

Chronic daily headache: Understanding and treating a common malady

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ABSTRACT

Chronic daily headache affects 4%-5% of the general population, half of whom have transformed or chronic migraine and half of whom have chronic tension-type headache. The overuse of prescription and nonprescription medications, particularly analgesics, is a prime contributor. Treatment may include stopping the offending medications, bridge therapy for withdrawal symptoms, preventive and acute pain therapy, and nonpharmacologic techniques such as lifestyle changes and behavioral therapy.

Chronic daily headache represents a group of primary and secondary headache disorders that remain poorly understood and are often inappropriately managed. Generally considered to consist of headaches that occur 15 or more days a month for 4 or more hours a day for at least 6 months, chronic daily headache affects an estimated 4%-5% of the general population.¹ There is a female preponderance of 2:1 to 4:1. The prevalence of chronic daily headache is not thought to change appreciably with age. Onset is typically in the 30s.¹

Primary headache disorders (such as migraine, tension-type, and cluster headaches) can be divided into two groups based on duration (Table 1, page 26).² In the general population, chronic tension-type headache occurs in approximately 1%-3% and chronic migraine (also called transformed migraine) occurs in 1%-2%.³⁻⁷ The latter group are much more likely to be referred to a tertiary care center.^{8,9} Primary headaches lasting 4 or more hours are often associated with the overuse of prescription or nonprescription medications.^{9,10}

The secondary headache phenomenon known as medication-overuse headache (rebound headache, drug-induced headache, or medication-misuse headache) typically begins with using an agent to treat the pain of an intermittent headache such as episodic migraine or episodic tension-type headache.² Over time, the persistent pain may cause patients to overuse the medications, leading to the overuse headache that may be superimposed on the original headache. It appears there usually is a history of migraine, as suggested by the observation that arthritis patients who use analgesics long-term but do not

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Table 1

Types of primary chronic daily headache
Headache duration < 4 hours
Cluster headache
Chronic paroxysmal hemicrania
SUNCT syndrome
Hypnic headache
Idiopathic stabbing headache
Headache duration ≥ 4 hours
Chronic tension-type headache
Chronic migraine
New daily-persistent headache
Hemicrania continua

Key: SUNCT = short-lasting unilateral neuralgiform headache with conjunctival injection and tearing.
 Source: Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, 2nd edition. Cephalgia 2004;24(suppl 1):1-152.

have a significant history of migraine do not develop medication-overuse headache.¹¹

Analgesics, particularly butalbital, opioids, acetaminophen and aspirin, and ergotamine tartrate (Ergomar), are known to cause medication-overuse headaches.¹² Some headache specialists believe that combination analgesics are especially likely to cause them. One recent study found that medications containing butalbital are most commonly overused.⁹ In addition to the pathophysiologic mechanisms we will outline later, overuse of butalbital-containing medications is probably related to their addictive properties as barbiturates.

Episodic headache can be transformed or progress to daily headache when any of these medications, even at low doses, are taken regularly more than 2-3 times a week. It does not appear to be the total dose, but rather the frequency of use, that leads to development of medication-overuse headache.¹⁰ The original primary headache may persist for a mean of about 10 years, but can last more than 20 years before chronic daily headache develops.

The frequency of medication overuse varies by setting. Population-based studies indicate that about one third of chronic daily headache patients overuse symptomatic medications.^{13,14} In contrast, data from tertiary treatment centers suggest that this figure may be as high as 80%,⁹ which probably reflects the difficult nature of overuse headache. Clearly, not all patients with chronic

daily headache overuse medications, suggesting that the chronicity may be a natural transformation from an episodic primary headache^{1,9} and that chronic daily headache may develop precipitously as a new daily-persistent headache.²

Chronic daily headache has been associated with several patient characteristics, including habitual snoring, female gender, lower educational level, being previously married, and low alcohol consumption, although a cause-and-effect relationship has not been established for any of these.¹⁵ Psychiatric comorbidities such as depression and

Table 2

Brief headache screen
1. How often do you get severe headaches (that make it difficult or impossible to continue normal function?)
a) daily or almost daily d) 1 month or less
b) 3-4 days a week e) almost never
c) 2 weeks to 2 months
2. How often do you get mild or less severe headaches?
a) daily or almost daily d) 1 month or less
b) 3-4 days a week e) almost never
c) 2 weeks to 2 months
3. How often do you take pain relievers or any medication to relieve headache symptoms?
a) daily or almost daily d) 1 month or less
b) 3-4 days a week e) almost never
c) 2 weeks to 2 months
4. How often do you miss some work or leisure time because of headache?
a) daily or almost daily d) 1 month or less
b) 3-4 days a week e) almost never
c) 2 weeks to 2 months
5. Are you satisfied with the current medication you use to relieve your headaches?
a) yes b) no
6. Are you taking daily prescription medication to prevent headaches?
a) yes b) no
If no, do your headaches trouble you enough to take daily preventive medication?
a) yes b) no

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anxiety are seen more commonly in adults and children with chronic daily headache than in those with other types of headache.^{16,17} An estimated 64%-90% of patients with chronic daily headache have some psychiatric comorbidity.^{16,17} Again a cause-and-effect relationship has not been proven,^{5,18} but the combination of psychiatric distress and chronic daily headache is a major determinant of the overall level of functional impairment and quality of life.¹⁹

Physiologic origins of chronic daily headache

Preliminary data suggest that several mechanisms contribute to the development of chronic daily headache. Repeated activation of trigeminal nociceptors can lead to the upregulation and finally sensitization of higher-order nociceptive-processing neurons in the central nervous system. These functional changes may underlie the allodynia and hyperalgesia in patients with chronic daily headache and other chronic pain syndromes.²⁰ Some data suggest that dysfunctional periaqueductal gray matter may be responsible for the evolution of episodic migraine into a pattern of chronic daily headache.²¹ It has also been postulated that an impairment of serotonergic pathways is the link between chronic daily headache and psychiatric comorbidities.¹⁹ Other peripheral mechanisms may contribute, but evidence is lacking.²⁰

The path to diagnosis

In clinical practice, the first diagnostic priority is to distinguish primary from secondary headache and then to assess the role of medication overuse in the patient with a primary headache. The importance of a correct diagnosis cannot be overemphasized, as management varies significantly depending on the cause. Normally, the diagnosis of chronic daily headache can be made on the basis of clinical history and physical and neurologic examinations. Physical examination is performed primarily to rule out an organic disorder. A structural abnormality found on examination of the head, eyes, ears, nose, and throat usually necessitates referral to rule out secondary or contributing causes.

A series of screening questions can be useful (Table 2)²² to identify the key features that differentiate medication-overuse from other headache

Table 3

Clinical features of medication-overuse headache

- Usually preceded by an episodic headache disorder that is managed with frequent use of analgesics, decongestants, triptans, ergot alkaloids or dihydroergotamine mesylate (Migranal, D.H.E. 45), or muscle relaxants, often in excessive quantities
- Refractory, daily, or nearly daily
- Varies in severity, type, and location from time to time
- Low threshold for head pain
- May be brought on by physical or intellectual effort
- Accompanied by asthenia, nausea, or other gastrointestinal symptoms; restlessness, anxiety, or irritability; difficulties with memory or concentration; or depression.
- Use of large quantities of ergot alkaloids or triptans may result in cold extremities, paresthesias, diminished pulse, hypertension, light-headedness, muscle pain of the extremities, leg weakness, depression
- Drug-dependent rhythmicity with frequent early morning (2 AM to 5 AM) headache
- Symptomatic medications provide some short-term (few hours) relief
- Prophylactic medications are ineffective unless symptomatic medications are discontinued
- Withdrawal symptoms, particularly worsening headache, occur when symptomatic medication is discontinued

Sources: Diener HC, Katarava Z. Analgesic/abortive overuse and misuse in chronic daily headache. *Curr Pain Headache Rep* 2001;5:545-550.

Zed PJ, Loewen PS, Robinson G. Medication-induced headache: Overview and systematic review of therapeutic approaches. *Ann Pharmacother* 1999;33:61-72.

Mathew NT. Transformed migraine, analgesic rebound, and other chronic daily headaches. *Neurol Clin* 1997;15:167-186.

types (Table 3).^{12,23,24} Overuse headache varies in severity, type, and location from time to time. A person with episodic migraine originally who develops analgesic-overuse headache typically experiences a tension-type headache plus intermittent migraine attacks. One whose original headache is episodic tension-type often develops increasingly frequent tension-type headaches that improve after medication withdrawal.¹² Another important feature of overuse headache is a drug-dependent rhythmicity with a high predictive value for early morning headaches.²⁴

Several other issues should be explored, includ-

MIDAS QUESTIONNAIRE

INSTRUCTIONS: Please answer the following questions about ALL your headaches you have had over the last 3 months. Write your answer in the box next to each question. Write zero if you did not do the activity in the last 3 months.

1	On how many days in the last 3 months did you miss work or school because of your headaches?	<input type="text"/> <input type="text"/>	days
2	How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1 where you missed work or school)	<input type="text"/> <input type="text"/>	days
3	On how many days in the last 3 months did you not do household work because of your headaches?	<input type="text"/> <input type="text"/>	days
4	How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? (Do not include days you counted in question 3 where you did not do household work)	<input type="text"/> <input type="text"/>	days
5	On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?	<input type="text"/> <input type="text"/>	days
TOTAL		<input type="text"/> <input type="text"/>	days
A	On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day)	<input type="text"/> <input type="text"/>	days
B	On a scale of 0-10, on average how painful were these headaches? (Where 0 = no pain at all, and 10 = pain as bad as it can be)	<input type="text"/>	

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Note: A MIDAS score above 10 indicates significant disability that should be seen by a clinician to improve treatment.

Figure 1 This instrument is known to have good test-retest reliability and correlates well with clinical judgment about the need for medical care. It also has good correlation with detailed headache diaries.

ing a thorough medication history of all prescription, nonprescription, and herbal medicines. Particular attention should be paid to temporal relationships between changes in medications (addition, dosage adjustment, or discontinuation) and headache onset and differences in severity or frequency. Increasing use of any type of medication to relieve headache pain is a red flag for rebound headache. Similarly, patients may report that previously effective preventive medications no longer work. Any psychiatric comorbidities, especially depression and anxiety, should be explored. Asking, "What else is going on in your life?" may help uncover important psychosocial issues.

Two instruments are helpful in assessing the impact of headache symptoms on quality of life. The Migraine Disability Assessment (MIDAS) is a brief, self-administered questionnaire designed to quantify headache-related disability over a 3-month period (Figure 1).²⁵ The MIDAS score has been shown to have moderately high test-retest reliability and correlates well with clinical judgment regarding the need for medical care.²⁵ It also exhibits good correlation with a detailed headache diary.²⁵ The second instrument, the Headache Impact Test, is a 1- to 2-minute questionnaire that measures the effect of the headaches on the patient's ability to function at work,

home, and school and in social situations²⁶ (available at: <http://www.headachetest.com>).

Diagnostic imaging is usually unnecessary without evidence or suspicion of a structural abnormality.²⁷ Occasionally, serum or cerebrospinal fluid analysis or cervical spine imaging may be warranted. Magnetic resonance imaging (MRI) of the brain is considered the imaging modality of choice. Techniques such as positron-emission tomography (PET) or high-resolution MRI can identify abnormal nociceptive pathways but are not yet applicable to general clinical practice.²¹

Elements of successful management

Management goals are to limit the impact of the headaches on functioning and quality of life by reducing their frequency, severity, and duration. This typically requires a reevaluation of preventive and acute treatments. A critical first step is to verify that the diagnosis of chronic daily headache is correct, followed by implementing a management plan with pharmacologic and nonpharmacologic therapies. If the diagnostic reevaluation shows that medication overuse plays a central role in chronic daily headache (signifying rebound headache), an aggressive management plan that includes discontinuation of the offending medications and a bridge strategy should be developed and implemented.

- *Medication withdrawal* One of the most common errors in managing chronic daily headache is to start prophylactic therapies without discontinuing the agent being overused. It is also important to emphasize that abrupt discontinuation usually results in profound escalation of headache intensity (withdrawal headache). This is why it is so difficult for patients to stop taking the overused medication on their own and why the process is readily perpetuated. Even after total discontinuation and termination of the rebound event, normalization of the headache process and response to standard medications may take weeks or even months.¹⁰

For the patient with rebound headache, several steps need to be taken (Table 4). Chief among these is discontinuing the offending drug, since clinical experience indicates that medical and behavioral headache treatments will not work if the patient continues taking daily symptomatic medications.^{10,12} Patient characteristics determine

Table 4

Management principles for medication-overuse headache

- Provide patient education
- Discontinue offending medications
- Initiate bridge therapy for withdrawal headache
- Initiate preventive therapy
- Select therapy for acute management
- Address psychosocial issues

whether therapy will be in an outpatient or inpatient setting.¹² Patients with a shorter duration of medication overuse, those who use only one substance, and those who have support of family and friends or are highly motivated themselves can usually be treated as outpatients.¹² Those who have not responded to outpatient management, who have a longer history of medication overuse—especially of barbiturates, opioids, or tranquilizers—or who have psychiatric comorbidities may require hospitalization.¹²

Ergot alkaloid, nonopioid, or triptan medications can be discontinued abruptly in some persons but may require tapering in others. Opioids, barbiturates, and benzodiazepines should be withdrawn slowly, perhaps over 2 weeks, depending on dose and duration of use.^{12,28}

- *Bridge therapy* For inpatients, bridge therapy for withdrawal headache (acute management with selected agents to break the cycle) often includes combined dihydroergotamine mesylate (Migranal, D.H.E. 45) and metoclopramide (Clopra, Maxolon, Reglan, etc.), known as the Raskin protocol,²⁹ unless the medication being overused is an ergot alkaloid or a triptan.¹²

Other bridge therapy options can be used for inpatients or outpatients (Table 5, page 32). A nonsteroidal anti-inflammatory drug (NSAID), triptan, or prednisone (Deltasone, Meticorten, Orasone, etc.) is generally very effective for withdrawal symptoms, including headache, nausea, vomiting, arterial hypotension, tachycardia, sleep disturbances, restlessness, anxiety, and nervousness.^{12,30} Most experience with NSAIDs has involved naproxen sodium (Naprelan), although other agents such as ketoprofen (Orudis, Oruvail) have also been used.^{23,31} Clonidine HCl (Dura-

Table 5

Options for bridge therapy of withdrawal headache	
Agent	Dosage
Naproxen sodium (Naprelan)	550 mg bid x 7d, then 550 mg qd x 7d
Meclofenamate sodium	100 mg tid x 7d, then 100 mg bid x 7d
Prednisone (Deltasone, Meticorten, Orasone, etc.)	60 mg qd x 1d, then titrate downward by 10 mg q 2-3 d over 2 wk
Raskin protocol	Initial doses of metoclopramide (Clopra, Maxolon, Reglan, etc.), 10 mg IV, plus dihydroergotamine mesylate (D.H.E. 45), 0.5 mg IV, with subsequent dosing to abort headache followed by a variety of medications to prevent recurrence

Source: Raskin NH. Treatment of status migrainosus: The American experience. *Headache* 1990;30(suppl 2):550-553.

Table 6

Options for preventive therapy with comorbidities	
Comorbidity	Agent
Anxiety	SSRI, SNRI, gabapentin
Bipolar disorder	Valproic acid
Depression	Antidepressant
Epilepsy	Anticonvulsant
Fibromyalgia	Antidepressant
Insomnia	Tricyclic antidepressant

Key: SNRI = serotonin-norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

clon) is helpful for symptoms of opioid withdrawal. The initial dose is 0.1-0.2 mg tid, titrated up or down. Phenobarbital (Bellatal, Solfoton) should be used if high doses (more than 15 tablets a day) of a butalbital-containing combination drug are discontinued abruptly.

Other options for inpatient management include diphenhydramine HCl or a neuroleptic such as droperidol (Inapsine). Regardless of the bridge therapy used, headache intensity may actually in-

crease during withdrawal, but it will decline by the end of the first or second week.²⁸ Whether the offending symptomatic medication is abruptly discontinued or tapered over 2 weeks, bridge therapy should be continued for 2 weeks. Typical withdrawal symptoms last 2-10 days (average, 3.5 days),¹² although they may persist for 2-4 weeks.²³

• *Preventive therapy* needs to be instituted concomitantly or within a few days of starting bridge therapy. An antidepressant or anticonvulsant is typically used, although the agent chosen is guided by the comorbidity (Table 6). A sedating tricyclic antidepressant (TCA) such as amitriptyline HCl (Elavil) or doxepin HCl (Sinequan) may be best for a patient with insomnia or another sleep disorder. A selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor is appropriate for someone with an anxiety or mood disorder, although neither is as effective as a TCA for treating chronic daily headache. An anticonvulsant may be helpful in a patient with epilepsy or bipolar disease.

The preventive medication should be started at the lowest possible dosage to avoid side effects and then increased over 2-4 weeks. Amitriptyline, for example, should be started at 10 mg hs, with a maximum 50-75 mg hs. Fluoxetine HCl (Prozac, Sarafem) is initiated at 20 mg qd and increased to 40 mg qd after 1 month, if tolerated.³² Valproate (Depakote, Depakene) is started at 250 mg po bid, increasing to 500 mg po bid after 2 days if tolerated.³³ Dosage is adjusted to maintain blood levels of 75-100 µg/mL. Another option is intravenous valproate (Depacon) started at 15 mg/kg, followed by 5 mg/kg q 8 h.³⁴ Topiramate (Topamax) may be initiated at 12.5 or 15 mg and increased by 12.5 or 15 mg per week to a total dosage of 100 mg weekly. Finally, tizanidine HCl (Zanaflex) in doses as high as 24 mg/d has been shown to improve headache severity over 12 weeks.³⁵ After 2 months of therapy, the dosage of the preventive medication should be reassessed, particularly if improvement in headache frequency is less than 50%. Preventive therapy should be continued for 6 months or longer.

• *Acute therapy* may include a triptan or an NSAID, but an accurate diagnosis of the original headache is important since triptans are effective

Table 7

Options for acute management of chronic daily headache	
Agent	Dosage
Aspirin	1,000 mg po once
Ibuprofen	800-1,200 mg po once, then 400 mg prn
Naproxen sodium (Naprelan)	825 mg po once, then 550 mg, 1 h later
Frovatriptan succinate (Frova)	2.5 mg po q 2 h x 3 (max, 7.5 mg/24 h)
Naratriptan HCl (Amerge)	2.5 mg po q 4 h x 2 (max, 5 mg/24 h)
Rizatriptan benzoate (Maxalt)	5-10 mg po q 2 h x 3 (max, 30 mg/24 h)
Sumatriptan succinate (Imitrex)	25-50 mg po q 2 h x 2-4 (max, 200 mg/24 h) OR 20 mg intranasally q 2 h (max, 40 mg/24 h) OR 6 mg SC q 2 h x 2 (max, 12 mg/24 h)
Zolmitriptan (Zomig)	2.5-5 mg po q 2 h x 2 (max, 10 mg/24 h)
Dihydroergotamine mesylate (Migranal, D.H.E. 45)	1 spray in each nostril; wait 15 min, then 1 additional spray OR 0.15-1.5 mg IV, IM, or SC injection q 8-12 h (under physician supervision)

Key: IM = intramuscular; IV = intravenous; max = maximum; SC = subcutaneous.

Source: Adapted from Drug Facts and Comparisons. St. Louis, Mo: Wolters Kluwer Health, Inc; 2003.

treatment for migraine.³¹ When a triptan is not effective, dihydroergotamine is a reasonable alternative unless contraindicated²³ (Table 7³⁶). Patients may be taught to self-administer dihydroergotamine by intramuscular or subcutaneous routes; the agent is also available as a nasal spray. A trial of the selected medication should last 2-4 weeks and be strictly limited to no more than 2 or 3 acute episodes a week.

• *Nonpharmacologic measures* are critical to achieving management goals. Patients should adopt regular patterns of sleeping, eating, and exercise and be encouraged to avoid headache triggers such as caffeine, nicotine, artificial sweeteners (aspartame), and monosodium glutamate. Behavioral management techniques have been shown to produce additional benefits beyond pharmacotherapy alone.^{10,37} Greater benefit (more than 60% reduction in total headache hours) is seen in patients who have headaches that last fewer than 15 hours per day or who have at least 1-2 headache-free days per week.³⁸

The focus of these therapies is not on preventing headaches but on reducing their severity, associated disability, affective distress, and the patient's over-

reliance on medications. The objective is to enhance patients' quality of life and increase their sense of personal headache control. Initial efforts are directed toward managing pain and preventing mild pain from progressing to disabling pain. The most commonly used techniques are relaxation training, biofeedback training, and cognitive-behavioral (stress-management) therapy.³⁷

Before and throughout the period of medication withdrawal, frequent, open communication with the patient is essential. This will help ensure that the goals of therapy are clear and the factors that might affect short- and long-term success are identified and addressed. Communication is enhanced if patients keep a diary to track headache severity, their use of symptomatic and preventive medications, triggers, and disability. An excellent diary

form is available online from the New England Center for Headache (<http://www.headachenech.com/patients/calendar.html>).

It should be noted that up to 60% of patients return to medication overuse after preventive medication is withdrawn, despite experiencing a period of significant improvement after withdrawal, explanation of the analgesic rebound problem, and implementation of an effective prophylactic medication program.³⁷ In such situations, the management process—medication withdrawal and bridge therapy—must begin again. Referral to a headache specialist, if not previously done, is recommended.

When should a patient be referred?

In several situations, referral to a headache specialist may be appropriate including when a secondary headache is diagnosed or when the diagnosis is uncertain. Referral may also be warranted when a patient has complicated or multiple comorbidities, when selecting appropriate therapies is difficult, or when treatment is unsuccessful. The latter includes situations in which overused medications cannot be successfully withdrawn, head-

aches cannot be prevented despite maximal dosages of preventive medications, or the patient is repeatedly noncompliant. Finally, referral may be advisable when it is not possible to provide the considerable time and resources required for patients with chronic daily headache, particularly rebound headache.

Conclusion

Chronic daily headache is a common syndrome affecting 4%-5% of the general population. It is often complicated by the overuse of symptomatic medications, particularly analgesics. Diagnosis of the original headache is critical to management, especially since it often coexists with medication-overuse, or rebound, headache. The most important management step for this type of headache is discontinuing the offending medications. Long-term success requires bridge therapy to reduce symptoms during medication withdrawal and then effective preventive and abortive medications. Nonpharmacologic measures provide additional benefit. Comprehensive management can lead to a significant reduction or elimination of rebound headache in up to 80% of patients. ■

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SELF-EXAMINATION

- Chronic daily headache refers to headaches that occur at least ____ days a month for ____ or more hours a day for 6 months or more.
 - 10; 2
 - 10; 4
 - 15; 2
 - 15; 4
 - 20; 4
- Which of the following statements about medication-overuse headache is false?
 - It typically begins with using a medication to treat an episodic headache.
 - Patients usually have a history of migraine.
 - The total dose of a medication is a more important contributor to rebound headache than the frequency of use.
 - Analgesic overuse is usually responsible.
 - Episodic tension-type headache can progress to chronic daily headache if the patient regularly takes analgesics more than 2-3 times a week.
- Which of these headache types is associated with headache duration of less than 4 hours?
 - cluster headache
 - hemicrania continua
 - chronic migraine
 - chronic tension-type headache
 - new-onset daily persistent headache
- In a patient with chronic daily headache, all of these agents except _____ are appropriate for treating the stated comorbidity.
 - tricyclic antidepressant for insomnia
 - selective serotonin reuptake inhibitor for anxiety
 - gabapentin for fibromyalgia
 - valproic acid for bipolar disorder
 - serotonin-norepinephrine reuptake inhibitor for depression
- Of these statements about treating chronic daily headache, all except _____ are true.
 - A person with a rebound headache who has overused an analgesic for 4 years can undergo withdrawal therapy as an outpatient.
 - The Raskin protocol is used for inpatient withdrawal from a triptan.
 - Clonidine may be used to manage symptoms of opioid withdrawal.
 - Preventive therapy should be instituted at the same time or within a few days of starting bridge therapy.
 - Preventive therapy should be continued for at least 6 months.

Answers at end of reference list.

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■ *Answers: 1)d, 2)c, 3)a, 4)c, 5)b*