Section 1

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Introduction

Headache is a nearly universal symptom. Migraine and other headaches can be highly disabling, and impose a significant burden, both in economic terms and in personal suffering. For migraine alone, missed workdays and disability at work have been estimated to cost American employers approximately $13 billion per year (Hu et al). Head pain is a common complaint by patients presenting to physicians’ offices and emergency departments (Barton). The characteristics and treatment of the primary headaches disorders including migraine, tension-type, and cluster will be discussed, as well as secondary headache disorders (including benign-appearing recurrent headache due to underlying disease). The recognition and treatment of chronic daily headache and its relationship to medication overuse will also be addressed.

Clinical Symptoms And Signs: Approach To The Patient

To properly diagnose a patient presenting with headache it is necessary to take a careful history and examine the patient. The history should include the date of onset, duration and timing of the headache attacks, as well as the frequency, severity, duration of pain episodes, triggers, quality of the pain, factors increasing and decreasing the pain, previous and current medications (including over-the-counter remedies), social history and family history. History of trauma, other medical conditions, and a psychiatric history should be obtained. A careful and complete history is important in earning the patient’s confidence and in establishing the correct diagnosis. A complete medical and neurologic examination, based on clues from the history or other physical findings, should
be performed on every patient complaining of headache. Head and neck examination is particularly important. The results of this evaluation will dictate the physician’s choice of additional investigations.

Neuroimaging (CT scanning or MRI), blood work, lumbar puncture, angiography, etc., are necessary when a secondary cause of headache is suspected. Testing is generally not indicated when history and examination are strongly consistent with a primary (benign) headache disorder. When neuroimaging is suggested by history or examination (see Table 6-1—“Red Flags” in Headache), MRI is usually superior to CT, although CT scanning is best when acute intracerebral or subarachnoid hemorrhage is suspected. Lumbar puncture is appropriate in three settings: 1) suspicion of meningitis or encephalitis, 2) suspicion of subarachnoid hemorrhage or 3) suspicion of high or low intracranial pressure. Prior to LP, neuroimaging to rule out intracranial mass is usually necessary.

Table 6-1—“Red Flags”—Clues to diagnosing secondary causes of headache

- Sudden onset
- Progressive worsening
- Constant pain
- Change in pattern
- Effort-induced pain
- Positional pain
- Onset in middle age or later
- Recent head trauma
- Setting of chronic illness (e.g., cancer, AIDS)
- Fever, abnormal vital signs
- Any neck stiffness
- Change in personality or behavior
- Neurologic findings on examination

Secondary Headaches

Secondary headaches include those headaches resulting from known structural or pathologic causes. Some can be exceedingly difficult to sort out from primary causes such as migraine and tension-type headache. The following case report is presented to stimulate thinking about secondary headaches that may mimic primary headache disorders.

Case Report (Part 1)

Case 6-1. A 20-year-old man came to the office complaining of pain over his forehead and into the left orbit. He rated the severity of his pain as a 10/10. He was previously seen in another office where he was diagnosed with tension-type headache and given acetaminophen/caffeine/butalbital (Fioricet®), resulting in mild relief. He had continued pain. He had been given 28 Fioricet®, of which only seven remained after 20 hours. He complained of nausea and had vomited once at home. He denied photophobia, fever, ear or abdominal pain.

He has a history of asthma and had had an upper respiratory tract infection about two weeks prior to his presentation with stuffy nose, cough and tearing eyes. He had been coughing green-brownish material for the three days. Medications included albuterol (Proventil®) and acetaminophen (Tylenol®). On examination he had equal pupils that were round and reactive to light without tearing, injection or nystagmus. He was able to read and count fingers in both visual fields. His fundi showed what was thought to be early papilledema. He had marked tenderness on palpation of his left frontal sinus and was non-tender to
palpation over the other sinuses. He had a non-focal neurological examination. His initial temperature was 100.4° orally and vital signs were stable. A stat head CT scan without contrast was arranged and read as normal.

The course and workup of this patient will be discussed later. This case illustrates the potential hazard of diagnosing a primary headache disorder too soon as will be seen later.

Because of a number of shared clinical features among the many causes of headaches, diagnostic problems may occur. These problems may be grouped into four categories and are reviewed below (Mathew, 1994).

1. **Organic conditions presenting with acute headache that may cause difficulty in diagnosis.**

   Clues to diagnosing secondary (threatening) headaches include: new, worsening, or constant headaches, sudden onset of headache, a deficit on neurological examination (including abnormal mental status), abnormal vital signs, a history of trauma, older age, or a history of drug abuse or systemic illness.

   - Intracranial aneurysms
   - Unruptured—“sentinel headache,” “thunderclap headache”
   - Ruptured
     - Cerebral venous thrombosis
     - Encephalitis (e.g. herpes simplex encephalitis)
     - Carotid artery dissection, vertebral artery dissection
     - Cerebral venous thrombosis

Subarachnoid hemorrhage (SAH) from ruptured intracranial aneurysm is usually a dramatic clinical presentation. Some individuals collapse and expire immediately. Survivors generally have an explosive, severe headache with nausea and/or vomiting. Seizures may occur, as can stupor or coma. On examination, stiff neck (Brudzinski and Kernig signs), hypertension, and subhyaloid ( preretinal) hemorrhages may be found, as well as focal neurologic deficits. Work-up proceeds promptly to a CT scan, which if negative (CT misses 10–15 percent SAH) is followed by a lumbar puncture. If SAH is confirmed, a 4-vessel cerebral angiogram is performed (up to 20 percent of aneurysms are multiple). CT angiography in some centers is nearly as sensitive. Neurosurgical consultation is required.

Up to 5 percent of the general population harbors asymptomatic intracranial aneurysms. Unruptured intracranial aneurysms may cause headache due to sudden expansion or thrombosis within the aneurysm. If sufficient clinical suspicion is present, magnetic resonance angiography (MRA) or CT angiography may be performed, or even conventional angiography.

Patients with encephalitis or meningitis usually have fever (unless on antipyretics or steroids), and stiff neck. (However, with patients in a deep coma, stiff neck may not be present). Headache is common, and focal neurologic deficits may develop. Seizures may occur, possibly followed by stupor and coma. CT scan or MRI is usually performed to rule out an abscess or other mass lesion, followed by a lumbar puncture.
Herpes simplex encephalitis, a progressive necrotizing encephalitis with a predilection for the temporal and frontal lobes, presents with fever and cognitive changes. Headache is common. MRI is positive early in some cases; polymerase chain reaction on CSF may be diagnostic. Treatment with acyclovir is initiated as soon as the diagnosis is suspected to try to limit the degree of brain damage. Neurologic and infectious disease consultation is appropriate.

Dissection of the carotid or vertebral arteries may occur spontaneously, or in the setting of trauma or underlying vascular disease. Symptoms include neck pain, headache, and neurologic deficits in the distribution of the involved blood vessel. The dissection may be revealed by ultrasound, MR angiography, CT angiography, or conventional angiography.

Cerebral venous thrombosis (CVT) may be present with headaches, seizures, paraparesis (cortical parasagittal leg area), or other focal neurologic deficits. Predisposing conditions include pregnancy (or the immediate post-partum period), dehydration, cancer, coagulation disorders, or trauma. CVT is often missed with conventional neuroimaging. MR angiography is generally very sensitive.

2. Organic conditions associated with recurrent headaches mimicking primary headache disorders

- Symptomatic cluster headaches
- Posterior fossa brain tumor
- Arteriovenous malformation
- Cough and exertional headache due to intracranial lesion (generally posterior fossa)
- Antiphospholipid antibody syndrome
- Isolated CNS vasculitis
- Pheochromocytoma

The pain of cluster headache is so severe that many patients feel certain there must be an underlying mass lesion. Imaging is generally normal. However, symptomatic cluster headache may be due to a lesion in or near the cavernous sinus. The duration of the pain attacks may become progressively shorter, and a fixed neurologic deficit may appear.

Cough headache is usually a sudden head pain triggered by coughing or other Valsalva maneuvers. The headache is sudden in onset and severe, but brief (seconds or minutes). It may be followed by a longer duration posterior or holocranial dull ache. Perhaps 10–20 percent are due to a posterior fossa lesion such as a Chiari malformation. MRI is indicated as part of the evaluation. (CT is a poor choice as it is less sensitive for lesions in the posterior fossa due to bony artifact). If imaging is negative, treatment with indomethacin is usually dramatically effective. Lumbar puncture may also be therapeutic (Raskin, 1995).

Sex may trigger headaches in several ways. First and most disturbing is the sudden onset “explosive” or “orgasmic” headache which mimics and must be differentiated from SAH. CT, LP, even angiography, may be required. Secondly, the “pre-orgasmic” muscle contraction type
headache may be precipitated (gradual onset, without nausea or vomiting). Both of these are considered primary headaches as causes have not been identified. Lastly, a postural headache may follow intercourse, presumably due to a nerve root sleeve or other dural tear with CSF leakage. The headache is relieved by recumbency and aggravated by standing, as is typical for “low-pressure” headaches such as the post-LP headache.

Antiphospholipid antibodies (the lupus anticoagulant, anticardiolipin antibodies, antiphosphatidylserine antibody) may occasionally be associated with migraine with prolonged (1 hour) aura or migrainous infarction. A previous history of recurrent miscarriages or venous thrombosis should arouse suspicion. An elevated partial thromboplastin time (PTT) on routine coagulation testing and a false positive VDRL may provide a clue to their presence.

CNS vasculitis may be present with headaches, seizures, and focal neurologic deficits. Laboratory parameters consistent with collagen vascular diseases may be present, but may be absent if disease is confined to the CNS (a privileged area). Imaging may reveal strokes; CSF may contain red and white cells, and rising protein. Angiography may demonstrate beading of blood vessels, segmental narrowing or occlusions. Occasionally meningeal biopsy is performed. Rheumatologic, neurologic, and neurosurgical consultation may be necessary.

Mild essential hypertension is typically not associated with headache. Severe paroxysmal elevations of blood pressure, as occurs with pheochromocytoma or the tyramine reaction in patients on MAO inhibitors, is associated with headache. The headache of pheochromocytoma is generally paroxysmal—sudden, but brief (less than one-hour duration). Dramatic elevations of blood pressure, with tremor and diaphoresis occur. The headache is often holocranial, pounding, and nausea/vomiting may be present. A 24-hour urine evaluation for products of the tumor (VMA, metanephrines) is diagnostic.

3. **Organic conditions associated with chronic persistent headache or facial pain, often without abnormal physical findings**
   - Arnold-Chiari Malformation-Type 1
   - Idiopathic intracranial hypertension (pseudotumor cerebri) without papilledema
   - Temporomandibular joint (TMJ) dysfunction
   - Giant Cell Arteritis (temporal arteritis)

Arnold-Chiari Malformation-Type 1 (without other malformations) can produce a secondary cough headache or more non-descript aching head pain. Patients may eventually develop diplopia, vertigo, ataxia from brainstem compression, but this is unusual.

Idiopathic intracranial hypertension (IIH, “pseudotumor cerebri”) typically presents with headache and signs of increased intracranial pressure such as papilledema. However, some patients do not exhibit papilledema, and diagnosis hinges then on finding increased opening pressure on lumbar puncture.
Temporomandibular joint dysfunction (TMD) may produce headache, but jaw pain radiating to the ear is generally noted. Clues include “popping” and clicking” at the joint, increased pain on use (chewing, talking, laughing), and limitation of jaw opening (less than 30 mm). TMD usually responds to physical measures such as physical therapy, heat, and massage. Non-steroidal anti-inflammatory medications are of use as well. Surgery is usually best avoided.

Giant cell arteritis (“temporal arteritis”) is usually manifested as temporal pain, often constant, sometimes with jaw claudication (increased pain with jaw use). The scalp and superficial temporal arteries may be tender. Most patients are over 50 years old and have an ESR over 50 mm/hr. Untreated, this disease carries a significant risk of blindness and stroke. If the diagnosis is suspected, prednisone is started immediately (60–80 mg per day initially), the patient is then sent for temporal artery biopsy (due to patchy involvement, a substantial length of vessel needs to be obtained. If one side is negative, the opposite side should be considered for biopsy).

4. Intracranial pathology occurring in a patient with established primary headache
   • Brain tumor
   • Brain Abscess
   • Subdural hematoma

Carrying the diagnosis of a primary headache type, such as migraine, in no way prevents a patient from developing a second type of headache. Brain tumors certainly can occur in patients who also have primary headache disorders. Therefore, if a patient with an established headache disorder develops new or progressive signs or symptoms, or becomes refractory to previously effective therapy, the possibility of the presence of a secondary headache should be considered.

Case Report (Part 2)
Case 6.1 (continued). Examination of the patient’s CSF showed 3 mononuclear cells with protein 22, glucose 77, and later, negative cultures. His blood WBC was 15,000. Later in the evening, after the results of the brain CT became available, he was diagnosed as having migraine or cluster headache. The next morning his temperature reached 102.5° (rectal) and he complained of chills. Subsequently his temperature rose to 104.1° (oral) with normal vital signs. His left eyelid and conjunctiva became swollen, with tenderness to percussion over the left frontal sinus.

He was admitted and treated with nafcillin 2 grams and cefuroxime 1.5 grams, intravenously. Acetaminophen and ibuprofen were prescribed for his pain. Repeat CT scan of the brain this time with additional views of the paranasal sinuses showed fluid collections in both maxillary and ethmoid sinuses, as well as the left frontal and sphenoid sinuses. He underwent bilateral intranasal antrostomies, a left intranasal ethmoidectomy and a left sphenoidotomy. Subsequently his WBC normalized and he did well, with complete resolution of headache.

This case illustrates the potential hazard of diagnosing primary headache disorder too soon. Over 100 secondary causes of headache are possible, many
of which may mimic primary headache (Levin 2002). **Table 6-2** lists the most commonly encountered causes.

**Table 6-2—Differential diagnosis of secondary causes of headache**

<table>
<thead>
<tr>
<th>Category</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vascular</strong></td>
<td>Subarachnoid hemorrhage&lt;br&gt;Arteriovenous malformation&lt;br&gt;Cerebral venous thrombosis</td>
</tr>
<tr>
<td><strong>Infectious</strong></td>
<td>Meningitis—bacterial, viral, fungal, protozoal, Lyme disease, syphilis&lt;br&gt;Encephalitis&lt;br&gt;HIV infection&lt;br&gt;Subdural empyema&lt;br&gt;Brain abscess&lt;br&gt;Sinusitis&lt;br&gt;Dental abscess</td>
</tr>
<tr>
<td><strong>Trauma</strong></td>
<td>Subdural hematoma&lt;br&gt;Intracerebral hematoma&lt;br&gt;Carotid or vertebral dissection&lt;br&gt;Post-concussive syndrome&lt;br&gt;Occipital or supraorbital neuralgia&lt;br&gt;Dural leak—low pressure syndrome</td>
</tr>
<tr>
<td><strong>Autoimmune</strong></td>
<td>Vasculitis affecting CNS&lt;br&gt;Giant cell arteritis&lt;br&gt;SLE</td>
</tr>
<tr>
<td><strong>Metabolic/Toxic</strong></td>
<td>Thyroid disease&lt;br&gt;Pheochromocytoma&lt;br&gt;Drug intoxication or adverse effect&lt;br&gt;Hyperparathyroidism&lt;br&gt;Oxygen abnormalities—COPD, sleep apnea, altitude sickness&lt;br&gt;Carbon monoxide toxicity&lt;br&gt;Anemia</td>
</tr>
<tr>
<td><strong>Idiopathic</strong></td>
<td>Trigeminal neuralgia&lt;br&gt;Benign intracranial hypertension (pseudotumor cerebri)</td>
</tr>
<tr>
<td><strong>Neoplastic</strong></td>
<td>Glioma&lt;br&gt;Meningioma&lt;br&gt;Pituitary region mass&lt;br&gt;Cerebellopontine angle tumor (e.g. acoustic neuroma)&lt;br&gt;Lymphoma&lt;br&gt;Metastatic tumor of brain, skull, meninges</td>
</tr>
<tr>
<td><strong>Structural, Psychiatric</strong></td>
<td>Depression, Anxiety&lt;br&gt;Hydrocephalus&lt;br&gt;Chiari malformation&lt;br&gt;Upper cervical spine disease&lt;br&gt;Epilepsy</td>
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Diagnosis And Management Of Primary Headaches

International Headache Society diagnostic criteria are now used to classify and diagnose headache (IHS Headache Classification Committee). We will discuss the major primary headache disorders (migraine and tension-type) and their management. Patients often complain about headaches when they interfere with their routine—our goal is to keep this interference to a minimum.

Migraine

Migraine is a common problem, affecting approximately 6 percent of children, 6 percent of men, and 18 percent of women (Stewart). It is an episodic headache that is often a unilateral throbbing pain associated with photophobia, phonophobia, nausea and vomiting. It is made worse by exertion. If there are neurological symptoms associated with the headache it is called “migraine with aura” (IHS1.2; old term: “classic migraine”), without these symptoms it is known as “migraine without aura” (IHS 1.1; old term: “common migraine”).

The object of therapy is to ameliorate or terminate patients’ migraine attacks, and when necessary, to reduce the frequency and severity of attacks via behavioral treatment, lifestyle changes, and preventative pharmacotherapy. Migraine is often precipitated by various triggers (i.e., foods, menses, sun glare, missing a meal, stress, sleep deprivation, etc.). Therapy begins with identification and modification or avoidance of these triggers when possible.

It is also important to be sure other medications are not contributing to headache causation. A number of medications and substances have the potential to directly cause headaches in some patients (see Table 6-3). Additionally, the overuse of symptomatic medication such as analgesics can transform migraine into a chronic daily headache. This is termed analgesic rebound or medication overuse headache (MOH) and is a significant problem in headache management. The mechanism of MOH is not well understood, but most, if not all, medications used for acute relief of migraine can lead to increased frequency of headaches in susceptible individuals. The frequency of analgesic use necessary to cause MOH seems to vary with respect to medication type and individuals, but restricting acute treatment to twice weekly is generally sufficient to prevent this phenomenon.

When MOH does occur, prophylactic medication is ineffective and the offending medications must be stopped. Preventive pharmacotherapy is thus usually appropriate when patients need to use acute headache medications more than 2 days per week, if the headaches do not respond to abortive medications, (perhaps resulting in visits to the emergency room), or if the patient has had complicated migraine (a prolonged neurologic deficit, or migrainous infarction).
Prophylactic Treatment

Prophylactic therapy is initiated to reduce the frequency, duration, and severity of migraine attacks. Fortunately, a number of good choices exist. Patients in the childbearing years requiring preventative treatment generally should be using an effective form of contraception. However, oral contraceptives may not be appropriate for some migraine patients.

It generally takes two to three months to ascertain a medication’s preventative effect. Ideally, therapy starts with the lowest dose which is increased slowly until headache control is achieved or unacceptable side effects are encountered. (“start low, go slow”). After the headaches are controlled for six months or more the medication may be gradually decreased and stopped, as tolerated. Preventative migraine therapy choice should be guided by co-morbid/co-existent conditions such as mitral valve prolapse, Raynaud’s phenomenon, epilepsy or, depression, since one can often choose a drug that might help both headache as well as a coexistent condition. In addition, it is essential to avoid medications which might exacerbate a coexisting illness.

The major classes of prophylactic drugs include beta-blockers, anticonvulsants, calcium channel drugs, and heterocyclic antidepressants. There are also several miscellaneous drugs, which are sometimes useful (Ward, 2000).

### Antidepressant

**Amitriptyline, Nortriptyline, Doxepin**

Many patients with migraine have co-morbid depression. If sleep disturbance is prominent, consider using a heterocyclic antidepressant. Amitriptyline (Elavil®, others) has the most support in the literature. Its effect on migraine is separate from its effect on depression. Its mechanism of action may be through modulation of serotonergic and noradrenergic pathways. Start patients on a 10 mg or 25 mg bedtime dose and increase the dose slowly to achieve headache control. Doses of 150 mg or less are generally employed. Side effects include weight gain, dry mouth, cardiac arrhythmias, urinary retention, blurred vision, and constipation. The medication should be avoided in patients with untreated glaucoma and prostatic hypertrophy. The dry mouth side effect can be managed by using hard sugarless candies or with pilocarpine (Salagen®) 5–10 mg tid.

Nortriptyline (Pamelor®, others) may be tried if the side effects of amitriptyline are unacceptable. It causes less drowsiness. Again, the initial dose is generally 10–25 mg HS, but as it is also available in a liquid formulation, even lower doses can be employed if necessary. Doxepin (Sinequan®) is another potential
option, and is also available in a liquid form. Heterocyclic antidepressants are contraindicated in patients with cardiac arrhythmia, narrow angle glaucoma, prostatism, and uncontrolled seizures (Saper).

Antidepressants exemplify the fact that medications within the same pharmacologic group produce various side effects that are more, or less, acceptable to each individual patient. If one agent is poorly tolerated, consider either a lower dose or a trial of another agent in the same family.

Beta-Adrenergic Antagonist Drugs
Propranolol, Timolol, Metoprolol, Nadolol, Atenolol

The beta-blockers are widely used for the prevention of migraine. They were discovered to have an effect serendipitously, and are postulated to work via an effect on 5-HT2 receptors, preventing the generation of nitric oxide. Propranolol (Inderal®) and timolol (Blocadren®) have FDA indications for migraine prevention. Propranolol is often the first choice and is used in doses ranging from 40–320 mg daily, in divided doses. It is also available in several extended-release forms that can be given once or twice daily. Nadolol (Corgard®) can be given once daily, as can atenolol (Tenormin®). Side effects are common and include hypotension, bradycardia, fatigue, weight loss, and bronchospasm (Welch).

This class of medications is contraindicated in patients with asthma, diabetes, Raynaud's phenomenon, depression, and sometimes heart failure. Some authorities avoid beta-blockers in migraine with aura.

Calcium-Channel Blocking Drugs
Verapamil, Diltiazem, Amlodipine

This class of drugs is especially useful in those migraineurs suffering from Raynaud's. Verapamil (Calan®, Isoptin®, others) is the best studied. Like other preventative agents, benefit may not become apparent for weeks to months (Welch). Verapamil is usually started at doses of 80 mg twice or three times a day. It may be increased to 480 mg per day as tolerated. There are sustained-release formulations (Calan SR®, others) that may be used once or twice daily, to enhance compliance. Common side effects include constipation, hypotension, and pedal edema. The vasodilation associated with some drugs in this category (particularly nifedipine [Procardia®]) occasionally causes a migraine-like headache.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

Naproxen, Naproxen Sodium

These drugs have a role in both acute and preventative migraine therapy (see below). Naproxen (Naprosyn®) has been demonstrated to be an effective prophylactic in clinical trials. It decreases the intensity and duration of headache, nausea, vomiting, and other analgesic use. It may be particularly useful for predictable menstrually-associated migraine attacks. The initial dose is 550mg naproxen sodium (Anaprox DS®) BID beginning two days prior to the expected onset of headache and continued through the usual time of headache susceptibility (Raskin, 1988). Patients may be switched to another NSAID to find the most effective and tolerable relief.

Aspirin

Aspirin is useful in migraine prophylaxis (Welch). A single 325 mg dose daily
may reduce the frequency of migraine attacks. Side effects of aspirin and other NSAIDs are well known and include dyspepsia, gastritis, and GI hemorrhage. These side effects can be ameliorated with concurrent treatment with misoprostol (Cytotec®). It is given as 200 mcg tablets 4 times a day, with meals. The dose may be reduced if necessary to 100 mcg 4 times a day.

**Anticonvulsants**

*Valproic Acid, Gabapentin, Topiramate.*

Migraine is known to be co-morbid with epilepsy. Valproic acid (Depakote®, others) has an FDA indication for migraine prevention. It is usually administered as the enteric-coated formulation, Depakote® with superior GI tolerability. The initial dosage is usually 250 mg BID. After 6–8 weeks, the dose may be increased to 500 mg BID, and eventually to 750 mg BID. A once-a-day formulation is available. The most important parameter to monitor is headache control. Blood levels do not correlate with clinical effect. Side effects include GI irritation, tremor, hair loss, weight gain, and hepatic dysfunction. Pancreatitis occurs rarely. Spina bifida may occur during pregnancies in fetuses exposed to valproic acid.

Gabapentin (Neurontin®) has been reported to have efficacy in selected migraine patients (Ward, 2000). It is not hepatically-metabolized and has little potential for drug interaction. Adverse effects do include cognitive impairment in some patients. Dosing typically begins at 300 mg tid, and may be slowly raised as high as 1200 mg tid.

Topiramate (Topamax®) has been shown in randomized controlled trials to be effective in preventing migraine (Brandes, Silberstein). Adverse effects include metabolic acidosis and paresthesias as well as occasional sedation and cognitive dysfunction. This drug is a weak carbonic anhydrase inhibitor, and therefore should not be given to patients with a history of renal stones. Higher doses are often associated with significant sedation. It is actually associated with weight loss, which may be of benefit to some migraineurs. For migraine prevention, dosing is begun at 15–25 mg at HS, and slowly raised to as high as 100 mg BID.

Lamotrigine (Lamictal®) seems promising as migraine prophylaxis. But adverse effects include severe skin rash.

**Miscellaneous Headache Preventive Agents**

*Methysergide, Cyproheptadine*

Numerous other drugs have been used as for migraine prophylaxis, with variable success, and often limited support in the literature. Methysergide (Sansert®) has an FDA indication for migraine prevention. It is highly and rapidly effective, but its use is limited by rare but serious side effects including retroperitoneal, cardiac valvular, and pulmonary fibrosis. Therefore it cannot be given for longer than 6 months without a “drug holiday” of at least one month. Other side effects are related to vasoconstriction and include: chest pain, abdominal pain, cold numb painful extremities with or without paresthesiae, and diminished or absent pulses. These effects usually regress when the medication is stopped. Nausea and vomiting may also occur. The medication may make patients feel strange (chemically similar to LSD), especially at the initiation of therapy. The 2 mg tablet is started once daily for 3–4 days, then increased slowly to tid or qid. Methysergide is often useful for intractable episodic cluster headache. It is no longer available in the US but is available in Canada.
Cyproheptadine (Periactin®) is an agent with anti-serotonergic, antihistamine, and calcium channel blocking properties. It has been advocated particularly as a preventative agent for children with migraine. The usual starting dose is 2 mg (1/2 a 4 mg tablet) twice or thrice daily. The dose may be increased slowly, usually to 4 mg twice or three times daily. It is available as syrup as well, enabling lower dosage titration. Side effects include sedation and weight gain.

Symptomatic Migraine Treatment

Simple Analgesics

Aspirin, Acetaminophen, Combinations

Both aspirin and acetaminophen are superior to placebo in decreasing migraine pain (Welch). Aspirin is the most commonly used non-prescription analgesic selected by patients for the management of headache pain. An initial dose of 975–1000 mg is recommended at the onset of the attack. Subsequent doses of 650–1000 mg every 4 hours may be given as needed (maximum 4–6 grams in a 24-hour period). Buffered and effervescent forms of aspirin may reduce gastric irritation. Delayed absorption with enteric-coated aspirin precludes the use of this product in acute pain management. Aspirin is also available for rectal administration. It has been used intravenously with good results (Welch) but is only available outside of the USA.

Acetaminophen is a non-prescription alternative in patients who cannot tolerate aspirin. Several pain models demonstrate the equivalent analgesic efficacy of aspirin and acetaminophen on a milligram to milligram basis. A study in patients with tension and tension-vascular headaches observed no difference between 1000 mg acetaminophen and 650 mg aspirin in relieving headache pain.

Gastric stasis may occur during a migraine attack and impedes the absorption of medications, such as aspirin and acetaminophen. Concomitant administration of metoclopramide (Reglan®) significantly increases serum concentrations of both these agents, by increasing gastrointestinal motility. (Volans). Oral medications may be limited in their utility by their incomplete absorption and the frequent vomiting accompanying migraine. The use of the rectal route of administration is available for aspirin and acetaminophen. Codeine and other drugs may also be prepared in this fashion by pharmacists (Ward). Dependence can occur in patients who use these products uninterrupted for 48 hours or more.

Aspirin and acetaminophen are commonly combined with caffeine and/or butalbital to enhance analgesic activity and are sold as Fiorinal®, Esgic® and Fioricet® (with acetaminophen). This combination works for many patients with headache, but is very prone to cause medication overuse headache. When this occurs, it is important to detoxify these patients from all rebound-producing medications, including simple analgesics, when using excessive quantities (e.g., more than two days a week).

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Naproxen Sodium, Ketorolac

Nonsteroidal anti-inflammatory drugs (NSAID) may be considered good choices in first line abortive therapy of migraines, due to their effectiveness and lack of a dependency cycle. Naproxen (Naprosyn®) is the most frequently studied NSAID for the treatment of migraine. Naproxen and naproxen sodium (Anaprox/Anaprox DS®) achieve peak plasma concentrations after 2 and 1 hour,
respectively. Naproxen sodium is preferred for abortive therapy because onset of analgesic activity corresponds with its earlier peak plasma concentration.

Ketorolac (Toradol®), the first parenteral NSAID available in the United States, is effective in the treatment of migraine. However, relief from pain and disability with I.M. ketorolac are significantly less than the combination of IV DHE 45® and metoclopramide. Ketorolac may also be administered intravenously.

Other NSAIDs found to be effective in the treatment of migraine include diclofenac sodium, flufenamic acid, flurbiprofen, ibuprofen and mefenamic acid (See Table 6-4). The most common adverse effect with all NSAIDs is dyspepsia.

**Table 6-4 — Dosing Guidelines For NSAIDs For Treating Migraine**

- Naproxen sodium (Anaprox®) 550 mg–850 mg BID
- Diclofenac sodium (Voltaren®) 50–100 mg in 2 divided doses
- Flufenamic acid Not available in the United States
- Flurbiprofen (Ansaid®) 300 mg in 2–4 divided doses
- Ibuprofen (Motrin®, Advil®) 600–800 mg TID
- Indomethacin (Indocin®) 25–50 mg TID
- Mefenamic acid (Ponstel®) 500 mg, then 250 mg every 6 hours
- Toltenamic Acid Not available in the United States

**Antiemetics**

**Metoclopramide, Chlorpromazine, Prochlorperazine, Promethazine**

Antiemetics are useful in the management of disabling nausea and vomiting frequently associated with migraine headaches. In addition to antiemetics properties, metoclopramide (Reglan®) can also reverse the gastric stasis accompanying migraine attacks. Metoclopramide enhances the effectiveness of analgesics such as aspirin, acetaminophen, naproxen as well as ergotamine in migraine by improving absorption (Raskin, 1988). It should be used sparingly as it may cause dystonia and akathisia, especially in adolescents (Welch). Keeping the dose below 30 mg per day decreases the chance such a reaction will occur. Patients should be warned of the potential dystonic reaction and have 25 mg of diphenhydramine (Benadryl®) available. Administration of a narcotic analgesic (e.g., meperidine-Demerol®) or anticholinergic agents may antagonize increased gastrointestinal motility produced by metoclopramide

Recent studies suggest that some antiemetics may be useful as single agents in the treatment of migraine attacks. Controlled studies have shown intravenous chlorpromazine (Thorazine®) 0.1 mg/kg and prochlorperazine (Compazine®) 10 mg effectively terminate migraine attacks (Lane/Jones cited in Raskin 1988) Chlorpromazine may be useful when treating migraine with intravenous dihydroergotamine (DHE-45®) (Welch). Chlorpromazine and prochlorperazine may cause tardive dyskinesia that occasionally is irreversible. Promethazine (Phenergan®) suppositories (12.5 mg–25 mg–50 mg) are effective in treating nausea and vomiting, with little likelihood of dystonia.

**Isometheptene**

Isometheptene (Midrin®) is suitable for patients to try for mild to moderate
migraine attacks. Midrin® contains isometheptene in combination with dichloralphenazone (a sedative) and 325 mg of acetaminophen. It is generally well-tolerated. Adverse reactions are unusual. Isometheptene is a vasoconstrictor possessing antispasmodic activity. It was more effective in treating mild to moderately severe migraine in a placebo-controlled trial (Raskin 1988). In a comparative trial, no difference in headache duration was observed between Midrin® and ergotamine/caffeine (Cafergot®). However, the incidence of nausea and vomiting was significantly lower with Midrin® (6.5 percent versus 24.6 percent). The recommended dose for Midrin® is 2 capsules at the onset of the attack, followed by 1 capsule every hour as needed, up to a maximum of 5 capsules per 12 hours.

Ergot Preparations

Ergotamine Tartrate, Dihydroergotamine

Ergotamine tartrate was a very important medication for symptomatic treatment of migraine. It is available in oral, rectal, and sometimes sublingual forms. Availability of some of these formulations has been intermittent. Dihydroergotamine (DHE-45®) is the only parenteral ergot available. The absorption rates of ergotamine are variable, depending on the route of administration. Caffeine enhances ergotamine’s absorption. Metoclopramide is likely to improve absorption of oral ergotamine (Welch). Parenteral treatment is most effective; rectal ergotamine achieves higher serum levels than the oral route. Therapeutic responses will, of course, vary among different patients and route and dose of medication.

Oral ergotamine (Cafergot®, Wigraine®, and others) is given initially as two 1 mg tablets followed by one tablet every 30 minutes until relief occurs. The dose is limited to 6 tablets daily and 10 tablets weekly. Nausea and vomiting are common side effects of the medication. Metoclopramide can be used to help control the nausea and vomiting associated with ergotamine.

Rectal ergotamine (Cafergot® or Wigraine®) is available in 2 mg suppositories. It is useful to take one-quarter to one-half of a suppository initially, followed by one-quarter every 30 minutes as needed to a maximum daily dose of two suppositories or 4 mg.

Gradual overuse of oral or rectal ergotamine may lead to dependency and the development of ergotamine headache. The patient develops a rebound or withdrawal ergotamine headache that is successfully treated with another dose of the drug. The total daily dose may slowly increase over years transforming a migraine headache into a chronic daily headache (Mathew, 1993). Other side effects include nausea, vomiting, abdominal pain, diarrhea, muscle cramps, paresthesias of the extremities, vasoconstriction and loss of pulses, and angina.

Dihydroergotamine (DHE-45®) is effective in aborting migraine, and is more effective than meperidine plus hydroxyzine and butorphanol (Raskin, 1986) (Silberstein, 1990) (Welch). Up to 90 percent of migraines treated with intravenous DHE 45® abated—it is also useful in treating drug-induced headache (Silberstein 1990). Patients can be taught to give themselves subcutaneous or intramuscular injections. DHE-45® comes in ampules (1 mg in 1 ml)—the dose may be titrated between 0.5–1.0 mg twice daily, as needed. The goal is to use the smallest effective dose.

Initially metoclopramide or another antiemetic should be taken prior to DHE-45®
to help control drug-induced nausea and vomiting. Many patients later find the metoclopramide is no longer necessary. The side effects of DHE-45® are similar to those of ergotamine but less severe. An intranasal formulation, Migranal®, is also available.

The ergots and their derivatives are contraindicated in patients with severe hypertension, peripheral vascular disease, ischemic heart disease and thrombophlebitis. They should be used cautiously in patients with peptic ulcer disease, bradycardia, renal and hepatic abnormalities. The ergots cannot be used with “triptan” drugs (see below) within 24 hours.

**Triptan medications**

Sumatriptan (Imitrex®) is the first medication engineered to work at the 5-HT receptor to treat migraine. It is an effective treatment and has been used extensively since it became available in the United States in 1993. Sumatriptan is currently available for patients orally, intranasally, and with an autoinjector for subcutaneous injection. Sumatriptan suppositories are available in some countries outside the USA.

Physicians may administer the drug without the use of an autoinjector. Subcutaneous sumatriptan reaches peak plasma level within 15 minutes. Extensive clinical trials have shown marked relief of head pain, nausea, vomiting, phonophobia, and photophobia within 1–2 hours after treatment with 6 mg in approximately 80 percent of patients. This formulation is most effective for headache occurring early in the morning (upon awakening), those which escalate to maximum severity rapidly, and those attacks with vomiting.

Oral sumatriptan (25, 50, and 100 mg) produces relief less rapidly, within 2 to 4 hours. Sumatriptan produced better relief from nausea and vomiting than ergotamine and had a similar effect to aspirin with metoclopramide. Intranasal sumatriptan is available in 5 mg and 20 mg single use devices (20 mg BID prn is the usual adult dose). It is another option for use during attacks with vomiting.

The side effects of subcutaneous, nasal, and oral sumatriptan are similar. Most common is an injection site reaction after subcutaneous administration. Also, flushing, heat sensation, chest pressure, heaviness, tingling and jaw or neck pain may occur. Occasional patients report chest pressure with pain going into the left arm suggestive of myocardial ischemia. After three million documented headache attacks treated with sumatriptan, 4 patients had documented myocardial ischemia (Welch). More extensive data suggests the occurrence of serious cardiac events is rare.

Usually side effects are mild to moderate in severity, short-lived, and resolve on their own. Some authorities advocate giving the initial dose of “triptans” under medical supervision. It is contraindicated to use “triptans” in patients with previous myocardial infarction, ischemic heart disease, Prinzmetal’s angina, or uncontrolled hypertension. They should only be used 24 hours before or after an ergot preparation is ingested. They should be avoided when patients are taking methysergide because of the vasoconstrictor properties of both medications.

Other “triptan” drugs available include zolmitriptan (Zomig®), naratriptan (Amerge®), rizatriptan (Maxalt®), eletriptan (Relpax®), almotriptan (Axert®), and frovatriptan (Frova®). In the USA, these agents are all presently available oral treatments, and zolmitriptan is available in nasal spray form. Zolmitriptan and rizatriptan are also available in rapidly dissolving tablets which are preferred by
some patients although they have not been shown to be more rapid or effective in clinical trials. Failure to respond to one triptan does not preclude a successful response to another (Ward 2000). These agents give superior results if used as early in the migraine attack as possible.

Narcotics

*Butorphanol, Codeine, Oxycodone, Hydrocodone, Meperidine*

Codeine has been shown to be superior to placebo in aborting a migraine attack (Raskin 1988). Butalbital, aspirin or acetaminophen, and caffeine combinations (see above) may become more effective in selected patients when codeine is added (Kunkel). These agents are potentially addictive: the addition of codeine increases the risk and severely limits its utility. Oxycodone (Percodan®) and hydrocodone (Vicodin®) have similar effects and concerns. Parenteral meperidine (Demerol®) is often used for the emergent treatment of migraine. It should be limited to those patients with infrequent attacks that cannot be treated effectively with another agent. This includes patients with peripheral vascular or coronary artery disease (Welch).

It is important to note that the efficacy of oral meperidine is approximately 25 percent of the IM preparation. Oral meperidine should be used in a very limited way for selected patients with severe migraine and as a rescue medication when other measures fail. Medication use should be closely monitored.

Transnasal butorphanol (Stadol NS®) has been used in the treatment of migraine. While US regulatory agencies formerly did not view it as a narcotic, it does contain the morphine molecule, and its major side effect is sedation. As a mixed agonist-antagonist, it may have less addiction potential, although this is controversial. Overuse may occur, and it seems capable of causing rebound. The initial dose of 1 mg (1 puff) in one nostril is approximately equipotent to 5 mg of morphine. Onset of action is rapid (minutes).

In pregnancy, there are very few medications that can be safely used. Acetaminophen, metoclopramide and meperidine can be used judiciously, as they are in FDA category B (Codeine is category C). Combination analgesics are to be avoided. Fortunately many migraineurs experience fewer headaches during pregnancy.

**Tension-Type Headache**

Previously known as muscle contraction headache and tension headache, the IHS classified it as tension-type headache: episodic. The episodic type is the headache that almost everyone experiences and usually responds to simple analgesics. The chronic type (more than 15 days per month) may be difficult to treat.

Patients with tension-type headache often complain of a dull ache across their forehead or in the back of their neck or both. It may feel as if a tight band is compressing the head. The pain location may vary and may even be unilateral at times. The neck muscles are usually tight. Patients do not often complain of photophobia, nausea or vomiting. Routine activity is generally not impaired, and there is less disability associated with headache episodes than there is with migraine. In primary tension-type headache the neurologic examination is normal, except for possible tightness/spasm in pericranial and cervical muscles. When the headache is chronic, depression and anxiety may be present.
Tension-type headache and episodic migraine headache may coexist. In addition episodic tension-type headache may be exacerbated or transformed to chronic tension-type headache by drug-induced or rebound headache caused by increasing symptomatic medication use over time. It is important to find out exactly how much medication the patient uses, including over-the-counter, and herbal, remedies, as well as prescription medications.

**Treatment of Tension-Type Headache**

Episodic tension-type headache may respond to the medications discussed for the symptomatic relief of migraine. Acetaminophen, aspirin, NSAIDs, and the isometheptene combination are the mainstays of episodic treatment. Chronic tension-type headache is difficult to treat. It is important that symptomatic medications are not overused leading to rebound headache. If so, the patient must be withdrawn from the offending medications. This often causes the patient to have a brief exacerbation of headache (“withdrawal headache”). DHE-45 may be used to treat this withdrawal headache (Raskin, 1986) (Silberstein). It takes approximately 8–12 weeks for the abused analgesics to “wash out” of the patient (Rapoport); only then may prophylactic medications, if necessary, become fully effective.

Incidentally, caffeine, present in medications, beverages and foods, often causes rebound headache. If the patient is taking over 500 mg daily, it is useful to slowly taper the caffeine ingestion. When the patient reports that caffeine ingestion provides headache relief within 1 hour, it virtually confirms the diagnosis of caffeine withdrawal headache.

Amitriptyline, nortriptyline or doxepin can be used for prophylactic therapy (see above). Elderly patients often cannot tolerate the smallest dose tablets or capsules because of their increased sensitivity to medication. Doxepin (Sinequan®) comes in a concentrate that may be added to juice or other drink. This gives precise control over the dose and permits these patients to be successfully treated. Nortriptyline is also available in liquid form.

Non-pharmacological treatments may also be useful. Biofeedback seems helpful, especially in combination with relaxation training and psychotherapy (Kunkel). Physical therapy and, if appropriate, an exercise program may be useful.

**Cluster Headache**

Cluster headache occurs predominantly in men and occurs daily in approximately 50 percent of patients, twice a day in 33 percent, and more often in the remainder. Attacks range in frequency from 8 (or more) a day to one every other day. The attack may last from 15 minutes to 3 hours, although the mean duration is 45 minutes. The attack often awakens the patient from sleep, occurring with the first stage of REM sleep (Kudrow). It is described as an extremely severe, boring pain that begins in or above one eye radiating to the frontal or temporal regions. The pain may also radiate into the teeth or the neck. It is associated with autonomic phenomena including ipsilateral rhinorrhea and lacrimation, nasal stuffiness, and conjunctival injection. A partial Horner’s syndrome may occur with the attack (miosis and ptosis). Most cluster headache patients feel the urge to pace about and find that they are unable to lie still during an attack (Kudrow).
The headaches of cluster patients usually occur in episodes or bouts lasting 2–4 months. During this time the attacks occur spontaneously or may be provoked by alcohol, histamine, or nitroglycerin. The time between bouts is a “remission” that may last from 1 month to 20 years, in episodic cluster headache. Occasionally, remissions are permanent. Some patients have chronic cluster headache, without remission.

There are some entities which may be misdiagnosed as cluster headache including:

- Migraine
- Trigeminal neuralgia
- Temporal arteritis
- Pheochromocytoma
- Cervical carotid artery dissection
- Chronic and episodic paroxysmal hemicrania

**Treatment of Cluster Headache**

**Symptomatic Treatment of Cluster Headache**

As in migraine, symptomatic treatment is the second line of defense against attacks, if prophylactic therapy fails (Ward 1997, 1998). Oxygen inhalation is effective and safe. The patient should be given 100 percent oxygen at 7 or more liters/minute via a facemask (non-rebreather). It has been effective in 90 percent of patients within 15 minutes (Kudrow). DHE-45® (1 mg) may be given IV to provide relief (preceded by an antiemetic such as metoclopramide 10 mg). Sumatriptan (Imitrex®) subcutaneously is highly effective in treating cluster attacks. Caution is advised, as many cluster patients are middle-aged males with multiple risk factors for coronary artery disease, a contraindication to the use of sumatriptan. Transnasal butorphanol (Stadol NS®) is another option.

**Prophylactic Treatment of Cluster Headache**

Many of the prophylactic treatments for cluster are similar to those for migraine. Patients with episodic cluster experience tremendous pain. Vigorous attempts to prevent the attacks are warranted. Treatment in the early phases of a cluster headache cycle with prednisone will usually stop the bout or decrease its severity within 24 hours. The initial dose is 60–80 mg daily instituted immediately. Then after 2–3 days at this level the dose is slowly tapered over 10–14 days. This immediate control permits the initiation of another medication that will be safer over the long-term than prednisone.

Prednisone can cause immediate bone loss, even when given for a short time. Bone loss may be prevented by taking Vitamin D 50,000 units weekly and calcium, one gram per day. Measures to protect the stomach (such as H2 blockers, antacids, or proton pump inhibitors) may be advisable.

Methysergide (Sansert®) is used as described under the treatment of migraine (see above). It tends to be most effective early in the course of the cluster cycle. It has been reported to have an efficacy of 65 percent (Kudrow).

Verapamil (Calan®, others) has been effective in several studies. Patients may require up to 480 mg per day (e.g., as Calan SR 240 BID) or, cautiously, even higher doses. Adding oral ergotamine 2 mg one hour prior to bedtime increases the effect of the verapamil (Kudrow). Lithium is effective in episodic cluster
and chronic cluster. The dose has to be gradually built up to avoid untoward reactions. This dose escalation takes place while controlling the cluster with the prednisone treatment. Lithium can be prescribed at 300 mg daily for three days then increased every three days until it is taken three times daily. It is necessary to follow the lithium serum level to monitor for toxicity. The concomitant use of diuretics, NSAIDS, and severe sodium-restricted diets are contraindicated, since this may cause toxicity. Thyroid function should be assessed in patients taking lithium as it can interfere with thyroid function. The symptoms of lithium toxicity include tremor, polyuria and mild nausea initially. Diarrhea, vomiting, drowsiness, muscular weakness, and incoordination occur with greater lithium intoxication. Stopping the lithium and monitoring the patient is necessary in this situation.

Valproic acid (Depakote®) appears to be another useful treatment for cluster headache. Recent studies suggest that for refractory cases, gabapentin (Neurontin®), and topiramate (Topamax®) might be useful. Combinations of verapamil and lithium, or verapamil and valproic acid, for example, may be effective when monotherapy fails.

When all medical treatment fails surgical treatment may be appropriate. Current surgical options include percutaneous radiofrequency lesions directed against the trigeminal ganglion, and deep brain stimulation of the hypothalamus. Both have risks for potential complications.

Less Common Primary Headaches

- Chronic Paroxysmal Hemicrania (CPH)
- Short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing (SUNCT)
- Hemicrania continua (HC)

Chronic paroxysmal hemicrania (CPH) is in many ways similar to cluster headache – periorbital location, severe pain intensity, usually accompanied by tearing and other autonomic facial symptoms – but duration of headaches is very brief, usually around 5 minutes, and headaches can occur many times per day. CPH affects young women predominantly, and is particularly responsive to indomethacin (25–50 mg tid).

SUNCT is characterized by even briefer paroxysms of pain (seconds), also in the periorbital region. Up to 200 attacks may occur per day. It too is usually accompanied by tearing and other autonomic facial symptoms, but it does not respond to indomethacin.

Hemicrania continua (HC) consists of constant unilateral head pain, also often accompanied by tearing, nasal congestion and other autonomic facial symptoms. Like CPH, HC is highly responsive to indomethacin.

Conclusion

Many different causes of headaches confront medical practitioners. A first step in the approach to the patient with headache is to rule out secondary causes, keeping common red flags in mind. Fortunately, the vast majority of patients with headache will be found to have a primary cause, such as migraine or tension-type headache. Many effective treatments are available for these conditions, but with primary headaches too, diagnosis is essential to ensure
proper treatment.

Self-Assessment Questions

1. A 35-year-old woman, with a past history of occasional migraine, has sudden onset of severe generalized headache and nausea, causing her to stop her activities and lie down. The headache persists and her family takes her to the emergency room. The primary diagnostic consideration for the examining physician is:
   A. migraine headache
   B. subarachnoid hemorrhage
   C. posttraumatic headache
   D. cluster headache
   E. none of the above

2. The above individual undergoes a noncontrast CT scan of the head which is read by the radiologist as negative. The next step for the examining physician is:
   A. administer an analgesic and observe for headache resolution
   B. lumbar puncture
   C. refer to a neurologist for his next available appointment
   D. schedule for an outpatient MRI and MRA of the brain
   E. administer 6 mg of sumatriptan subcutaneously

3. The following organic conditions can mimic recurrent primary headache disorders:
   A. pituitary adenoma
   B. cerebral arteriovenous malformation
   C. isolated CNS vasculitis
   D. pheochromocytoma
   E. all of the above

4. A 68-year-old female presents with a three week history of severe unilateral headache and scalp tenderness. She has had one episode, the day prior, of transient ipsilateral monocular visual loss, which has completely resolved. An erythrocyte sedimentation rate is 65 mm/hr. The following steps should be instituted:
   A. schedule cerebral angiography
   B. start prednisone, 60–80 mg/daily immediately
   C. obtain a stat CT scan of the brain.
   D. schedule for a temporal artery biopsy
   E. a,b,c
   F. b,c,d
5. Pick the one true statement among the following:
   A. oral or rectally administered ergotamines rarely lead to dependency, despite frequent use
   B. ergotamines and sumatriptan cannot be used concomitantly within 24 hours of each other
   C. ergotamine or sumatriptan can be used safely during pregnancy
   D. sumatriptan can be used safely six months after myocardial infarction
   E. dihydroergotamine has only marginal benefit in the treatment of migraine headache

6. The mainstay drug(s) for treatment for episodic tension-type headache are:
   A. ergotamines, sumatriptan
   B. beta-adrenergic antagonist drugs
   C. calcium channel blockers
   D. steroids
   E. aspirin, acetaminophen, non-steroidal anti-inflammatory drugs

7. Overuse of medications which symptomatically treat tension-type headache may lead to:
   A. transformed migraine
   B. cluster headache
   C. chronic daily headache
   D. hemicrania continua
   E. classic migraine

8. The following medication should not be used for migraine prophylaxis:
   A. valproic acid
   B. verapamil
   C. nadolol
   D. nortriptyline
   E. butorphanol

9. New-onset headache, followed shortly by confusion and/or seizures, may be secondary to:
   A. encephalitis
   B. brain abscess
   C. subdural empyema
   D. aseptic meningitis
   E. a,b,c
10. Label the following statements True (T) or False (F):

A. Valproate serum levels correlate with clinical effectiveness in migraine prophylaxis.

B. Metoclopramide may enhance analgesic absorption during a migraine attack.

C. Oxygen inhalation is a safe and effective treatment for cluster headache attacks.

D. Nonsteroidal anti-inflammatory drugs are an effective first line abortive therapy for mild to migraine headaches.

E. Fronto-maxillary headache, with associated local tenderness, is almost always due to a benign headache disorder.

Answers

1. B
2. B
3. E
4. F
5. B
6. E
7. C
8. E
9. E
10. A is False
    B is True
    C is True
    D is True
    E is False