Topics in Primary Care Medicine

The Clinician's Approach to the Management of Headache

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Headache is a ubiquitous complaint, yet it is one that often elicits anxiety in both patients and physicians. When a patient presents with headache, the clinician must answer the following questions: (1) Is the headache "worrisome" (secondary to underlying disease)? (2) If the headache is benign, what type is it? (3) How is the acute headache best treated? and (4) How may future headaches be prevented? The following review is intended to aid primary care physicians in answering these questions.

(Maizels M. The clinician's approach to the management of headache. West J Med 1998; 168:203–212)

Assessment: What Type of Headache Is It?

A headache evaluation should address the issues listed in Table 1. Many patients have more than one type of headache; the patient with constant daily headaches often has occasional incapacitating migraines. In assessing the patient's headache, each type should be considered and addressed.

Migraine

The International Headache Society has defined the criteria for migraines with and without aura (Tables 2 and 3);[1] the most recent definitions replace previous designations of "classic" and "common" migraine. *Migraine is never pain alone:* there must always be nausea or photophobia and phonophobia. Auras may or may not accompany the migraine; they are usually visual hallucinations and are typically described as flashing lights, zig-zag lines (the "fortification" phenomenon), or blind spots (scotoma). Clinicians also rely on certain patterns to aid in the diagnosis of a migraine. Headaches with reliable triggers (Table 4) and patterns (such as perimenstrual exacerbation with relief during pregnancy) are likely to be migrainous. It is also typical to notice relief of the headache after sleep.

Tension-type headache

The designation "tension-type" reflects the understanding that the headache is not directly related to muscle tenderness; rather, muscle tenderness may be a secondary phenomenon.[2] Episodic tension-type headache (TTH) is different from chronic TTH in that it occurs less than 15 days per month.[1] Many experts believe that TTH and migraine form a continuum and cannot be readily distinguished.[3] For instance, features that accompany migraine—such as unilateral headache, throbbing pain, nausea, or photo- and phonophobia—are occasionally seen in TTH, while neck muscle tenderness may be seen in migraine patients.[4] Many patients do have both migraine and TTH, and, in fact, a TTH can turn into a migraine. These facts lend further support to the idea of the existence of a headache continuum.

Pathophysiology of Migraine and TTH

The current understanding of migraine origin has evolved from vascular models,[5] to a trigeminovascular model,[6,7] toward a central neuronal model of migraine as a disturbance of the serotonergic system of the midbrain.[8] Activation of the dorsal raphe nucleus of the midbrain during migraine[9] has led to the concept of a "migraine generator." Receptors for serotonin (5-hydroxytryptamine, or 5-HT)-specific medications are identified in the midbrain,[10] and all migraine abortive and prophylactic medications influence the serotonin pathway.[11] In migraines, vascular changes are most likely secondary, rather than causative, phenomena.

A gene for the rare disorder familial hemiplegic migraine has been mapped to chromosome 19p13.[12] This discovery has raised speculation that a genetic basis for other forms of migraine may be found.

There has been little progress in our understanding of TTH. Olesen has proposed looking at migraine and TTH as integrations of vascular, supraspinal, and myofascial inputs:[13] the spectrum of symptoms is explained by the relative predominance of vascular as opposed to myofascial input. Some instances of what is currently called TTH may ultimately be found to be cervicogenic in origin.[14]

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ABBREVIATIONS USED IN TEXT

5-HT_1 = 5-Hydroxytryptamine
DHE = dihydroergotamine
CDH = chronic daily headache
NSAID = nonsteriodal anti-inflammatory drug
TCA = trycyclic antidepressant
TTH = tension-type headache

Headaches are also commonly believed to have a psychological basis, but related studies have had varying results. Many of these studies show that people afflicted with migraines (migraineurs) have high levels of anxiety or depression.[15] In one study, however, the Minnesota Multiphasic Personality Inventory (MMPI) patterns of patients with migraine headaches were normal; those of patients with TTH or combined migraine-TTH were moderately abnormal (indicating "neuroticism"); and those of patients with posttraumatic headache (daily headache following trauma) were abnormal.[16] Nonetheless, 67% of migraineurs identify emotion as a headache trigger.[17]

Chronic Daily Headache/Drug Rebound Headache

The phenomenon of drug rebound headache has been described as an unrecognized epidemic.[18] The mandate of any primary physician is to prevent drug rebound and to recognize it when it occurs.

Chronic daily headache (CDH) is a low-grade daily headache, which may become severe at times and have migrainous features. CDH patients account for 40% of all patients referred to headache clinics.[19] The patient may not complain of daily headache, however. Frequent refills of symptomatic medication or recurrent visits to the emergency room should alert the physician to the possibility of CDH.

Mathew[20] described the transformation of episodic migraine into a daily headache. Mathew and colleagues[19] later studied 630 patients with CDH (excluding those with posttraumatic headache): 78% had transformed migraine, 13% had chronic TTH, and 9% had what is known as new daily persistent headache. Patients with transformed migraines begin with a typical history of episodic migraine that, over the years, becomes more and more frequent and eventually occurs daily. Patients with new daily persistent headache note the onset of a headache over a day or two, which then persists daily. New daily persistent headache patients are difficult to treat, but their long-term prognosis is good: 30% have their symptoms resolve within 3 months, and 70% to 80% have theirs resolve in 6 to 12 months.[21]

In a landmark study of 200 patients with daily TTH, Kudrow[22] demonstrated that only those patients who stopped their daily use of analgesics improved. Withdrawal of daily medication, combined with amitryptiline prophylaxis, led to a 72% improvement (using an index of headache frequency and severity) within 4 weeks. Even without any prophylaxis, patients who withdrew from their daily analgesics showed a 43% improvement. Patients who continued daily analgesics, with or without prophylaxis, had little improvement. In a separate series of 200 patients, Mathew and colleagues[23] found a 78% and 52% improvement, with and without prophylaxis, respectively, in patients who successfully stopped their daily analgesic. Patients may require a "wash-out" period of 8 to 12 weeks or longer (to cleanse the body of the analgesic).[24]

Any symptomatic headache remedy may cause drug rebound headache, but it is most likely when using ergotamines, narcotics, and products that combine caffeine or butalbital with aspirin or acetaminophen.[23,25] Even patients who take as little as 1000 mg per day of aspirin or acetaminophen may develop drug rebound headache.[26] *Many clinicians believe that the frequency of use is most important, and they limit the use of all symptomatic medication to two days a week.*

TABLE 1.—*Evaluation of Chronic Recurrent Headaches*

History	*Physical Examination*
Age at onset; change in pattern over time	Funduscopic
Headache features	Myofascial—cervical spine; temporomandibular joint
quality (throbbing vs. dull)	Neurologic exam—cranial nerves, DTRs, motor, cerebellar
location (unilateral vs. bilateral)	
severity	
prodromal symptoms/aura	
associated symptoms	
nausea; photo- or phonophobia	*Laboratory Evaluation**
frequency/duration	CT/MRI
Triggering factors (see Table 4)	Lumbar puncture
Family history	
Psychosocial (lifestyle, sleep pattern, anxiety/depression)	
Previous evaluations (imaging studies, consultations)	
Medications—current and previous with responses and side effects	

* see text for indications

TABLE 2.—*Diagnostic Criteria for Migraine Without Aura*

A. At least five attacks fulfilling B to D
B. Headache attacks lasting 4 to 72 hours (untreated or unsuccessfully treated)
C. Headache has at least two of the following characteristics:
   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe intensity (inhibits or prohibits daily activities)
   4. Aggravation by walking stairs or similar routine physical activity
D. During headache at least one of the following conditions exist:
   1. Nausea and/or vomiting
   2. Photo- and phonophobia
E. No evidence of related organic disease

TABLE 3.—*Diagnostic Criteria for Migraine with Aura*

A. At least two attacks fulfilling criterion B
B. At least three of the following four characteristics:
   1. One or more fully reversible aura symptoms, indicating focal cortical or brainstem dysfunction.
   2. At least one aura symptom develops gradually over more than 4 minutes, or two or more symptoms occur in succession.
   3. No aura symptom lasts more than 60 minutes.
   4. Headache follows aura within an hour (or begins before or simultaneously with the aura).
C. No evidence of related organic disease

The proper treatment of drug rebound headache involves withdrawing the causative medication. *The addition of prophylaxis without withdrawal of the offending medication is a futile gesture.* Physicians must convey the good prognosis after drug withdrawal. Physicians should tell their patients to expect to feel worse for about two weeks before an improvement begins. Most patients can be abruptly withdrawn as outpatients, with the addition of amitryptiline (10 to 25 mg) as prophylaxis and a nonsteroidal anti-inflammatory drug (NSAID) such as naproxen for symptomatic relief.[27] Patients who abuse high doses of barbiturates or narcotics, or who cannot successfully withdraw on their own, should be referred to a headache specialist.

Treatment of the Acute Headache

There are several general principles to be followed in treating acute headaches. Physicians should base their selection of symptomatic medication on the past experience of the patient; the severity of the headache; associated symptoms; and side-effect profiles (Tables 5 and 6). Patients should be taught how to recognize early headache symptoms and treat them before the headache becomes disabling.

Aspirin and NSAIDs (such as ibuprofen[28] or naproxen[29]) are effective for most milder headaches, although they often require high doses. Combination analgesics, such as aspirin or acetaminophen with butalbital and caffeine or isometheptene with acetaminophen and dichloralphenazone, are widely used. Caffeine increases the analgesic effect,[30–32] but combination products are prone to cause rebound headache.[33]

More severe headaches are treated with ergotamine combinations, the efficacies of which are probably equal to those of NSAIDs and mixed analgesics.[34] Patients should be instructed to determine the maximum dose they can tolerate without nausea, and take it as soon as possible in the attack. Ergotamine is poorly absorbed orally, but suppositories yield blood levels 20 to 30 times higher.[35] Patients willing to use a suppository should titrate their dosage to avoid nausea.

Headaches accompanied by strong nausea, or headaches that have not completely responded to the above medications, may be treated successfully by adding an anti-emetic. Anti-emetics improve the delayed absorption of medications caused by gastric stasis during a migrainous episode. Anti-emetics such as metoclopramide may be combined with any other migraine medications.

TABLE 4.—*Common Migraine Triggers*[65,103]

Emotion/stress/relief from stress
Specific foods
   aged cheeses (tyramine)
   nitrite/nitrate containing foods
   MSG
   chocolate
   caffeine
   alcohol
Skipping meals
Menses
Change in sleep pattern (too much or too little)
Glare

Treatment of the Most Severe Headache

More severe headaches often require parenteral therapy. Dihydroergotamine (DHE), a derivative of ergotamine tartrate, is underused in the treatment of severe headache.[36] DHE may be given intramuscularly (IM), subcutaneously (SQ), or intravenously (IV) and recently was approved for intranasal use. Its efficacy is comparable to sumatriptan (see below)—its onset of action is slower but it has less chance for relapse—and it is a cost-effective alternative. In addition, DHE, in contrast to ergotamine, does not cause drug rebound headache.[37,38] Patients can readily be taught to use DHE at home, and it is effective when other migraine treatments have failed.

Repetitive IV DHE (Table 7) is the treatment of choice for refractory migraine, status migrainosus (migraine lasting longer than 72 hours),[36] and chronic intractable headache (a chronic headache that has been refractory to treatment).[39] Premedication with metoclopramide or prochlorperazine[40] is required.

Sumatriptan is a specific 5-HT_1 (serotonin$_1$) receptor agonist and is a major advancement in the treatment of migraines. Six milligrams of sumatriptan given SQ relieves migraine pain and the associated symptoms in

TABLE 5.—*Principles of Acute Treatment*

Tailor prescription to the patient and to the headache severity;
Treat headache symptoms early, with maximal tolerated doses;
Consider adding anti-emetics to other treatments; and
Limit symptomatic medication to two days per week.

TABLE 6.—*Medications for Symptomatic/Abortive Treatment of Headache*

Drug	*Dose/route/ frequency*	*Remarks*	*Side effects (SE)/ Contraindications (C)*
MILD HEADACHES			
Aspirin NSAIDs naproxen ibuprofen others	Use maximal tolerated doses at onset; e.g., naproxen 775 mg, ibuprofen 1200 mg.		SE: GI intolerance, bleeding, fluid retention; C: peptic ulcer disease, Coumadin; use with caution in CHF, renal insufficiency
Aspirin or acetaminophen, butalbital, caffeine (Fiorinal, Fioricet)	1–2 at onset, repeated every 4 hours; maximum, 4 per day	HIGHLY PRONE TO DRUG REBOUND: Limit use to 2 days per week	SE: sedation and same as for aspirin (above)
MORE SEVERE HEADACHES			
Isometheptene, dichlorphenazone, acetaminophen (Midrin)	2 at onset, then 1 every hour to maximum of 5	Vasoconstrictor-sedative combination	SE: dizziness; C: glaucoma, severe renal or liver disease, CAD, hypertension; concomitant MAO-Is
Ergotamine tartrate, caffeine (Cafergot)	1–2 orally at onset; may repeat within 30 minutes and every four hours; maximum 5 per day	HIGHLY PRONE TO DRUG REBOUND: Limit use to 2 days per week	SE: nausea, abdominal pain, paresthesias, chest tightness; ergotism (ischemia of extremities) C: CAD, PVD, hypertension, renal or liver diseases, sepsis, pregnancy
Metoclopramide (Reglan)	10 mg orally, intramuscularly, or intravenously	Combine with any other agent to increase efficacy	SE: dystonic reactions; avoid use in children
MOST SEVERE HEADACHES			
Dihydroergotamine (DHE)	1 mg intramuscularly or subcutaneously, up to every 8 hours; 2 mg intranasally; see also intravenous protocol	Low rate of relapse; ideal for persistent headache	SE and C: same as for ergotamine, but does not cause drug rebound headache
Sumatriptan succinate (Imitrex)	6 mg subcutaneously; 25–100 mg orally; 5–20 mg intranasally; for relapse, may repeat one dose within 24 hours	High rate of relapse; subcutaneous is drug of choice for severe migraine or rapid onset of symptoms.	SE: atypical sensations (tingling, numbness, warmth, cold, heaviness), flushing, chest pain, neck pain; C: CAD or Prinzmetal angina; hemiplegic or basilar migraine. Do not use within 24 hours of ergots or MAO-Is

Abbreviations: CAD = coronary artery disease; CHF = congestive heart failure; PVD = peripheral vascular disease; MAO-Is = monoamine oxidase inhibitors
Note: All agents may be combined with anti-emetics for greater effect. Drugs are listed in groups of approximate order for increasing severity of headache.

about 80% of patients,[41–44] with relief beginning within 10 minutes and peaking in two hours. In these studies, however, headache recurred in about 40% of patients, most likely because of sumatriptan's short half-life.[45] A second dose of sumatriptan is effective in treating headache relapse,[46] but it is not helpful if the first dose was ineffective.[41,42] If given during a migraine's aura phase, sumatriptan will not shorten the aura nor prevent the headache:[47] patients with aura should be instructed to take the medication only after the headache phase begins. Drug rebound has not been reported in longitudinal studies of sumatriptan[48,49] but has been reported in isolated cases in which patients have used the medication daily for an extended period of time.[50,51] Oral doses of sumatriptan (25mg to 100 mg) also relieve headache in 70% to 80% of patients,[52,53] with greater effect as the dose is increased. Relief may take about two to four hours, as opposed to the rapid relief achieved with subcutaneously administered sumatriptan.

Subcutaneous sumatriptan provided greater relief than DHE one hour after being given (78% versus 57%) but not at three and four hours afterward. Additionally, the rate of headache recurrence within 24 hours was 2.5 times greater for sumatriptan than for DHE (45% versus 18%).[54] Both sumatriptan and DHE have recently become available as intranasal preparations.

Because coronary blood vessels also contain 5-HT_1 receptors, coronary vasoconstriction is a concern when

TABLE 7.—*Raskin Protocol for IV DHE for Intractable Migraine*[104]

1. Insert heparin lock.
2. Premedicate with metoclopramide 10 mg IV, slow push; wait 5 to 10 minutes.
3. DHE 0.5 mg IV:
   - if nausea occurs or headache is relieved within 1 hour, next dose of DHE is given after 8 hours, reduced to 0.3 mg to 0.4 mg
   - if headache is relieved without nausea, repeat 0.5 mg every 8 hours.
   - if neither nausea nor headache is relieved, repeat 0.5 mg after 1 hour (without metoclopramide). If tolerated, subsequent dose of DHE is 1.0 mg every 8 hours. If not tolerated, dose 0.75 mg every eight hours.
4. Repeat doses of DHE, determined above, every 8 hours; premedicate with metoclopramide for the first six doses.
5. Patients with risk factors for coronary artery disease should have electrocardiographic monitoring.
6. Patients may need to continue self-dosing with subcutaneous or intramuscular DHE.

using sumatriptan: it is contraindicated in patients with coronary artery disease or Prinzmetal's angina. The manufacturer recommends a cardiac evaluation for patients with cardiac risk factors including hypertension, hypercholesterolemia, diabetes, obesity, smoking, and a strong family history of heart disease, as well as for men over the age of 40 and postmenopausal women.[55] Patients with such risk factors should be given the first dose of sumatriptan under medical supervision. Chest pain is reported in 4.5% of patients taking SQ sumatriptan, but documented cardiac events are rare and are mainly seen in patients with previously noted cardiac risk factors.[56]

Newer triptans will soon be available, but it is still too early to see significant differences between them that would lead physicians to choose one over another. Concerns for the cost of the triptans may relegate them to second-line therapy. SQ sumatriptan should be considered a first-line treatment where rapid relief of severe headache symptoms is desired. DHE is particularly useful for prolonged headaches, or where relapse has occurred. Polymodal therapy (combinations of anti-emetics, NSAIDs, and 5-HT_1 agonists) should be used whenever a single agent is not effective.[57]

A patient who presents to the emergency room with a severe headache may require IV fluids and anti-emetics (Table 8). Dopamine antagonists—prochlorperazine,[58,59] chlorpromazine,[60] and metoclopramide[61] have all been reported to be highly effective.[62] There are, however, side effects, which can include dystonic reactions and tardive dyskinesia (manageable with dramamine).

TABLE 8.—*Alternatives to Narcotics in the Emergency Room*

DHE 1.0 mg IM or IV (see Raskin protocol—Table 7)
Sumatriptan 6 mg sq
Chlorpromazine 12.5 mg IV
  repeat every 20 minutes to maximum 37.5 mg
  (pre-medicate with 500 ml saline)
Metoclopramide 10 mg IV
Ketorolac 60 mg IM[105]

Abbreviations: IM = intramuscular; IV = intravenous; sq = subcutaneous

Prophylactic Therapy: Preventing Future Headaches

The treatment of recurrent headaches begins with the interview, not with the prescription. Patient satisfaction with the initial consultation predicts success better than any other specific intervention.[63] One study showed that patients referred to a neurology clinic were more interested to have an explanation of the causes of their headache than to receive treatment.[64] Attention to trigger factors (Table 4) may reduce migraine frequency by 50%.[65] Depression must be sought out and treated. Physicians also should focus on the lifestyles of the patients: a correlation of headaches with "daily hassles" has been documented.[66] Regular exercise and stress reduction (through biofeedback, meditation, and so on) help the patient become an active participant in the management of his or her headaches. Physicians should be aware that patients with daily rebound headache cannot be treated without the withdrawal of their medication. *Failure to identify all of these aspects often leads to what is known as a "drug-resistant headache."* (Table 9)

TABLE 9.—*Causes for Refractory Headaches*

Common
  Drug rebound headache (including caffeine-induced)
  Inadequate therapy:
    abortive (too little, too late; failing to use anti-emetics and polytherapy when needed)
    prophylactic (not allowing at least six weeks to determine efficacy or failing to use all appropriate agents)
  Lack of attention to trigger factors
  Lack of attention to depression and psychosocial factors
  Lack of a therapeutic physician-patient relationship
Uncommon
  (Structural causes for headache missed on CT scan)
    Chiari I malformation*
    Idiopathic intracranial hypertension with or without papilledema**
    Spontaneous intracranial hypotension**

* requires MRI for diagnosis
** requires lumbar puncture for diagnosis

TABLE 10.—*Prophylactic Medications for Headache*

Medication	*Therapeutic Range*	*Special Indications*	*Side Effects (SE)/ Contraindications (C)*
Beta-blockers: propranolol (Inderal) metoprolol (Lopressor) atenolol (Tenormin) nadolol (Corgard)	Determined by pulse, blood pressure, and tolerance	Migraine without tension-type headache; associated hypertension or angina	SE: fatigue, depression, impotence C: asthma; bradycardia; congestive heart failure; diabetes mellitus
Tricyclic Antidepressants: amitryptiline (Elavil); imipramine (Tofranil); nortryptiline (Pamelor)	10 mg–25 mg; increase as tolerated	Tension-type headache; migraine with tension-type headache; depression; sleep disturbances	SE: sedation, dry mouth, constipation, blurred vision, postural hypotension, cardiac arrhythmias; C: cardiac conduction abnormality, glaucoma, urinary retention
Divalproex sodium (Depakote)	500 mg–1500 mg per day	Migraine, tension-type headache, chronic daily headache	SE: nausea, vomiting, hair loss, tremor, weight gain, polycystic ovaries; C: liver disease
Calcium-channel blockers (Verapamil)	Determined by pulse, blood pressure, and tolerance	Prolonged aura; hemiplegic migraines; associated hypertension or angina	SE: constipation, fluid retention, bradycardia/ hypotension
NSAIDs	Naproxen 550 mg twice a day, and others	Relatively weak efficacy	See Table 3
Methysergide (Sansert)	1 mg per day; increase by 1 mg per day every three days; up to 8 mg per day, given three times a day	Limit to refractory migraine due to serious side effects; limit use to six months at a time, with two months off	SE: Retroperitoneal, cardiac, or pulmonary fibrosis; chest, abdominal, or limb pain from ischemia; nausea, sedation, dizziness, depression; C: arteriosclerosis; lung, renal, or liver disease; peptic ulcer disease; pregnancy
Phenelzine (Nardil)	15 mg three times a day, maximum 90 mg a day	Limit to refractory migraine due to risk of hypertensive crisis	SE: hypertensive crisis; orthostatic hypotension; central nervous system stimulant effects; gastrointestinal upset, constipation, urinary retention

Physicians should offer prophylactic medication if: severe attacks occur more than 2 to 3 times per month; attacks cannot be readily controlled with abortive medication; attacks occur after prolonged aura; or patients use daily symptomatic medication.[67] Prophylaxis reduces migraine frequency by 50% to 60%.[38]

Selecting which preventive agent to use is based on comorbid conditions and side effect profiles (Table 10 and Figure 1). First-line agents are tricyclic antidepressants and beta-blockers. Divalproex sodium is also effective but often poorly tolerated. Calcium-channel blockers and NSAIDs are less effective but may be used before giving drugs that have greater side effects. Third-line agents, methysergide and monoamine oxidase inhibitors, may be quite effective, but they require thorough knowledge of their use and side effects.

Many experts consider beta-blockers to be the drugs of choice for the prophylactic treatment of migraines.[36] A meta-analysis of 53 studies of 2403 migraineurs treat-

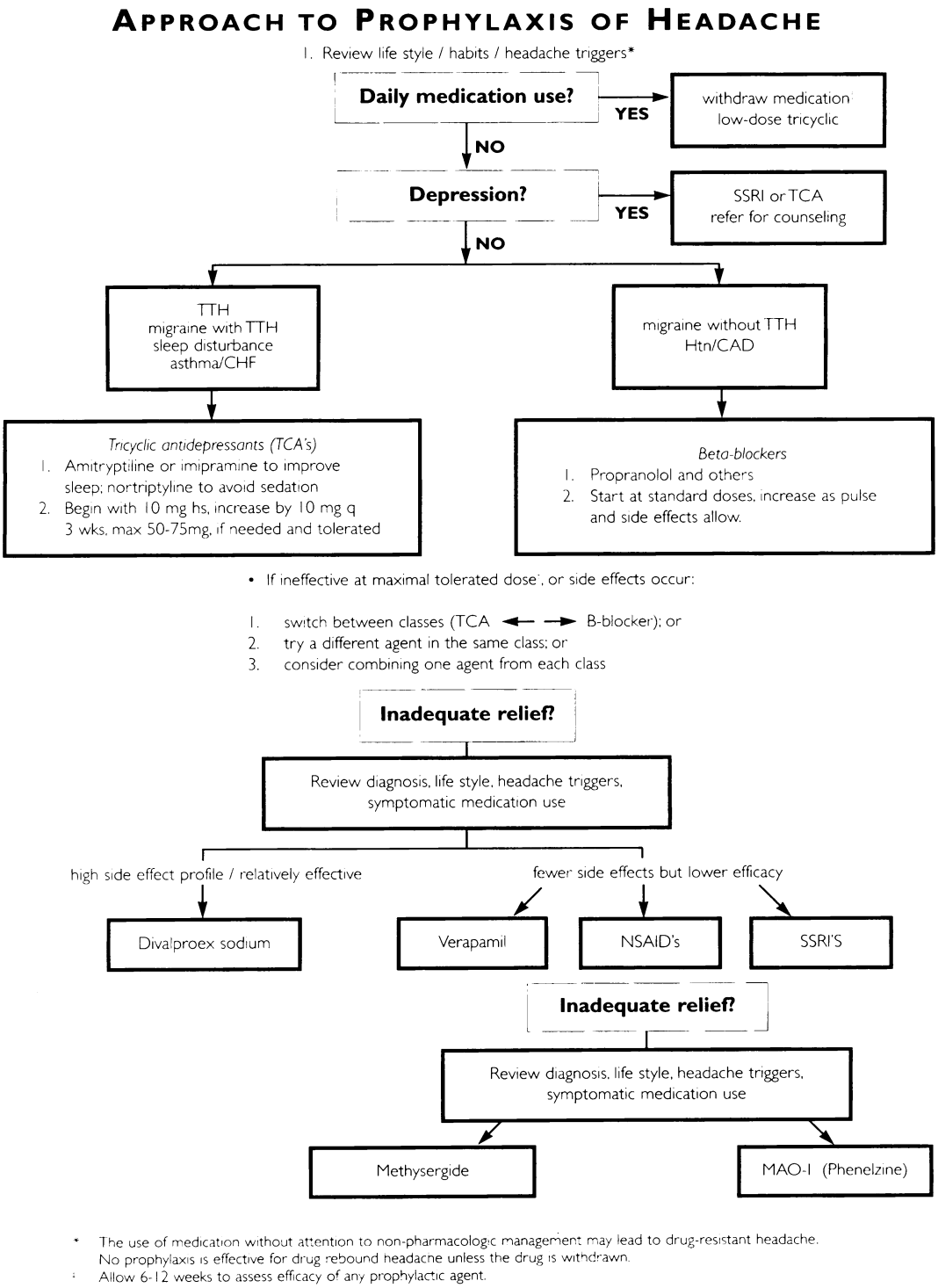

Figure 1.—This figure illustrates the approach to prophylaxis of headache.

ed with propranolol found about a 50% reduction in migraine activity (using an index of headache frequency and severity). There was little difference noted between using 120 mg or less a day or more than 160 mg a day.[68,69] Metoprolol, atenolol, nadolol, and timolol[68–77] all appear to be effective, with small differences among them. Patients may respond to one, although they did not to another.

TABLE 11.—*Guidelines for Neuroimaging of Headache*

Consider Imaging
1. Migraine associated with:
seizure disorder
neurologic signs or symptoms other than aura
2. Any headache associated with:
unexplained neurologic symptoms (including change in personality or cognition)
systemic symptoms (fever, weight loss, cough)
history of cancer
3. New onset of headache after age 50
4. Severe headache triggered by cough, coitus, or exertion
5. Any headache that cannot be confidently diagnosed as a "primary" benign headache
6. Sudden severe headache ("thunderclap headache")
7. Marked change from previously stable headache pattern
Imaging Not Necessary
Migraine, stable pattern
No Guidelines
Tension-type headache

Tricyclic antidepressants (TCAs) are the prophylactic drugs of choice for TTH[78] and are also effective in preventing migraines[79] independent of depression.[80] Amitryptiline significantly reduces the severity, frequency, and duration of migraine attacks.[81] Amitriptyline is effective within the first month,[79] whereas the effectiveness of beta-blockers has a much slower onset. Amitryptiline is the only TCA with established efficacy for migraines, although all TCAs are equally effective when used in other chronic pain conditions.[82] A sedating TCA (amitryptiline or imipramine) is appropriate for patients with sleep disturbance; nonsedating TCAs such as nortriptyline may be used otherwise. TCAs have been shown to be more effective at very low doses (10 mg to 25 mg) than at standard antidepressant doses.[83] Low doses will also minimize the common side effects of sluggishness upon awakening, dry mouth, constipation, and weight gain.

Selective setononin reuptake inhibitors, such as fluoxetine and paroxetine, are less effective for migraine than TCAs.[36] Selective setononin reuptake inhibitors should be considered for patients in whom depression is a significant contributor to the headache.

Divalproex sodium (Depakote) reduces the frequency of migraine attacks;[84,85] it may also be useful for CDH.[86] It is unclear if the efficacy of divalproex sodium is related to obtaining therapeutic drug levels. Side effects of nausea, weight gain, hair loss, and tremor limit its use. Fatal cases of hepatotoxicity have occurred in children under two, usually when receiving multiple medications. In adults, however, clinical monitoring may be more useful than monitoring liver function tests.[87] Recent studies of long-term use of divalproex sodium for seizures have shown the development of polycystic ovaries and elevated serum testosterone levels in women.[88]

Calcium-channel blockers, such as verapamil, show less demonstrated efficacy.[36,89] They may be useful for patients with prolonged aura or complicated migraine.[90]

Methysergide, a potent 5-HT_1 receptor agonist, should be reserved for truly refractory cases of migraine, because of the severe complication of retroperitoneal fibrosis. The monoamine oxidase inhibitor, phenelzine,[91] is similarly reserved because of its danger of hypertensive crisis triggered by tyramine-containing foods.

Is It a "Worrisome" Headache?

Both patients and physicians fear the possibility of headache as a symptom of brain tumor or hemorrhage. The "classic" brain tumor headache, which is worse in the morning, worse with Valsalva maneuvers, and associated with nausea and vomiting, is uncommon. Rather, *the brain tumor headache lacks diagnostic features*, is often mild and intermittent, and resembles a TTH.[92] In series of patients studied with modern neuroimaging, only 30%[93] to 50%[92] of brain tumor patients complained of headache. Instead, the initial presentation of brain tumors included focal signs or symptoms in 57% of patients, seizures in 9%, and isolated headache in only 8.2%.[93] All but one of the patients in the last group soon developed other neurologic symptoms or signs.

A review of the neuroimaging of 897 patients with migraines noted only four with abnormal scans (three tumors and one arteriovenous malformation).[94] Of these four, one tumor was incidental (the migraines continued after surgery) and two patients had seizure disorders. These findings led the American Academy of Neurology (AAN) to recommend that imaging is not warranted in patients with stable migraine who have no history of seizures and no neurologic signs or symp-

toms. Recommendations for imaging TTHs were not made because of insufficient evidence: case-finding rates varied from 2.4% in early studies to 0.4% in more recent studies.[95] Imaging guidelines are summarized in Table 11.

Unlike the dilemma of chronic headaches, the sudden onset of what a patient refers to as the "worst headache ever" is well recognized as a symptom of subarachnoid hemorrhage. However, only two-thirds of patients with a subarachnoid hemorrhage present with a headache;[96] neck pain and nausea are the other common symptoms. The accuracy of CT in finding such a hemorrhage is 92% on the first day, but falls to 58% by day 5.[97] Because CT detection is not 100% accurate, a patient should undergo lumbar puncture if CT results are negative for subarachnoid hemorrhage . Blood may not be evident in the cerebral spinal fluid for several hours after the hemorrhage, however, so a lumbar puncture should be timed appropriately. A warning, or "sentinel," headache preceded the hemorrhage by weeks or months in 15% to 95% of the patients questioned in various series.[98]

Some patients with a sudden, severe headache—called a "thunderclap headache"—and normal CT and lumbar punctures have been found through angiography to have an aneurysm.[99] A prospective series of 71 patients experiencing thunderclap headache followed for a mean of 3.3 years found no instance of ruptured aneurysm.[100] Because the true incidence of unruptured aneurysm in patients with thunderclap headache is unknown, however, one panel of experts recommends magnetic resonance angiography be performed on all patients meeting these criteria.[101]

Lumbar puncture should also be considered (after imaging studies have ruled out a mass) to diagnose the following: refractory CDH with increased intracranial pressure (with or without papilledema); spontaneous intracranial hypotension; and subacute headache of fungal, viral, or carcinomatous meningitis.[102]

Conclusion

Every presentation of headache requires care to exclude organic disease, and every presentation provides the opportunity to relieve suffering. No symptom more than headache gives a physician the chance to regain the time-honored role of "healer." A primary care physician who understands his or her patient is ideally suited to be a "headache expert."

Dedication

This article is dedicated to the memory of Rasoul Soudmand, MD, whose gentle soul embodied the ideals of the neurologist while always remaining a compassionate human being.

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