Headache is a common malady occurring in 90% of the population. Psychiatric disorders are common as well, and as a result, the 2 categories of conditions are likely to coexist in the same individuals. However, there is frequently a more complex interaction. Often the mutual progression of headache syndromes and psychiatric comorbidities interact to affect overall quality of life.

Many psychiatric syndromes and migraine (migraine being the most commonly disabling form of episodic headache) occur together in some individuals. There are numerous shared components, including family history and autonomic and sympathomimetic symptom complexes, as well as shared treatment with similar medications and behavioral regimens. Understanding the biologic connections and pathogenesis of these associated conditions should lead to improved diagnosis, treatment, and outcome in patient populations.

Characterization of headache types has been an active arena in clinical research. The International Headache Society lists several hundred headache types. However, most are phenotypes of conditions that often have complex and poorly understood genetic underpinnings.

Tension-type headache is the most prevalent form of head pain, but, by definition, is rarely disabling and is generally untreated or self-treated. Consequently, these individuals rarely come to medical attention. Migraine is the most common headache that presents to health care professionals. Twelve percent of the population in the United States is afflicted with migraine. Much of the burden of migraine is through the attendant psychiatric disorders.

Migraine is generally described as a condition of recurrent headaches, often unilateral and pulsatile, and often associated with photophobia, phonophobia, and nausea and exacerbated by movement. However, there are many variations of migraine. Up to 30% of migraines do not have pulsatile pain and the attacks are frequently bilateral, often leading to the misdiagnosis of tension-type headache.

The term migraine is often used in a general way to describe the state of a lowered threshold for the development of head pain. Many migraineurs have prodromal
symptoms occurring up to a day before the headache begins. These symptoms can include cold hands and feet, food cravings (for example, for chocolate), yawning, and a variety of mood changes, including depression or euphoria. Twenty percent of migraineurs experience focal neurologic complaints of an aura. The symptoms are often visual, but can be a sensory, language, motor, or a brainstem abnormality lasting up to an hour. A sequence of auras is common. An example would be a visual aura, followed by cheiro-orbital tingling, followed by numbness. This situation is likely because of activation followed by a metabolic depression involving the primary visual cortex, the primary somatosensory cortex, and the primary motor cortex. The aura symptoms commonly, but not invariably, precede the headache. Migraine headaches characteristically last 4 to 72 hours and are often followed by postdromal symptoms such as malaise and depression, which can last up to a day. During the postdromal period, migraineurs are vulnerable for a brief recurrence of the headache with exertion or a Valsalva maneuver.

Specific pathologic features are observed in the genesis of migraine attacks. Migraineurs seem to have a hyperexcitable cerebral cortex. This characteristic has been shown in various ways. Transcranial magnetic stimulation of the occiput produces phosphenes in all individuals, but a lower intensity is needed to produce this effect in migraineurs.

Cortical spreading depression (CSD) might be the common denominator for various migraine causes. Although this wave can be seen in other conditions, it is convincingly seen in migraine with aura. Less clear is the frequency of occurrence in migraine without aura, because it is difficult to study asymptomatic migraines in the earliest stages of attacks. CSD was originally identified by Leão after stimulating the cortex of rabbits. A wave spreading 3 to 6 mm/min spread across the cortex, posteriorly to anteriorly, first activating, and then depressing neuronal activity. Lashley, observing his own migraine auras, calculated that the observed symptoms during the aura correlated with a slow march of cortical activity at a rate of 3 mm/min. Positron emission tomography studies in spontaneous migraine attacks showed a spreading bilateral oligemia. Unlike in the older vascular theory, it has been observed that the headache in a migraine attack begins at a time of continued reduction in cerebral blood flow, making cerebral vasodilation an unlikely source of the head pain. The vascular changes in aura seem to be after neuronal changes. A wave of CSD or other factors occurring during a migraine activates trigeminal nociceptors in the meninges, leading to localized vasodilation, meningeal inflammation, and pain transmission. The vascular changes, long believed to be the fundamental cause of aura, are therefore likely secondary to the neuronal changes brought on by this wave, first exciting, then depressing neuronal activity.

Plasma protein extravasation also occurs in the dura. Because migraine pain follows meningeal inflammation and activation of nociceptors in the meninges, it is not surprising how similar the symptoms of meningitis are to a severe migraine. The trigeminal nerve innervates the pia and the meningeal arteries, and CSD activates trigeminal afferents. Therefore, the pain of migraine is typically referred to the trigeminal nerve distribution, commonly its first division, notably the eye and the temple. The presynaptic terminal of the trigeminal nerve contains vasoactive neuropeptides including neurokinin A, substance P (SP), and calcitonin gene-related peptide (CGRP). Activation of the trigeminal sensory C fibers in this region causes release of the neuropeptides, leading to vasodilatation and plasma protein extravasation.

It is possible that the predilection of a brain to develop CSD and its fundamentally hyperexcitable state relate to the psychiatric comorbidities that accompany migraine. Later in an attack that has not been terminated, abnormalities of central processing
occur as second-order trigeminal neurons are activated. This situation leads to cutaneous allodynia, in which the stimuli, which are not normally painful, cause a painful reaction, and migraineurs find it uncomfortable to brush their hair, loosen their ties, and remove their jewelry. Because sensory fibers converge centrally, the pain becomes generalized in the migraineurs’ head and less pulsatile. The cervical region becomes involved and they are often misdiagnosed as having tension-type headaches. This central sensitization is caused by involvement of wide dynamic range neurons in the trigeminal nucleus caudalis, which receive C fibers from the trigeminal ganglion. Increased amounts of glutamate, serotonin, nitric oxide, CGRP, and SP amplify the input received from $A_b$ fibers.

A genetically driven vulnerability for these attacks likely underlies the disorder of recurrent migraine attacks. This situation likely involves multiple genes interacting with environmental triggers over time. Studies of migraine family trees provide evidence for this genetic basis. First-degree family members experiencing migraine with and without aura have a higher than expected prevalence of the same type of migraine. Monzygotic twins have a higher concordance for migraine, when compared with dizygotic twins. This finding suggests that although there is a significant genetic component to migraine, it cannot entirely explain its prevalence and severity. Only in familial hemiplegic migraine have genes been convincingly identified; these are associated with ion channelopathies.

**PSYCHIATRIC COMORBIDITIES WITH MIGRAINE**

Comorbidity means that 2 conditions occur in the same individual more often than expected by chance. Psychiatric comorbidities are a common presentation in sufferers of migraine headache.

**Migraine and Depression**

Depression is the most common psychiatric comorbidity with migraine and often poses a challenge in the treatment of both disorders. Those with migraine have an odds ratio for depression of 2.5. This risk is more highly associated with women than men. In addition, the incidence of depressive symptoms is higher in those with a longer history of headaches and with a higher attack frequency. Those with tension-type headaches do not suffer from this increased risk of depression when compared with controls. There is no proof that migraine frequency is increased because of the presence of anxiety or depression.

Migraine and depression share a bidirectional comorbidity, suggesting that there is some shared component to the cause of both disorders. There is also a bidirectional risk for suicidality in migraineurs and depressed patients. It has recently been shown that the inheritability of migraine decreased in those individuals who are depressed. There are no significant qualitative differences in the migraines seen in mildly compared with severely depressed individuals.

When migraine becomes chronic and transformed from its episodic form, there is an even higher likelihood of a comorbid psychiatric condition. One study showed 78% of these individuals with chronic migraine have psychiatric disorders. These disorders were major depression in 57% of cases, dysthymia in 11% of cases, panic disorder in 30% of cases, and generalized anxiety in 8% of cases. Depression and anxiety disorders were more frequently encountered in female migraineurs. However, there was no increased risk of generalized anxiety disorder in this group.

In chronic daily headache (subtypes not defined), the risk of major depression and panic disorder is 1.5 to 2 times more likely in women, compared with the general population.
There may be sex-related differences in the variety of comorbid conditions. One study suggested that only migrainous women, and not migrainous men, suffered from an increased risk of anxiety, depression, somatic complaints, and hysteria.22

The relationship of affective disorders and migraine is unclear. Does migraine trigger affective disorder in some whereas affective disorder triggers migraine attacks in others? In general, affective disorders present before migraine symptoms.11 It is possible that depressed individuals have a lower threshold for pain and these patients may experience a greater number of headaches. However, no genetic link to both migraine and depression has been identified.

Treating both migraine and comorbid depression is challenging. Not all antidepressant medications are effective for migraine therapy. The serotonin reuptake inhibitors, which are widely used in the treatment of depression, are generally not useful in the prevention of migraine. Amitriptyline has level-A evidence for the treatment of migraine, but is commonly not used in sufficient amounts to treat major depression, should that be comorbid. Other tricyclic antidepressants, notably doxepin, nortriptyline, and protriptyline, have level-C evidence for efficacy in migraine. Venlafaxine is more potent in its ability to inhibit serotonin reuptake compared with norepinephrine. It seems that 75 to 150 mg can treat migraine.23,24 Mirtazapine, known to enhance serotonergic and noradrenergic neurotransmission, might be helpful in the treatment of both conditions.25

Bipolar disorder is another significant psychiatric condition comorbid with migraine. There is a lifetime prevalence of migraine in these individuals of 40% (44% in women and 31% in men). This relationship is particularly prominent with individuals with bipolar II disorder, who have a migraine prevalence of 65% (75% in women and 40% in men).26 There are some differences in their psychiatric presentation as well. Depression, rather than mania, is the reason for a medical consultation, followed by a flip of depression into mania after treatment with antidepressant medication.

**Migraine and Anxiety**

Just as migraine is comorbid with depression, it is also comorbid with generalized anxiety disorder, with 11% of migraineurs having an anxiety disorder as opposed to 2% of the general population.27

Migraineurs with depression and anxiety tend to suffer more severe migraine attacks and respond poorly to their headache treatment. In addition, they are more likely to overuse their acute migraine agents.28 This situation could contribute to an increased chance of developing the syndrome of medication-overuse headache (MOH), a chronic condition.

**Migraine and Panic**

A significant relationship of migraine to panic disorders has long been identified.29 Migraineurs are 12 times more likely to have panic attacks compared with the general population.30 There is a crossover of symptom complexes in these disorders. Some migraine attacks can be accompanied by panic symptoms such as anxiety, palpitations, feelings of cold extremities, and fear of imminent death.31

Autonomic symptoms such as nausea, vomiting, and dizziness are commonly reported in both disorders.29 It is possible that those with a panic disorder and migraine sufferers share a fundamental abnormality of autonomic regulation. Because those with panic disorder tend to somatize, it is also possible that the symptoms, which lead to the diagnosis of a panic disorder, are exaggerated, and more often reported by patients and health care professionals.
Social phobias and migraine are also associated comorbid conditions. The stresses and daily hassles that complicate migraine are also reported in these syndromes.

**Migraine and Stress**

Three-quarters of migraineurs report that there were triggers of their attacks, with 80% stating that stress is a major trigger.\(^{32}\) The concept of stress is often ambiguous. The inability to reach a goal, whether the cause is internal or external, can be a significant stressor to individuals. The stress of the headache disorder itself is often significant. Often the headache occurs, not at the height of the stress, but when the stressor is withdrawn. Stress is often protective for the development of attacks. There is evidence that stress can produce analgesia.\(^{33,34}\)

The sympathetic nervous system and the hypothalamic-pituitary-adrenal axis are activated acutely during a stressful situation. Corticotrophin-releasing hormone (CRH) is released as part of this response, leading to cortisol release from the hypothalamus, leading to epinephrine release. Subsequently there is activation of the \(\beta\)-endorphin and dopaminergic systems. However, should this response be long-term, pronociceptive and immunosuppressive systems become activated.\(^{35}\) This factor, along with others, can lead to activation of \(N\)-methyl-\(d\)-aspartic acid and \(\mu\) opioid receptors.\(^{36}\) Proinflammatory mediators such as interleukin \(\beta\) (IL-\(\beta\)), tumor necrosis factor \(\alpha\), IL-6, and nitric oxide are also subsequently activated. Stress also affects mast cells located in the dura. CRH, released during stressful situations, activates and degranulates mast cells, which are located near the trigeminal afferents in the meninges and dura.\(^{37}\) These events could easily trigger a migraine attack.

Adolescents have reported stress to be the major trigger of headaches in 40% of individuals.\(^{38}\) Cognitive coping strategies can be used and reduce the likelihood of the stressor triggering a headache attack. In an adolescent diary study, these strategies reduced the incidence of attacks occurring the day after the stressor, but not the day of the event.\(^{39}\) The severity of such hassles of daily life is correlated with the frequency and intensity of headaches.\(^{40}\) These daily events may be more important to the perpetuation of chronic headaches than specific life events.

Posttraumatic stress disorder (PTSD) has always been pervasive, but of even more recent concern given the large number of soldiers recently returning from war. Of those soldiers returning from the Iraq war who have been diagnosed as having PTSD, 32% list headaches as a significant complaint.\(^{41}\)

Confounding the high prevalence of headache in soldiers is the fact that mild head trauma is seen in half of these individuals who seek care for headaches. This situation could cause a new headache or enhance a preexisting primary headache disorder. Mild head trauma, as opposed to severe trauma, is more likely to trigger headaches.\(^{42,43}\)

Orofacial pain, often associated with headache, is also rendered more disabling in those with a history of traumatic life events. A total of 42% of individuals with both orofacial pain and headaches reported traumatic life events and their Migraine Disability Assessment Scores of headache disability were significantly higher than those not reporting such events.\(^{44}\)

PTSD is associated with an enhanced activation of the amygdala and limbic system when confronted with threats. This activation is associated chemically with an increased sympathetic drive and activation of the hypothalamic-pituitary axis.\(^{45,46}\)

A history of violence is not commonly shared with a treating physician. One study reported that this information was discussed with only 15% of patients.\(^{46}\) This percentage may be increased by specifically inquiring about these past events when obtaining a patient history. Despite this reduced reporting, a history of physical, and particularly sexual, abuse is commonly reported in sufferers of chronic daily
headache. Up to 29% of those with chronic daily headaches report a history of physical abuse and up to 31% report a history of sexual abuse. Among migraine syndromes, the prevalence is even higher, with physical or sexual abuse reported in 42%. In those with PTSD and migraine, 65% report a history of physical or sexual abuse.

An association of migraine with a history of physical child abuse has been identified. The occurrence of child abuse nearly doubled the risk of the development of migraine in individual patients.

The treatment of comorbid headache and PTSD is unclear. Selective serotonin reuptake inhibitors (SSRIs), used widely to treat PTSD, are commonly ineffective, or may even enhance migraines. Tricyclic antidepressants and venlafaxine may have a positive effect on both conditions. Some alternatives might be mirtazapine, venlafaxine, or nefazodone, which might have a positive effect in the treatment of both conditions. Atypical antipsychotics, such as olanzapine, quetiapine, and rispirdone, may also be efficacious in the treatment of both conditions.

Certain psychiatric syndromes may be seen in younger patients. Adolescents with tension-type headaches have not been found to have any more psychopathic symptoms when compared with headache-free individuals. However, adolescents with migraine exhibit 3 times the number of conduct problems, hyperactivity, inattention, and emotional symptoms when compared with headache-free adolescents.

**Migraine and Borderline Personality Disorder**

The incidence of borderline personality disorder in the general population is 2%, but in the headache population, particularly in those with comorbid psychopathology and medication overuse, the incidence is higher. This situation makes headache management particularly challenging. Treatment recommendations and pitfalls of management in this particular population are reviewed by Saper. Pharmacotherapy, psychotherapy, good communication between treating practitioners to avoid splitting, treatment contracts, and heightened awareness by the practitioner about counter-transference issues are emphasized.

**Migraine and Psychosis**

Psychotic disorders are also comorbid with headache syndromes. Schizophrenia has been associated with a low incidence of headache, as well as other pain disorders. Such individuals often have an impaired awareness of somatic events in general as well as a blunted affective response to pain. However, Kuritzky and colleagues and Ayata and colleagues have disputed this and reported that schizophrenics had more complaints of more frequent headaches and headaches of longer duration than controls.

Migraineurs are genetically predisposed to a great many psychiatric comorbidities. It seems that psychiatric syndromes can shape the experience of headache attacks for sufferers and the frequency of symptom reporting. The presence of migraine may also be associated with behavioral and learning problems at school. Environmental factors such as physical and psychological trauma also play a role in severity and frequency of attacks as well as response to treatment. It is therefore important that these comorbid disorders be identified and their treatment included in a comprehensive migraine management plan.

**THE TREATMENT OF MIGRAINE**

There are different treatment approaches to managing migraines depending on the frequency and severity of attacks as well as associated medical and psychiatric conditions.
Acute medications are those generally used to abort individual attacks. The triptans are said to be migraine specific, but can relieve many forms of headache. Therefore it is important not to assume that a positive response to a triptan is a diagnostic test of migraine. These agents are agonists of the 5-HT\textsubscript{1B} and 5-HT\textsubscript{1D} receptors. They block vasodilatation and neurogenic inflammation. Because meningeal noceceptors are activated in a migraine, the triptans also seem to block pain transmission of these noceceptors before their synapse with the trigeminal nucleus caudalis, which is where the second-order trigeminal neurons originate. There is little evidence that triptans can enter the central nervous system and whether this ability has any therapeutic implications. Once the migraine attack has advanced to the point that there is central sensitization, this class of drugs is unlikely to be effective. These medications block the peripheral activation but not the self-sustaining central effects of the migraine attack.

Since the triptan era, the US Food and Drug Administration (FDA) has mandated that current agents seeking approval for the acute treatment of migraine reduce not only pain but also light and sound sensitivity and nausea. Unlike ergotamine tartrate and current formulations of dihydroergotamine, which often enhance nausea, triptans reduce this symptom.

Butalbital-containing agents are frequently prescribed in the treatment of migraine, but few data exist to support their efficacy in this setting. Butalbital is a barbiturate with a plasma half-life of 35 hours, but a clinical duration of action of only 4 to 6 hours. This quality means that even modestly frequent redosing can lead to drug accumulation. Butalbital-containing agents have been associated with an alarming risk for the development of MOH.

Nonsteroidal antiinflammatory agents are important agents for treating acute migraine attacks. Advantages of this class of medications in the treatment of migraine include that they rarely lead to the syndrome of medication-overuse headache, and they lack the psychoactive features that can lead to this syndrome. However, the frequent use of these agents can lead to renal or hepatic disease and gastric ulceration, and increase the risk of vascular disease.

Not all classes of medications used commonly for headache treatment have been proved to be helpful. Opioids should rarely be used in the treatment of migraine. Their efficacy in migraine is low for a variety of reasons. Opioid receptors are poorly represented in trigeminovascular neurons, which conduct head pain. Opioids can be proinflammatory, degranulating mast cells, which can enhance the inflammation in the meninges. CSD can be triggered by the presence of the most powerful excitatory amino acid, glutamate. The glutamate transporter enzyme, which is the enzyme that normally transports this acid back into the neuron, is blocked by opioids. If used frequently, these agents easily lead to the syndrome of MOH. Dysphoric individuals often self-treat their attacks with opioids to obtain relief of the dysphoria.

Preventive medications are generally used when frequency is greater than 1 or 2 attacks per week or when infrequent headaches are severe or long-lasting. Only 4 agents are approved by the FDA for prophylaxis of migraine: propranolol, timolol, divalproex, and topiramate. Methysergide, previously approved by the FDA for the prevention of migraine, is no longer on the market in the United States, although it is still used in other countries.

The mechanism of action of preventive antimigraine agents is unknown, although topiramate, valproate, propranolol, amitriptyline, and methysergide have all been shown to reduce CSD.\textsuperscript{58} Should this site of action prove to be predictive of antimigraine prophylaxis, this greatly assists in the development of these agents in the future. Previously, all currently used preventive drugs were found to reduce migraines when prescribed for other purposes.
There are important issues to consider when using antidepressants as preventive agents in migraine with bipolar and major depressive disorders.

Several agents used in the treatment of depression can be useful in the treatment of migraine. Although low doses of tricyclic antidepressants often suffice to suppress migraines, they would not be expected to adequately treat migraine with major depression. Of equal concern is that many with depression have bipolar disorder, which may be unrecognized by the clinician. Bipolar patients may become manic when exposed to antidepressants. It has been suggested that this effect is particularly prominent in migraineurs.\textsuperscript{26}

It is often recommended to use tricyclic antidepressants in migraineurs who experience difficulty in falling asleep and in maintaining sleep. However, the architecture of sleep that occurs with the use of these agents is abnormal.\textsuperscript{60}

SSRIs, which are better tolerated than tricyclic antidepressants, have not been convincingly shown to be effective in the prophylaxis of migraine. Some selective serotonin/norepinephrine reuptake inhibitors have some data, albeit limited, supporting their use in the treatment in a migraineur with comorbid depression.

$\beta$-Blockers have been useful in migraine prophylaxis. Several of these agents have been shown to be effective in the prevention of migraine, notably propranolol, atenolol, nadolol, nebivolol, and timolol. Because there is a high comorbidity of migraine and depression, and $\beta$-blockers have been said to cause depression, there is often concern about using such agents in migraineurs. Because of methodological and selection issues in the studies that originally led to this notion, it is not clear whether $\beta$-blockers can trigger depression.

Valproic acid has been shown to be an effective agent for the prophylaxis of migraine and is, in addition, a mood stabilizer. It is one of the preventive treatments for migraine approved by the FDA. This situation makes this agent a logical choice for a migraine preventive agent in a bipolar individual. Weight gain and risk of teratogenicity with pregnancy often limit its use.

Topiramate is also an effective agent for the prevention of migraine. The mood-stabilization studies for this agent have been largely negative. This agent also has FDA approval for migraine prophylaxis. Weight loss induced by the use of this drug is a nearly unique feature with migraine prophylactic agents. Paresthesias and taste perversions are troublesome but benign. Cognitive abnormalities, in particular difficulty with word retrieval, can be problematic.

Nonmedication treatments are also available in the treatment of migraine and can be effective when used in combination with medication therapy. Cognitive behavioral therapy and biofeedback both have level-A evidence for efficacy in the prevention of migraine.

A meta-analysis of 23 randomized controlled trials concerning the use of cognitive behavior therapy, relaxation, and biofeedback in children and adolescents with migraine and tension-type headache has documented their efficacy. A statistically and clinically significant reduction in headaches, associated with long-term improvement, was documented.\textsuperscript{61}

Medication interactions arise when psychiatric and headache syndromes are treated concurrently. Given the high comorbidity of migraine and depression, and the widespread use of triptans in the acute treatment of migraine, the serotonin syndrome has been of great concern. This interaction has been reported with SSRIs, serotonin- and norepinephrine-inhibiting antidepressants, and monoamine oxidase inhibitors, all capable of increasing serotonin levels. The prevalence of this interaction is low. It seems that activation of the $5-HT_{2a}$ receptor causes a serious serotonin syndrome, and triptans normally have no affinity for this receptor, being largely
5-HT₁b and 5-HT₁d agonists. Nonetheless, the FDA alert suggests that a fatal serotonin syndrome is possible when triptans are coadministered with some antidepressants. No convincing cases of the serotonin syndrome have been reported with the use of ergots, including bromocriptine.

**TENSION-TYPE HEADACHES**

Tension-type headaches are a commonly misunderstood variety of headache, although the most prevalent. However, because these headaches are rarely disabling, those individuals often do not seek professional care, and adequately self-treat. Originally named tension headache, it was ambiguous whether this term was referring to muscle tension or psychic tension. The term was later changed to muscle-contraction headache until it was recognized that muscle contraction was not an adequate marker of the presence or severity of these headaches. It is not clear that the current nomenclature of tension-type headache clarifies these issues.

The episodic form of tension-type headache is diagnosed by attacks lasting 30 minutes to 7 days. At least 2 of the following characteristics need to be associated with the pain: bilateral location; pressing, tightening, and nonpulsatile; mild or moderate in severity; and not aggravated by routine physical activity. In addition there cannot be nausea or vomiting, and photophobia or phonophobia can be present, but not both. Frequently when attacks are more severe and do not fulfill these criteria, they are termed migraines. If the attacks occur more than 15 times monthly, they are classified as chronic tension-type headaches. Chronic tension-type headache, as opposed to the episodic form, is disabling because of its chronicity. Many of these individuals, like those with chronic migraine, overuse acute medications, which are responsible for the transformation and perpetuation of the chronic pain.

It remains unclear whether the pain of tension-type headache is centrally located or emanates from extracranial skeletal muscles. Most likely, the brief episodes have a peripheral mechanism and the more continuous pain is centrally located. The electromyograms (EMGs) of peripheral muscles reveal some increase in activity in the chronic form, but not in the episodic form. The degree of physical hardness of the muscle and the degree of pain are not always correlated.

Emotional stress remains the most common trigger of these attacks. As in chronic migraine, the high numbers of daily hassles correlate with the number of headaches. Although there is not a clear correlation of chronic tension-type headache and depression, some depressive scales can be increased. Despite the high comorbidity of migraine with depression and panic attacks, this comorbidity has not been identified in those with tension-type headaches and headache-free individuals.

The medical treatment of episodic tension-type headaches generally involves simple analgesics such as nonsteroidal antiinflammatory medications. Ibuprofen and naproxen are most commonly used. The preventive treatment of chronic tension-type headache is more challenging. Most practitioners advocate the use of amitriptyline, which was found in a study to be effective as opposed to citalopram. One positive study in chronic tension-type headache also showed that there was no correlation between headache improvement and improvement in pericranial muscle tension or temporal muscle exteroceptive suppression of voluntary activity (ES2). In general, the doses of tricyclic antidepressants used are lower than those used for depressive syndromes. There is no evidence to support the use of benzodiazepines or botulinum toxin. There is weak evidence to support the use of tizanidine. Mirtazapine might also have some efficacy in chronic tension headaches. A recent meta-analysis of preventive drugs for tension-type headache concluded that none was effective.
EMG biofeedback has good evidence for efficacy in the treatment of chronic tension-type headache and should always be used, if available. This treatment, combined with relaxation training, can reduce headaches by 50%. It is unclear whether physical therapy, chiropractic therapy, occipital nerve stimulation, or acupuncture are efficacious.

**CHRONIC HEADACHE AND ITS TREATMENT**

Approximately 3% of sufferers from episodic migraine transform their attacks to a chronic form within a 1-year period. Several risk factors are known to be associated with this transformation, including medication overuse, the frequency of headaches at baseline, obesity, caffeine consumption, stressful life events, and depression. Major life events, particularly in those older than 40 years, often occur within 2 years of the transformation of episodic into chronic headaches. This association does not prove causality, because the major life event could lead to the overuse of psychoactive medications, leading to chronic daily headache.

MOH can occur in migraineurs who use large amounts of acute medications. It occurs in 1% to 2% of the population and affects 3 times more women than men. One-quarter of those with chronic daily headache can trace the cause to the overuse of acute medications. Over time, medication overuse can transform an episodic headache into chronic head pain with superimposed exacerbations. Migrainous individuals return to their pain-free state in between paroxysms, but there is a baseline pain in those with medication overuse.

MOH is more prevalent in migraineurs when compared with sufferers of neck or low back pain. Those with pain syndromes, but without migraine, do not develop headaches de novo and then progress in frequency and chronicity. This finding has been shown with several conditions, including arthritis, in which migraineurs taking analgesics for their joint pains developed chronic headaches. The prognosis for untreated MOH is poor and there may a point at which it is untreatable.

In those with MOH, there is an increased risk of depression. Other comorbidities seen in migraineurs with medication overuse include panic disorder, anxiety, and social phobias.

There are various reasons why those with psychiatric disorders are often those overusing medication. It is suspected that many individuals with medication overuse are self-treating a comorbid disorder. Anxious individuals might be attracted to barbiturates for their anxiolytic properties. Butalbital, a short-acting barbiturate with a long biologic half-life, is present in many preparations used to treat headache. Dysphoric individuals might be attracted to the use of opioids. Those with hypersomnia for a variety of reasons, including depression and various sleep disorders, might overuse caffeine in their diet and in medications. There are additional reasons why these individuals can increase their acute medications. Undertreating or delaying treatment of an acute attack commonly leads to incomplete relief. Often redosing follows. Fear of a headache (with little confidence that the pain can be terminated without using the acute agent), obsessional drug-taking behavior, and anticipatory anxiety all lead to this state.

The psychological profiles of those with MOH and the episodic form differed in some respects. The patients with MOH reported more hypochondriasis and health concerns on the MMPI-2 (Minnesota Multiphasic Personality Inventory, second edition).

Triptans and nonsteroidal antiinflammatory agents, also used in the treatment of migraine, had little likelihood of inducing and perpetuating headaches in a recent
study. This finding is in contradistinction to opioid, butalbital combination, and over-the-counter products with caffeine.86 These agents are generally devoid of psychoactive properties.

The treatment of MOH involves withdrawal of the overused agent, if present. This action is initially associated with a worsening of symptoms, generally followed by improvement. Regardless of treatment, the prognosis is poor with chronic MOH. There are many studies addressing this prognosis, and a representative study revealed that at 4 years following treatment, only one-third of these individuals remained off the offending medications.87 Preventive medications for chronic headache have not been well studied in the past, with most prevention studies excluding individuals with headache for more than 15 days monthly. Recent studies involving onabotulinumtoxin A in the chronic migraine have suggested modest efficacy.88 It seems that chronic migraines, even in the presence of medication overuse, can respond to this therapy. Topiramate prevention with the use of triptans for acute treatment was effective in converting chronic migraine into the episodic form.89 Fluoxetine, used in the treatment of depression and obsessive-compulsive behavior, did increase headache-free days and caused a mood improvement, including those without depression.90

MALINGERING AND DRUG SEEKING

Accusations of malingering and drug seeking are common in patients with headache, particularly in the emergency department setting, in which the practitioners often are unfamiliar with the individual and in which parenteral opioids are available and often used. Pain is a subjective and immeasurable experience. Malingering individuals intentionally feign or exaggerate painful symptoms with the hope of fooling the treating practitioner into prescribing an agent of their choice, often an opioid. Feigning illness in the emergency department setting is common and was discovered in 13% of emergency department patients in one study.91

Malingers typically have some external gain, which drives their behavior, although that factor may be elusive to the treating physician. These factors include using or selling narcotics and avoiding responsibilities. Many are antisocial and therefore have a history of additional antisocial behaviors other than drug seeking. Those with persistent malingering have little interest in a therapeutic outcome. However, even obvious malingering does not preclude the coexistence of a serious psychosocial or medical disorder that requires management. Malingers tend to dramatically present their complaints and, if any physical findings are noted, they are usually out of proportion to the purported pain. Skepticism by the physician is commonly met with hostility. Although the practitioner is obligated to share their concerns with the patient, this should be done in a nonjudgmental way, with the hope of breaking the repetitious pattern of medical office and emergency room visits.

Factitious pain is motivated by the desire of the individual to occupy the role of a suffering individual. This motivation is different from that of the malingerer. Those with Munchausen syndrome often self-inflict injury and try to produce a convincing medical syndrome.

COGNITIVE DECLINE

A transient cognitive disorder is associated with spells of migraine and cluster attacks.92 Does decreasing cognitive function result from recurrent migraine attacks? Deep white-matter lesion changes can be seen with frequent headaches, in particular
in women. The nature of these changes, whether they represent ischemic areas or abnormalities in the blood-brain barrier, is unknown. However, there is no evidence that migraine is associated with a cognitive decline.93

SUMMARY

Headache, and in particular, migraine, is often associated with comorbid psychiatric illness. The complex relationships between these disorders are slowly becoming understood. Successful management requires an integrated approach of neurologic and psychiatric management.

REFERENCES