over 4 to 10 days, the dose may be raised to 10 or 20 mg. The effective dose for migraine or tension headache varies widely, from 5 mg. per day to 60 mg. (or more). Formal studies on Prozac for headache prevention have yielded mediocre results. Most patients are on 20 mg. daily. Milder tension-type headache often responds to low doses (10 or 20 mg). As is true with tricyclics, lower doses of SSRI's are used for headache than for major depression. In some patients, SSRI's actually exacerbate headaches. Fluoxetine is an inhibitor of the 2D6 system, and to a lesser extent, 3A4.

Sertraline (Zoloft; generic is available.) Zoloft is available in 25 mg., 50 mg. and 100 mg. scored tablets. Zoloft is somewhat shorter-acting; elimination half-life is 26 hours of the parent drug and 62 to 104 hours of the active metabolite. Because the half-life is shorter than with Prozac, patients are occasionally able to stop Zoloft for one or two days and alleviate the sexual side effects. However, with

the shorter half-life, withdrawal syndrome is occasionally seen with Zoloft. I usually start with 25 mg., or 1/2 of a 25 mg. tablet, and slowly increase; the average antidepressant dose is 75 to 150 mg., but the usual headache dose is approximately 50 mg. While many patients are on 100 mg. or more for headaches, most patients are maintained on lower doses. The cost of the 50 mg. and 100 mg. tablets is approximately the same. In higher doses, Zoloft is a 2D6 and 3A4 inhibitor.

Paroxetine (Paxil; generic is available.) Paxil is conveniently available in 10, 20, 30 and 40 mg. tablets. Paxil CR (controlled release) is available in 12.5 and 25 mg. doses. The elimination half-life is 21 hours, with no active metabolite. Paxil is generally very well tolerated. I usually begin with 1/2 of a 10 mg. tablet and slowly increase to 10 or 20 mg.; many patients need 30 to 60 mg. for depression. Or, we start with 12.5 mg. CR and titrate as needed to 25 mg. CR. It is important to stop Paxil slowly in order to minimize withdrawal. Paxil (SSRI) withdrawal consists of one to several days (and occasionally longer) of flu-like symptoms, malaise, dizziness and asthenia. This often goes unreported to the physician. Managing the withdrawal can be difficult; at times, the addition of fluoxetine (Prozac) may help in weaning off of the short-acting SSRI. Paroxetine is a potent inhibitor of the 2D6 system and, to a lesser extent, 3A4.

Citalopram (Celexa; generic available.) Celexa is available in 20 and 40 mg. tablets, which are scored. The mean terminal half-life is about 35 hours. Celexa has a clean profile with regard to cytochrome P450 enzymes. It has been an outstanding antidepressant with a very good track record, and is well tolerated. Side effects are similar to the other SSRI's. As always, we start with low doses, half of a 20 mg. tablet for four to six days, then progress to 20 mg. per day. Withdrawal symptoms have been unusual with Celexa. Its use has mostly given way to Lexapro, but due to its lower cost, Citalopram is useful.

Escitalopram (Lexapro). Lexapro is a newer, more selective version of Celexa and has been fairly well tolerated. It is metabolized primarily by the liver. Lexapro has a favorable side effect profile, but side effects are similar to the other SSRI's. Lexapro is available in 10 and 20 mg. tablets. We start with 1/2 of the 10 mg. tablet for 4 to 6 days, and then increase to 10 mg. daily. Withdrawal symptoms are relatively unusual with Lexapro; it is fairly clean as far as drug interactions. Lexapro has risen to be one of the most prescribed antidepressants in the U.S.

Wellbutrin (bupropion; generic available) is actually an older antidepressant that is in its own class, aminoketone. Bupropion may work primarily through norepinephrine pathways. It is unlike tricyclics or SSRI's as it does not affect serotonin. Wellbutrin is available in lower doses. The XL form is dosed once daily, 150 mg. or 300 mg. The usual dose is 100 or 150 mg. slow release tablets once per day. For moderate to severe depression, the doses are pushed to 300 mg. or more per day.

The advantage of Wellbutrin (bupropion) is that sedation, weight gain and sexual side effects are much lower than many of the other antidepressants. In fact, weight gain has been no more than placebo and the sexual side effects are exceedingly low. While it is not as anxiolytic as SSRI's, the lack of sexual side effects and weight gain render this an excellent antidepressant. The efficacy for anxiety is somewhat less than with the SSRI's and Effexor, Pristiq or Cymbalta.

At higher doses, particularly at 300 mg. per day or more, people who are predisposed to seizures are at a slightly increased risk for seizure. This is dose-related and is approximately .1 % (1 out of 1,000) at 300 mg. per day, increasing to .4% at 400 mg. per day. In treating headache patients, we usually use lower doses. Bupropion is also utilized for smoking cessation under the name Zyban.

Remeron (mirtazipine). Remeron is available in 15 mg., 30 mg., and 45 mg. film-coated tablets, and is also available in dissolving tablets. Generic is available. Remeron enhances noradrenergic and serotonergic activity. Remeron is also an antagonist of histamine, which helps to explain its sedative effects. The usual dose is 30 mg. per day; however, we start with 7.5 or 15 mg. at night for a period of time before increasing to 30 mg. Somnolence is very common, but this is an advantage in agitated depressed patients with insomnia. Weight gain is commonly seen, and is a major limiting side effect. Overall, Remeron has fewer side effects than the older tricyclics. While its primary use is in depression, for which it is a very effective medication, headache is sometimes improved with Remeron. Remeron is commonly used as an adjunctive medication for severe, refractory depression. Due to Remeron's 5HT3 antagonist activity, it helps some patients who have IBS with diarrhea.

Effexor XR and Pristiq (venlafaxine). The long-acting Effexor XR is available in 37.5 mg., 75 mg. and 150 mg. doses. Effexor has been an outstanding antidepressant because of efficacy and tolerability. A generic is available, but does not always work as well. Pristiq is a newer form which is very well tolerated. Available in 50 and 100 mg. doses, it is usually started at 50 mg.; the final dose ranges from 50 to 100 mg. per day.

Basically, Effexor or Pristiq is an SSRI at low doses; at higher doses, norepinephrine, then dopamine, are affected. It is very well tolerated, with less weight gain and sexual side effects than some of the other antidepressants. Effexor has few interactions with cytochrome P450 enzymes, rendering it a fairly clean medication. We usually begin with 37.5 mg. and progress to 75 mg., with a typical dose in headache patients being 75 mg. or 150 mg. Effexor XR is particularly well tolerated. It is very useful in headache patients who have concurrent anxiety and depression. Sustained elevation in blood pressure may occur at higher doses, particularly 250 mg. per day or more. The lower doses have not increased blood pressure. While headache is a potential side effect of Effexor or Pristiq (and all of the others), it has been no more than the rate of placebo in studies. Nausea, constipation, somnolence, dry mouth, dizziness, insomnia and agitation are seen more than in placebo. However, if doses remain low, Effexor or Pristiq has been well tolerated. While Effexor or Pristiq is less effective than tricyclic antidepressants for pain or headache, its efficacy in anxiety and depression, and its tolerability render it an extremely useful medication.

Cymbalta (duloxetine). Cymbalta has two FDA pain indications, and is a very effective antidepressant. Cymbalta increases both serotonin and norepinephrine. It is available in 20, 30, and 60 mg. capsules, which should not be split apart. Cymbalta may be helpful for headache, as well as for anxiety/depression. The usual dose is 60 mg. daily for depression; starting dose is 20 or 30 mg., increasing over several days to weeks. Side effects include, among others, nausea, dry mouth, anxiety, fatigue, lethargy, sexual effects, and weight gain. Use with caution in patients with glaucoma. Cymbalta is a moderate CYP 2D-6 inhibitor. It has been much more effective for moods (anxiety and depression) than for pain.

THE BIPOLAR SPECTRUM

The comorbidity of migraine with anxiety and depression is well established, both in clinically based studies and in epidemiologic samples from community populations. The physiologic overlap between migraine and depression is considerable, and antidepressants or mood stabilizers often help both

conditions. Only 15% of those with bipolar syndrome have severe illness and mania. Most patients have much milder characteristics, with accompanying anxiety, depression and irritability.

In the vast majority of migraine patients who suffer from depression, anxiety is a complicating factor. The anxiety disorder often precedes the age of onset of migraine, with depression following at a later age. It is possible that poorly controlled migraine headaches may fuel the onset of depression, or depression may increase headache. However, it is more likely that shared environmental and genetic factors link migraine and depression.

The relationship between bipolar illness and migraine has not been as well studied as depression and migraine. However, in several studies, bipolar I and bipolar II were found to be increased in migraineurs. In our study, ("The Bipolar Spectrum in Migraine, Cluster and Chronic Tension Headache Patients", Robbins, L., *US Neurological Disease 2007 (2008)*, February 2008, Vol. 3, Issue II) we assessed 1000 consecutive migraineurs. The results were as follows: Bipolar I: 2.1 %; Bipolar II: 2.4%; Cyclothymic Disorder: 1.3%; Bipolar Disorder Not Otherwise Specified: 2.8%; Total Bipolar Spectrum: 8.6%. Recent studies have confirmed that at least 7% of headache patients fit into the bipolar spectrum, and 40 to 50% of bipolar patients have migraines.

The name "bipolar" greatly inhibits its diagnosis and acceptance. The mild end of the bipolar spectrum is basically depression, anxiety and agitation. It is the mild end that tends to be missed; look for those with persistently agitated, angry personalities, with frequent depression, excessive energy, and with a strong bipolar or depressive family history. A patient may not have clear hypomanic or manic episodes.

Soft bipolar signs include: early (teenage) depression, severe depression, quick-onset depression, agitated and angry depression, moody personality, very high anxiety, extreme mood swings and poor response to medication. Sleep disorders are common. Cyclical depression, for no apparent reason, with high anxiety, is common in bipolar depression. Another possible indicator of bipolar illness is an adverse reaction, including mind racing and severe anxiety, to antidepressants. Bipolar patients may react poorly to a number of other medications, including Sudafed, cortisone, sleep medicines and antihistamines.

When these patients are not diagnosed correctly, they are often are given a number of antidepressants, with predictable hypomanic results. Tricyclic antidepressants appear to have the highest propensity towards triggering mania, followed by the selective serotonin reuptake inhibitors (SSRI's). Any antidepressant can provoke hypomania (or full mania) in someone who is bipolar. Some patients do well on antidepressants, particularly if they are also on mood stabilizers. When a mood stabilizer is effective, the underlying agitation/anger/depression improves.

Whether the bipolar diagnosis is established or suspected, mood stabilizers often are very helpful for the moods and headaches. **Divalproex sodium** (Depakote) is effective for mania, hypomania, depression associated with bipolar disorder, and for headache prevention. Divalproex sodium has been extremely well studied for these conditions, and has become one of the primary migraine and chronic daily headache preventives. Lithium carbonate is not utilized as readily in the headache population, due to increased side effects as well as lack of efficacy for migraine. One or more of the newer antiepileptic drugs may prove to be helpful for bipolar disorders and/or migraine.

Carbamazepine (Tegretol) has some utility as a mood stabilizer, but not for migraine prophylaxis. The antiepileptic topiramate (Topamax) may improve moods in some patients. Oxcarbazepine (Trileptal) is a milder form of carbamazepine that may help mild bipolar illness.

Lamotrigine (Lamictal) is becoming one of the most commonly used mood stabilizers. It is one of the only effective medications for bipolar depression. Doses must be slowly titrated, due to severe allergic reactions seen in 1 or 2 out of 3000 patients. Lamictal may increase headache, but is usually well tolerated. The atypicals are also used for bipolar, and may help headache.

The recognition of increased comorbidity between migraine and bipolar illness has important clinical implications. By broadening our concept of the bipolar realm, we can improve outcome in these patients. Recognition of the milder end of the bipolar spectrum is crucial. Unfortunately, medications are often more effective for manic or hypomanic symptoms than for depression; the depression often goes untreated. Since bipolar patients are more often depressed than manic, many patients need an antidepressant in addition to a mood stabilizer, and may need up to four medications – for instance, lamotrigine, lithium, an antidepressant and an atypical.

THE USE OF ATYPICALS IN THE HEADACHE PATIENT

Atypicals, or antipsychotics, are poorly named. The majority of patients using these have never had psychosis. The newer atypical antipsychotics are useful in selected headache patients. For a patient with a moderate or severe personality disorder, the atypicals may ease the anxiety and/or depression. They can be an effective mood stabilizer in bipolar patients, and also are helpful for insomnia.

These medications can be useful as a headache abortive, primarily because of the induction of sedation and sleep. One commonly used atypical is quetiapine (Seroquel). The dosage may range from 25-300 mg. qhs. It is very important to use the lowest dose possible. The doses for headache patients with severe anxiety or insomnia tend are lower than the standard doses for schizophrenia. Seroquel is usually well tolerated, with sedation the next day being the primary side effect. Because of the risk of long-term side effects, particularly tardive dyskinesia and diabetes, these should only be used in the carefully selected patient where benefit outweighs risk. Patients must be aware of the possible side effects, such as weight gain.

Olanzapine (Zyprexa) has been utilized in a similar fashion. The usual dose is 2.5 or 5 mg. qhs; occasionally Seroquel or Zyprexa have been used on an as-needed basis with headache patients. While olanzapine (Zyprexa) is very effective, it does cause more weight gain, and possibly diabetes, than the other atypicals.

Risperidone (Risperdal) has been very effective, and we usually use low doses (0.25 or 0.5 mg. daily). These help induce sleep, and may offset nausea as well. The other atypicals may also be useful. Ziprasidone (Geodon) and aripiprazole (Abilify) are also available, and cause less weight gain. Abilify may initially cause anxiety or agitation. For some, Abilify has been remarkably effective in relieving depression. Asenapine (Saphris) is a new atypical which may be helpful in treating mixed episodes.

The atypicals are a very versatile group of meds, but they should be judiciously utilized, with informed consent. Sedation is the most common side effect to all of these atypicals, and the following are also seen: nausea, dizziness, restlessness, tremor, rash, weight gain, diarrhea or constipation. Hypomania

may occur. While QT prolongation may occur with any of the antipsychotics, this is possibly more of a concern with higher doses of ziprasidone (Geodon). The potential for some of these newer atypicals to cause an increase in blood sugar is a serious concern that may limit their use in some patients.

PERSONALITY DISORDERS

Some 10-15% of people have strong features of a personality disorder. There are a number of personality disorders, some of which are more dangerous and difficult than others. In general, characteristics of personality disorders include: lack of insight, poor response to psychotherapy or other therapeutic interventions, difficulty with attachment and trusting, sense of entitlement, and the creation of chaos and distress in family, friends and co-workers.

Personality disorders have a wide range of severity, from mild to very severe. They often flip between victim, rescuer, and persecutor. When they turn persecutor, they can be dangerous to the person that they have their sights set on. In general, therapy only helps people with personality disorders when followed over long periods of time. Seeing a therapist for several years may help to a degree, but goals and expectations are limited. The concept of "plasticity" of the brain is very important, as some people can improve naturally over time. One study of borderline personality disorder in adolescents indicated that by age 30, about 33% of the young people no longer had the disorder.

The following is a description of some of the more severe personality disorders. Many people do not fit neatly into these categories, but may have features of two or three types. The new version of the psychiatric classification manual, Diagnostic and Statistical Manual of Mental Disorders (DSM-V), may redefine these.

Paranoid Personality Disorder. These are people who tend to be distrustful, suspicious, and see the world as dangerous. They view themselves as constantly being mistreated. They are secretive and reluctant to confide in others. They doubt the loyalty of those around them, and believe they are being exploited or harmed. These patients bear severe grudges against others. They can become angry very easily and have a sense of entitlement. Paranoid personalities can become violent and dangerous; most spree killers are paranoid personality disorders. Some infamous world leaders, such as Joseph Stalin or Saddam Hussein, were most likely paranoid personalities.

Antisocial Personality Disorder. These people generally have no regard for the rights of others; they see themselves as better or superior, and tend to be irritable and impulsive. They are exploitative and very opportunistic; they may steal from the people around them and often have had trouble with the law. They frequently engage in fraudulent activities and make very good scam artists, such as the person who insinuates himself into a church group and ends up stealing all the funds. They generally have no remorse. Conduct disorder as a child often morphs into antisocial personality disorder.

Borderline Personality Disorder. These people have instability of mood, poor self image, and pervasive abandonment fears. There is an identity disturbance and major boundary issues. Borderlines usually demonstrate impulsiveness, suicidal behavior, and very quick shifts from depression to anxiety to irritability. There are usually chronic feelings of emptiness or severe "malignant" loneliness, plus anger and temper. Under stress they can become somewhat paranoid. Drug abuse or other addictive behaviors may occur. There are often sleep disorders with severe insomnia. Severe borderlines will perpetuate high-level drama and create chaos for everybody around them. They tend to split, which is,

they see people as wonderful or as terrible, with nothing in between. Examples include Adolph Hitler, and Glenn Close's character Alex, in the movie "Fatal Attraction." Borderline personalities can vary from mild to severe, and may become better, or worse, over time. Resources on this subject include Robert O. Friedel's book, Borderline Personality Disorder Demystified.

Narcissistic Personality Disorder. This is less common, where the people see themselves as being above others; they are grandiose, have a lack of empathy, and feel self-important with a deep sense of entitlement. They may be very vain and constantly require admiration. They are envious, arrogant, exploitative, and can be very angry. Examples include General George Patton, and Michael Douglas' character, Gordon Gekko, in the movie "Wall Street."

There are a number of other personality disorders that are not as dangerous for the people around them. Many patients do not have all of the characteristics of one particular personality disorder, but have aspects of a number of them. Personality disorder characteristics in people are often overlooked, and health care clinics may react and treat these patients in a dysfunctional manner. Treatment consists of maintaining limits and boundaries on the person, therapy with somebody who is experienced with personality disorders, and extending the weekly therapy for a prolonged time. Medications may help the anxiety and depression aspects, but no specific medications are considered very successful for personality disorders.