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Chronic headache: Stop the pain before it starts

Familiarity with the risks associated with medication overuse and the importance of headache prophylaxis is key to easing your patient's pain.

PRACTICE RECOMMENDATIONS

› *Treat medication overuse headache by withdrawing abortive therapy and initiating prophylactic therapy.* (C)

› *Select prophylactic medications that are first-line therapy for chronic migraine or tension-type headache and are appropriate for the patient's comorbidities.* (C)

› *Advise patients to limit intake of abortive headache medications to ≤9 per month.* (B)

Strength of recommendation (SOR)

- (A) Good-quality patient-oriented evidence
- (B) Inconsistent or limited-quality patient-oriented evidence
- (C) Consensus, usual practice, opinion, disease-oriented evidence, case series

CASE ▶ Eric K, age 25, is in your office, seeking help for chronic headache—which he's had nearly every day for the past 9 months. He says that the headaches vary in quality and intensity. Sometimes the pain is in the right temporal area; has a throbbing, pulsating quality; and is accompanied by nausea and photophobia. These headaches are incapacitating, with an intensity of 10 on a scale of one to 10. When they occur, the patient reports, all he can do is take migraine medication and lie down in a darkened room for several hours, until the pain goes away. He cannot identify any triggers.

He also gets headaches that are not incapacitating, but occur almost daily, the patient says, describing a dull bilateral pressure that usually begins in the afternoon and worsens until he takes headache medication. He denies any fever, chills, weight loss, visual changes, or tinnitus. His medical history is significant only for obesity, but a system review is positive for depression and insomnia. Physical examination reveals normal vital signs; normal head, eyes, ears, nose, and throat (HEENT); and normal fundoscopic and neurological exams.

Patients like Mr. K can be challenging for primary care physicians, but referral to a neurologist is indicated only in the most intractable cases. For the vast majority of patients with frequent headaches, family physicians can perform the diagnostic work-up and oversee treatment. This review will help with both.

What kind of headache?

While most headaches are sporadic in nature, the prevalence of "chronic daily headache" ranges from 3% to 5% worldwide.¹⁻³

Chronic daily headache is not a diagnosis, however, nor is it an indication that a patient has a headache every day. According to the International Classification of Head-



Acute headache medications should follow the “one and done” rule, eliminating the pain with a single dose.

ache Disorders (ICHD-II), chronic daily headache encompasses several distinct primary headache disorders that have a frequency of ≥ 15 times per month for at least 3 months. These disorders are also classified by duration, as long (>4 hours) or short.⁴

The text and tables that follow focus on the diagnosis and treatment of the 4 primary headache disorders of long duration—chronic migraine (CM), chronic tension-type headache (CTTH), hemicrania continua (HC), and new daily persistent headache (NDPH) (TABLE 1).^{4,5} Although medication overuse headache (MOH) is not a primary headache, it is included in this review because it often contributes to and complicates treatment of primary headache disorders. What’s more, most chronic daily headache syndromes are inextricably linked to medication overuse.^{6,7}

Which individuals are at risk?

Risk factors for chronic headache include female sex, older age, obesity, heavy caffeine consumption, tobacco use, low educational level, overuse of abortive headache medications, and a history of head and neck trauma.⁸ Episodic migraine (EM)—that is, migraines

that occur ≤ 14 times a month—is also a risk factor for chronic headache.

ICHD-II classifies EM as a progressive disease that transforms to CM at a rate of 3% per year.⁹ Transformation of EM to CM has been found to occur after as few as 5 days of barbiturates or 8 days of opiates per month.¹⁰

Patients with EM should be warned about the potential for migraines to become chronic and have their acute headache medications replaced with a prophylactic drug if the frequency approaches 2 per week.

Pinpointing the type of headache

An accurate diagnosis requires a thorough headache history and a HEENT and neurological examination. The history should include questions about the characteristics of the headache, including the location, intensity, frequency, timing, associated symptoms, previous headache diagnoses, and triggers, and address comorbidities, medication use, caffeine intake, and family history.⁸ In the absence of red flags—age >50 years, history of headache or systemic illness, sudden onset, or papilledema, among other findings that may indicate more serious conditions



A definitive diagnosis of chronic migraine is possible only in the absence of overuse of abortive headache medications.

(TABLE 2)⁷—advanced imaging and further work-up are not needed.

Migraine or tension headache?

Chronic migraine. To be classified as CM, the headache must have occurred ≥ 15 days a month for 3 months or more and have features of migraine, such as unilateral location, pulsating quality, and moderate to severe intensity. Migraines are aggravated by physical activity and associated with nausea and/or vomiting, photophobia, and phonophobia, and may or may not be preceded by aura. Common triggers include stress, menstruation, alcohol, skipped meals, dehydration, and chocolate. Migraines typically respond to ergots and triptans.^{4,5}

■ **Partial treatment.** Patients with CM often take medication early in the course of a headache. This sometimes results in a partially treated migraine that develops into a headache with tension-type features, such as a bilateral location, a pressing quality, and mild-to-moderate intensity, as well as a possible transformation to MOH. This is most likely to occur in patients who have migraines without an aura.

To avoid partial treatment, medications for acute migraine should be taken within 30 minutes of an attack, in a dose that's sufficient to relieve the pain within 2 hours, with no need for a second dose—a protocol known as “one and done.” Efficacy of a triptan can be improved by adding a nonsteroidal anti-inflammatory drug (NSAID).¹⁰

A definitive diagnosis of CM is only possible in the absence of medication overuse.^{4,5} A patient who is overusing abortive headache medication and whose headache meets the criteria for CM should be given a diagnosis of probable CM instead.

■ **Chronic tension-type headache.** In addition to traits common to tension headaches, CTTH may be associated with mild nausea, photophobia, or phonophobia (but typically only one such feature at a time). There may also be tenderness to palpation of the pericranial muscles. Unlike migraine, CTTH is not affected by physical activity.

Here, too, overuse of headache medication is often a factor and should be stopped, if possible, before a definitive diagnosis of CTTH can be made.

■ **Headache with overlapping features.**

It is possible for a patient to have chronic headache with features of both migraine and tension headache. Advise patients whose headaches have varying characteristics to keep a headache journal to determine which features are more prominent. Patients with smart phones can download a free app, such as iHeadache or My Headache Log Pro, to be used for this purpose.^{11,12}

When to suspect medication overuse headache

MOH is sometimes referred to as a rebound headache or drug-induced headache. Headaches associated with medication overuse have variable intensity. Patients with MOH often awaken from sleep with a headache, and neck pain is highly prevalent.¹⁰

■ **Quantifying overuse.** According to ICHD-II, overuse is defined as using a single abortive headache medication ≥ 10 times a month or using 2 or more such drugs ≥ 15 times a month.⁵

Triptans have the potential to cause MOH more quickly and in lower doses compared with other acute headache medications. However, analgesics—especially combination products such as butalbital/acetaminophen/caffeine (Fioricet)—are most frequently associated with the development of MOH.^{13,14} NSAIDs have less potential to cause MOH and are sometimes given as bridge therapy for patients who are discontinuing their acute headache medication.

Less common primary headache disorders

Hemicrania continua, a rare cause of chronic daily headache, is unilateral, without shifting sides, and the intensity is moderate to severe—and unrelenting. HC is associated with autonomic features such as lacrimation, ptosis, and nasal congestion.

■ **New daily persistent headache** is characterized by an out-of-the-blue onset of a headache that becomes unremitting soon after it develops. To receive a diagnosis of NDPH, the patient must have a headache that started suddenly and has continued for 3 months or more.

Most patients diagnosed with NDPH are

TABLE 1
Diagnosing and treating chronic headache^{4,5}

Type of headache	ICHD-II diagnostic criteria	First-line treatment
Chronic migraine	<ol style="list-style-type: none"> 1. Headache fulfilling criteria for migraine without aura ≥ 8 days/month 2. Headache occurs ≥ 15 d/mo for ≥ 3 mo 3. No overuse of medication 4. No secondary headache 	Prophylactic therapy: <ul style="list-style-type: none"> • TCAs • SNRIs • Anticonvulsants • Beta-blockers • Botulinum toxin A Limit acute medication; avoid triggers; initiate lifestyle modification
Chronic tension-type headache	<ol style="list-style-type: none"> 1. Headache fulfilling criteria for tension-type headache 2. Occurs ≥ 15 days/mo for ≥ 3 mo 3. No overuse of medication 4. No secondary headache 	Prophylactic therapy: <ul style="list-style-type: none"> • Amitriptyline • Venlafaxine • Mirtazapine Limit acute medication; avoid triggers; initiate lifestyle modification
Medication overuse headache	<ol style="list-style-type: none"> 1. Headache occurs ≥ 15 days/mo 2. Single abortive medication use ≥ 10 days/mo or combination therapy ≥ 15 days/mo for ≥ 3 mo 3. Headache developed or worsened during medication overuse 	Discontinue overused acute meds; provide headache education; bridge with NSAIDs, prednisone, or botulinum toxin A; begin prophylactic medication
Hemicrania continua	<ol style="list-style-type: none"> 1. Headache for ≥ 3 mo 2. All of the following characteristics: <ul style="list-style-type: none"> • Unilateral pain without side shift • Daily and continuous, without pain-free periods • Moderate intensity, but with exacerbations of severe pain 3. At least one of the following on the same side as the pain: <ul style="list-style-type: none"> • Conjunctival injection and/or lacrimation • Nasal congestion and/or rhinorrhea • Ptosis and/or miosis 4. Complete response to therapeutic doses of indomethacin 	Indomethacin
New daily persistent headache	<ol style="list-style-type: none"> 1. Headache for ≥ 3 mo 2. Characteristics of tension-type headache (but migrainous features are common) 3. Unrelenting from onset or within 3 days of onset 4. No medication overuse 	Rule out secondary causes; treat according to migrainous or tension features of headache

ICHD-II, International Classification of Headache Disorders; NSAIDs, nonsteroidal anti-inflammatory drugs; SNRIs, serotonin-norepinephrine reuptake inhibitors; TCAs, tricyclic antidepressants.

TABLE 2

Beyond headache: Red flags warrant additional testing⁷

Red flag	Condition(s) to rule out
Age of onset >50 y	Giant cell arteritis, mass lesion, stroke
No prior history of headache OR change in characteristic from prior headaches	Cancer, aneurysm, stroke, cerebral sinus thrombosis, infection
“Thunderclap” headache	Ruptured aneurysm
Signs or symptoms of systemic illness (eg, fever, chills, weight loss)	Meningitis, encephalitis, cancer
History of systemic illness, such as cancer, autoimmune disease, or HIV	Brain metastasis, mass lesion, autoimmune meningitis, thrombosis
Headache brought on by change in head position or Valsalva maneuver	Spontaneous CSF leak or Chiari malformation
Occipital location of headache (in children)	Brain tumor
Neurological symptoms	Mass lesion, encephalitis
Papilledema	Idiopathic intracranial hypertension, cerebral sinus thrombosis

CSF, cerebrospinal fluid; HIV, human immunodeficiency virus.

➤ Ask patients whose headaches have varying characteristics to keep a headache journal, and let them know that there are free apps for smart phones designed for this purpose.

able to recall, to the day, when the headache started. More than 50% report a precipitating event, such as a viral illness, a stressful experience, or surgery.¹⁵ ICHD-II defines NDPH as having the characteristics of a tension headache. Notably, however, migrainous features are also common, and neurologists often diagnose NDPH with either migrainous or tension-type features.¹⁶

The sudden onset of NDPH is a red flag and, like other red flags, always warrants further work-up. Magnetic resonance imaging with gadolinium is preferred to computed tomography. Magnetic resonance venography or lumbar puncture may also be considered.^{15,16}

Review comorbidities, rule out secondary causes

Patients who suffer from frequent headaches have a high prevalence of depression, anxiety,^{17,18} sleep disorders,¹⁹ obesity,²⁰ irritable bowel disease, fibromyalgia,²¹ temporomandibular joint disorder,²² and chronic fatigue syndrome. Treatment of these disorders may increase the efficacy of headache treatment. Conversely, overuse of headache medications can make comorbidities harder to treat.

Treating chronic headache: Which drugs are best?

A multimodal approach combining pharmacologic and nonpharmacologic therapies is usually required for patients with chronic headache. The particular therapy and prognosis depend on the type of headache a patient has and the presence of comorbidities (TABLE 3).^{6,7,23,24}

Choice for migraine prophylaxis? Here’s what the evidence tells us

Although most studies of the benefits of prophylaxis have involved patients with episodic or frequent migraine rather than CM, extrapolation of the findings to patients with CM is not unreasonable. And, although dozens of pharmacologic and complementary therapies have been studied for migraine prophylaxis and certain classes of drugs have been identified as effective, there are very few head-to-head trials comparing agents.

The American Academy of Neurology and the American Headache Society published a summary of the evidence in 2012.²³ Key findings: The types of medication with the most evidence to support their use as first-line agents for CM are antidepressants, anticonvulsants, and beta-blockers.

TABLE 3

Consider comorbidities in prophylaxis selection^{6,7,23,24}

Comorbidity	What to choose	What to avoid
Depression	Venlafaxine	—
Bipolar disorder	Valproic acid	Venlafaxine, amitriptyline, mirtazapine
Insomnia (CM)	Amitriptyline	—
Insomnia (CTTH)	Mirtazapine	—
Obesity	Topiramate	Amitriptyline
Hypertension	Metoprolol, propranolol	—
Cardiac conduction abnormalities	—	Amitriptyline
Fibromyalgia	Amitriptyline, tizanidine	—

CM, chronic migraine; CTTH, chronic tension-type headache.

■ **Antidepressants**, especially tricyclics (TCAs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), have been found to be effective. Chief among them are amitriptyline, a TCA, which is inexpensive and may be beneficial for patients with coexisting insomnia due to its sedating effect, and venlafaxine, an SNRI, which may help treat comorbid depression.²³ Amitriptyline is associated with weight gain and can prolong the QT interval at higher doses. There is insufficient or conflicting evidence of the value of selective serotonin reuptake inhibitors for migraine prophylaxis.

■ **Anticonvulsants** that have been studied most extensively for migraine are topiramate and sodium valproate. Both have level A ratings for established efficacy.²³ Topiramate has also been shown to be noninferior to amitriptyline in reducing migraine frequency and is associated with weight loss, rather than weight gain.²⁵ (Topiramate and valproic acid should be avoided in women who are hoping to become pregnant.) Gabapentin has conflicting evidence and is not recommended for migraine.²³

■ **Beta-blockers** that appear to be most effective as prophylaxis for CM are propranolol, metoprolol, and timolol.^{23,26} Any of these would be the obvious choice for a patient with comorbid hypertension. Beta-blockers can take several months to have an effect on migraines, however. Their use as CM prophylaxis may be limited by their adverse effect

profile, which includes erectile dysfunction, bradycardia, and hypotension, although the lower dosage needed for migraine prophylaxis may be a mitigating factor. Calcium channel blockers are commonly prescribed for migraine, but there is little evidence to support their use for CM.²³

Other medications that are likely effective for migraine prophylaxis include naproxen²⁴ and tizanidine²⁷ (a muscle relaxant). Complementary and alternative treatments that appear to be effective include magnesium, feverfew, butterbur, and riboflavin, although the benefits may not be noticeable for several months.²⁴

■ **Botulinum toxin A** is the only medication approved by the US Food and Drug Administration for prevention of CM. It is generally considered to be a second-line agent because of its high cost and the need for training and expertise to administer it. Botulinum toxin A is not effective as prophylaxis for EM.²⁸

Treating other headache syndromes

Chronic tension-type headache. Treatment of CTTH applies similar principles to those of CM, and amitriptyline and venlafaxine—as well as mirtazapine, a sedating SNRI—have evidence to support their use for this type of headache.²⁹ Overall, however, CTTH therapies have not been studied as extensively as those for migraine. There is conflicting evidence of the value of anticonvulsants



Triptans, simple analgesics, and ergots can be safely withdrawn at once or with a slow wean over a 4- to 6-week period.

➤ **Beta-blockers are an obvious choice for headache prophylaxis in patients with hypertension, but their use may be limited by their adverse effects profile.**

for prophylaxis of CTTH, and botulinum toxin A has been shown to be no better than placebo.³⁰

■ **Medication overuse headache.** Prophylactic medications are not effective in patients who are overusing acute headache medications, and patients with MOH should be instructed to stop the offending drugs. Withdrawal of triptans, simple analgesics, and ergots—either cold turkey or with a slow wean over 4 to 6 weeks—is fairly safe and can be done in an outpatient setting. Concomitant use of prednisone, long-acting NSAIDs, or botulinum toxin A can be used as “bridge therapy” to relieve acute pain. Start the patient on a prophylactic medication based on the best estimate of his or her baseline headache and comorbidities.^{31,32} For patients who have been overusing opiates or barbiturates, most experts recommend inpatient treatment to manage withdrawal symptoms and prevent complications.¹⁰

Most patients with MOH will improve with drug withdrawal, but some will be left with the same disabling headaches that caused them to overuse medication in the first place. For such patients, weekly office visits during the withdrawal period may be helpful. After completion of the bridge therapy, they will likely require abortive headache treatment, but its use must be limited to no more than twice a week. Referral to a specialty headache clinic may be appropriate for such patients.

■ **Hemicrania continua.** The treatment for HC is indomethacin. A 2- to 5-day course typically results in complete recovery.

■ **New daily persistent headache.** For patients with NDPH, the first step is ruling out secondary causes. Once that has been done, most experts recommend trying to characterize the headache as having features of either migraine or tension and treating accordingly with preventive therapy. If acute headache medication is still needed, limit the quantity you prescribe and stress the importance of taking it no more than twice a week.

CASE ▶ Mr. K receives a diagnosis of MOH and probable CM. You explain the way MOH develops and how his medication use has

contributed to the escalation of his headaches, and ask him to stop all the headache medications he has been using and to keep a headache journal. You prescribe meloxicam as a short-term bridge therapy and low-dose venlafaxine, which is increased to 150 mg/d over the next 4 weeks; recommend riboflavin 400 mg/d; and refer Mr. K to a neurologist for botulinum toxin A.

You ask him to return in 4 weeks and explain that because he has successfully stopped the overuse of acute headache medications, he can begin taking them again—provided he limits their use to no more than twice a week.

Nonpharmacologic measures can help, too

Lifestyle modification can play an important role in the treatment of chronic daily headache. Advise patients of the importance of proper sleep hygiene, regular exercise, stress reduction, and a healthy diet, as well as avoiding known triggers and minimizing intake of caffeine. Tell patients that biofeedback, cognitive behavioral therapy, and physical therapy may play a role in conjunction with pharmacotherapy, especially for CTTH,^{26,29,33} but that hypnosis, acupuncture, chiropractic manipulation, transcutaneous electrical nerve stimulation, and hyperbaric oxygen have too little evidence to recommend for or against their use.^{26,34}

In discussing treatment for chronic headache and the goals of therapy with a patient with chronic headache, it is important to be frank. Explain that while a complete cure is not always possible, a decrease in both the frequency and severity of headaches and an improvement in the quality of life and the patient’s ability to function are realistic goals.

CASE ▶ At the 3-month follow-up, Mr. K reports that his headaches are down to less than twice a week, and that he is undergoing cognitive behavioral therapy for depression. For acute headache pain, he takes sumatriptan 100 mg with ibuprofen 800 mg, and is careful not to do so more than twice a week. **JFP**

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Advise patients of the importance of proper sleep hygiene, regular exercise, stress reduction, and a healthy diet, as well as avoiding known triggers and minimizing intake of caffeine.

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