

# HEADACHE MEDICINE

## QUESTIONS AND ANSWERS

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DARA G. JAMIESON



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QUESTIONS AND ANSWERS



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## QUESTIONS AND ANSWERS

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# PREFACE

**H**EADACHES ARE AN ALMOST UNIVERSAL EXPERIENCE with most people noting at least one headache in a lifetime. Most headaches are mild and transient, and do not warrant a visit to a health-care provider. However, almost thirty million Americans suffer from chronic disabling headaches that impact their quality of life. Individuals of all ages, from young children to the elderly, may suffer from headaches with certain headache types present at a specific age. Most headaches are primary, not associated with any underlying anatomic or physiologic abnormality. Rarely a headache is secondary to a disease or disorder with risk of neurologic injury or even death.

Patients with headaches may consult a variety of different medical specialists, including neurologists, internists, emergency medicine physicians, otorhinolaryngologists, family practitioners, gynecologists, psychiatrists, and pediatricians. Many specialists must evaluate these patients and distinguish between trivial or troubling headache types. In an effort to assess the ability of medical specialists to treat headaches, the United Council of Neurologic Subspecialists (UCNS) has designated headache medicine as a subspecialty concerned with the diagnosis and treatment of head and face pain. The UCNS has developed an examination with 200 multiple-choice questions to certify physicians who have exhibited expertise in headache medicine either through completion of a headache medicine fellowship or through extensive

clinical experience. *Headache Medicine: Questions and Answers* is an interesting and informative way to study for the UCNS headache medicine examination as the contents of the book parallels the UCNS headache medicine examination categories. Medical students and neurology residents will also find this book to be useful to assess and expand their knowledge of headache medicine prior to medical school examinations and the resident in-service examinations. Self-assessment through the multiple questions in this book is also a motivating way for established practitioners to appreciate their familiarity with headache treatment and to acquire new information.

I have been able to use the enormous amount of information gleaned in writing this book in my clinical practice and I have enjoyed every minute of researching and writing. I hope that those who use this book to learn more about headache medicine will find the information useful and intriguing. And for those of you using this volume to study for examinations covering headache topics, I wish you the best of luck.

Dara G. Jamieson, MD  
*New York, New York*

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My husband, Ehud Lavi, MD is the inspiration for my interest in headache medicine. I have been trying for over a quarter of century to cure his headaches and I look forward to many more decades of learning from him about neuropathology and headaches. Dr. Lavi kindly supplied the neuropathological images for this book. A. John Tsiouris, MD of Weill Cornell Medical Center was most generous in supplying me with neuroradiologic images. I thank both of them so very much for their help with this book.



# HEADACHE MEDICINE

QUESTIONS AND ANSWERS





# 1

# HEADACHE EPIDEMIOLOGY AND COMORBIDITY QUESTIONS

1. Which of the following statements best describes the association between migraine and cardiovascular risk?
  - A. Migraineurs have not been proven to be at increased cardiovascular risk.
  - B. Male migraineurs are at increased cardiovascular risk only when they have multiple traditional vascular risk factors.
  - C. Women who have ever had a migraine headache are at increased risk of cardiovascular disease.
  - D. The risk of myocardial infarction (MI) is increased in women with active migraine with aura.
  - E. The increased cardiovascular risk in men with migraine with aura is a contraindication to their use of triptans.
2. Which of the following causes of vestibular symptoms is associated with migraine?
  - A. Perilymph fistula
  - B. Vestibular neuronitis
  - C. Labyrinthitis
  - D. Benign paroxysmal positional vertigo (BPPV)
  - E. Medications
3. ID Migraine is a simple, brief, easy-to-use, well-validated symptom-based diagnostic screener. Which of the following headache features of ID Migraine is the best predictor of a diagnosis of migraine?
  - A. Pain on one side
  - B. Moderate to severe pain
  - C. Phonophobia
  - D. Throbbing pain
  - E. Disability

4. Which of the following is **not** a risk factor for the development of chronic daily headache (CDH)?
- A. Obesity
  - B. Snoring
  - C. High socioeconomic status
  - D. Head injury
  - E. Stressful life events
5. Which of the following cardiac conditions is most closely linked to migraine?
- A. Coronary artery disease
  - B. Patent foramen ovale (PFO)
  - C. Spontaneous echo contrast
  - D. Coarctation of the aorta
  - E. Long Q-T syndrome
6. Which of the following best describes gastric stasis in migraine patients?
- A. Migraine patients may suffer from gastric stasis both during and between acute migraine attacks.
  - B. Gastric stasis delays the gastrointestinal absorption of all triptans during a migraine.
  - C. Migraine patients rarely experience clinically relevant delayed gastric emptying during an attack.
  - D. Gastric stasis is the main underlying mechanism of nausea.
  - E. All of the above
7. What is the approximate prevalence of PFO in patients with migraine with aura?
- A. <10%
  - B. 10–20%
  - C. 20–40%
  - D. 40–60%
  - E. 60–80%

- 8.** Which is statement best describes motion sickness and migraine?
- A. Migraine and tension-type headaches (TTH) are equally associated with motion sickness.
  - B. Patients with migraines are just as likely as nonmigraineurs to enjoy reading in the car.
  - C. Motion sickness in young children suggests a predisposition to developing migraine.
  - D. Traveling in aircraft and trains is associated with more motion sickness than riding in buses and boats.
  - E. Migraineurs with motion sickness would rather ride in the back seat than drive.
- 9.** The 1-year prevalence of migraine in the United States is approximately:
- A. 3% in men.
  - B. 12% in men.
  - C. 6% in women.
  - D. 18% in women.
  - E. 20% in both men and women.
- 10.** The association between migraine and increased ischemic stroke risk is greatest in:
- A. Younger women with migraine with aura.
  - B. Younger men with migraine with aura.
  - C. Younger women with any type of migraine.
  - D. Older women with any type of migraine.
  - E. Older men with any type of migraine.
- 11.** Which of the following psychiatric conditions is most closely linked to migraine?
- A. Bipolar disorder
  - B. Depression
  - C. Neuroticism
  - D. Attention deficit disorder
  - E. Schizophrenia

- 12.** Chronic daily headache (CDH) is associated with:
- A. Higher economic status.
  - B. Obesity.
  - C. Male gender.
  - D. Never being married.
  - E. Under-utilization of medication.
- 13.** What is the prevalence of primary CHD in the U.S. population?
- A. <1%
  - B. 1%
  - C. 4%
  - D. 8%
  - E. 12%
- 14.** The peak incidence of migraine without aura in males is in which age range?
- A. 5–8 years
  - B. 10–11 years
  - C. 14–17 years
  - D. 20–25 years
  - E. 28–32 years
- 15.** The peak incidence of migraine without aura in females is in which age range?
- A. 5–8 years
  - B. 10–11 years
  - C. 14–17 years
  - D. 20–25 years
  - E. 28–32 years
- 16.** Which population group is most likely to suffer from a headache pain lasting 10–180 minutes that awakens the patient from sleep, more days of the month than not, without autonomic features?
- A. Infants
  - B. Prepubescent children
  - C. Teenagers
  - D. Middle-aged men
  - E. Elderly individuals

- 17.** According to data from the Women's Health Study (WHS), increased risk of which of the following is found in women with migraine with aura?
- A. Ischemic stroke
  - B. Myocardial infarction (MI)
  - C. Myocardial revascularization
  - D. Death from a vascular cause
  - E. All of the above
- 18.** Sinus headaches are distinguished from migraine headaches by the presence of:
- A. Change in weather as a trigger.
  - B. Allergen exposure as a trigger.
  - C. Pain in a bilateral maxillary distribution.
  - D. Nasal congestion.
  - E. None of the above
- 19.** Which of the following statements best describes migraine headaches in young children?
- A. Migraines are very rare in pre-pubescent children.
  - B. Migraines are more common in girls than boys under age 7 years.
  - C. Chronic headaches rarely impact a child's quality of life.
  - D. Migraines in children are generally of shorter duration than in adults.
  - E. Migraine headaches in young children are generally in an occipital location.
- 20.** What is the most common pathogen associated with adult community-acquired bacterial meningitis?
- A. Streptococcus pneumonia
  - B. Neisseria meningitidis
  - C. Haemophilus influenza
  - D. Listeria monocytogenes
  - E. Staphylococcus aureus
- 21.** Which saint may have suffered from migraines?
- A. St. Peter
  - B. St. John
  - C. St. Catherine
  - D. St. Paul
  - E. St. Matthew

- 22.** Which of the following is most commonly found in children evaluated in the emergency department for an acute headache?
- A. Head trauma
  - B. Brain tumor
  - C. Migraine
  - D. Upper respiratory tract infection
  - E. Meningitis
- 23.** Which of the following markedly increases the risk of ischemic stroke in women with migraine with visual aura?
- A. Hypertension
  - B. Diabetes
  - C. Myocardial infarction (MI)
  - D. Elevated total cholesterol
  - E. Cigarette smoking
- 24.** Sleep disturbances in children with headaches:
- A. Occur rarely and are of little clinical significance.
  - B. Are associated with migraine, but not tension-type, headaches in children.
  - C. Are more severe in children with more severe migraines.
  - D. Are not associated with behavioral problems.
  - E. Include insomnia, but not parasomnias.
- 25.** Which gynecological condition is associated with migraine headaches?
- A. Cervical cancer
  - B. Endometriosis (EM)
  - C. Uterine myomata
  - D. Cervical dysplasia
  - E. Bicornate uterus
- 26.** Which of the following migraine comorbid conditions has the strongest association with a history of physical, emotional, or sexual abuse in migraine patients?
- A. Endometriosis (EM)
  - B. Fibromyalgia
  - C. Irritable bowel syndrome (IBS)
  - D. Tremor
  - E. Seizures

- 27.** Which of the following migraine comorbid conditions is associated with increased migraine frequency and severity?
- A. Obesity
  - B. Depression
  - C. Anxiety
  - D. Morbid obesity
  - E. All of the above
- 28.** Which of the following is the most important trigger in increasing the risk of occurrence and persistence of headache and migraine?
- A. Odors
  - B. Menstruation
  - C. Stress/stress relief
  - D. Alcohol
  - E. Fatigue
- 29.** What is the most common postdrome symptom reported by migraine patients?
- A. Tiredness
  - B. Nausea
  - C. Irritability
  - D. Lingering headache
  - E. Weakness
- 30.** Migraine patients with premonitory symptoms:
- A. Report tiredness, mood change, and gastrointestinal symptoms.
  - B. Generally report symptoms lasting less than 4 hours.
  - C. Are more likely to have multiple migraine triggers.
  - D. Are more likely to have postdrome symptoms.
  - E. All of the above
- 31.** Approximately what percentage of patients with migraine headaches report symptoms of cutaneous allodynia with their headaches?
- A. <5%
  - B. 20%
  - C. 40%
  - D. 60%
  - E. 80%



- 32.** Which statement describes generalized anxiety disorder (GAD)?
- A. Generalized anxiety disorder (GAD) is a short-term situational reaction to stress.
  - B. Onset of symptoms generally occurs in adolescence.
  - C. Generalized anxiety disorder has a lifetime prevalence of 4–7%.
  - D. The clinical course of GAD rarely exceeds 5 years.
  - E. All of the above
- 33.** Which of the following diary writers did *not* describe suffering from severe headaches?
- A. Samuel Pepys
  - B. Ann Frank
  - C. James Boswell
  - D. Virginia Woolf
  - E. Fyodor Dostoevsky
- 34.** What is the approximate prevalence of recurrent headaches in adolescents?
- A. 60–80%
  - B. 30–40%
  - C. 10–20%
  - D. <5%
  - E. None in the adolescents but close to 100% in their parents
- 35.** Migraine headaches may increase the risk of:
- A. Subarachnoid hemorrhage (SAH).
  - B. Hydrocephalus as a complication of SAH.
  - C. Rebleeding as a complication of SAH.
  - D. Delayed ischemic neurological deficit as a complication of SAH.
  - E. None of the above
- 36.** Which of the following may be a risk factor for CDH?
- A. Head and neck injury
  - B. Medicinal and dietary caffeine
  - C. Childhood stressors
  - D. Habitual snoring
  - E. All of the above

- 37.** Fibromyalgia:
- A. Is diagnosed by specific laboratory testing.
  - B. Is most common in adolescent and young women.
  - C. Is associated with arthritis and headaches.
  - D. Is treated with exercise, cognitive behavioral therapy, and medication for anxiety.
  - E. Is rarely diagnosed in women with chronic daily headache (CDH).
- 38.** Migraine confers an increased risk of which complication of pregnancy?
- A. Ischemic stroke
  - B. Gestational hypertension
  - C. Preeclampsia
  - D. Eclampsia
  - E. All of the above
- 39.** What is the most likely diagnosis for a patient with a stable pattern of episodic, disabling headaches and a normal physical examination?
- A. Tension-type headaches (TTH)
  - B. Medication overuse headaches (MOH)
  - C. Migraine headaches
  - D. Sinus headaches
  - E. Idiopathic intracranial hypertension (IIH)
- 40.** A 28-year-old woman with sinus headaches since her teens reports once-a-week bifacial and periorbital pressure and pain triggered by change in weather, allergies, and stress. When her headaches with nasal congestion and nausea occur, she likes to rest in a quiet, dark room in order to sleep. Various suggestions by multiple physicians have been made to treat her headaches. Which of the following recommendations do you prefer?
- A. Start antibiotics at the first sign of sinus pressure.
  - B. Have her deviated nasal septum straightened, along with shaving off the bump on her nose.
  - C. Initiate treatment with allergy injections.
  - D. Use a triptan at the onset of facial pain.
  - E. Use antihistamines and inhalational steroids as needed.

**41.** Which of the following is the most common trigger of an acute migraine headache?

- A. Change in weather
- B. Stress or relief from stress
- C. Alcohol
- D. Specific foods
- E. Change in sleep

**42.** Match the migraine population with the best estimate of the age of peak incidence. The answer may be used once, more than once, or not at all.

- |                                     |                       |
|-------------------------------------|-----------------------|
| A. Boys with migraine without aura  | 1. Around 5 years old |
| B. Boys with migraine with aura     | 2. 10–11 years old    |
| C. Girls with migraine without aura | 3. 12–13 years old    |
| D. Girls with migraine with aura    | 4. 14–17 years old    |
|                                     | 5. 18–21 years old    |

**43.** Headache is associated with which of the following chronic gastrointestinal complaints?

- A. Nausea
- B. Diarrhea
- C. Constipation
- D. Reflux
- E. All of the above

**44.** Which of the following has been shown in a case-control study to be associated with migraine headaches in adults?

- A. Restless legs syndrome (RLS)
- B. Parkinson's disease
- C. Spasmodic dysphonia
- D. Cervical dystonia
- E. All of the above

45. A 30-year-old woman has migraine headaches approximately twice a month. She takes a triptan for the headaches and is on medication for depression. On review of symptoms, she reports abdominal pain occurring episodically or after eating, relieved by urgent diarrhea. She also has irregular bowel habits with episodic constipation. What is causing her gastrointestinal symptoms?
- A. Gall bladder disease
  - B. A side effect of her medication for depression
  - C. A side effect of magnesium prophylaxis of migraine headaches
  - D. Irritable bowel syndrome (IBS)
  - E. Celiac sprue
46. Which of the following statements best describes the relationship between PFO and migraine?
- A. Migraine with and without aura are similarly associated with patent foramen ovale (PFO).
  - B. Atrial septal defects and PFOs are similarly associated with migraines.
  - C. Migraine is more common in young patients with cryptogenic stroke who have a PFO.
  - D. The prevalence of migraine is not increased in patients with PFO.
  - E. White matter lesions seen on the MRI of migraineurs indicate the presence of a PFO.
47. Which geographic area has the *lowest* adjusted prevalence of migraine?
- A. Africa
  - B. Asia
  - C. Europe
  - D. South and Central America
  - E. North America
48. Obesity is defined as a body mass index (BMI) in the range of:
- A.  $<18.5 \text{ kg/m}^2$
  - B.  $18.5\text{--}24.9 \text{ kg/m}^2$
  - C.  $25.0\text{--}29.9 \text{ kg/m}^2$
  - D.  $30.0\text{--}34.9 \text{ kg/m}^2$
  - E.  $>35.0 \text{ kg/m}^2$

**49.** Women with migraine with aura:

- A. Have a similar risk of myocardial infarction (MI) to that of women without migraine aura.
- B. Have an increased risk of hemorrhagic stroke.
- C. Have an increased risk of ischemic stroke, even corrected for vascular risk factors.
- D. Do not have an increased risk of cardiovascular disease (CVD).
- E. All of the above

**50.** Which American President suffered from migraine headaches, but was not known to have had a stroke?

- A. Thomas Jefferson
- B. Woodrow Wilson
- C. Richard Nixon
- D. Millard Fillmore
- E. Chester A. Arthur

**51.** Which of the following is associated with headaches in patients with systemic lupus erythematosus?

- A. Raynaud's phenomenon
- B.  $\beta_2$ -glycoprotein-I antibodies
- C. Depression
- D. Active lupus disease
- E. All of the above

**52.** Risk of which of the following is *not* increased in patients with migraine headaches?

- A. Arterial dissection
- B. Subarachnoid hemorrhage (SAH)
- C. Ischemic stroke
- D. Myocardial infarct (MI)
- E. All of the above

**53.** Tension-type headache:

- A. Has a lifetime prevalence of about 80%.
- B. Is the most common form of headache.
- C. Is more common in younger, than in older, individuals.
- D. Is more prevalent in women.
- E. All of the above

- 54.** Which of the following is more common in migraineurs, as compared to nonmigraineurs?
- A. Elevated blood pressure response to stress
  - B. Syncope
  - C. Orthostatic hypotension
  - D. Resting tachycardia
  - E. All of the above
- 55.** Which of the following is associated with cutaneous allodynia?
- A. Female gender
  - B. Depression
  - C. Increased body mass index
  - D. Increased headache frequency
  - E. All of the above
- 56.** What is the most common neuropsychiatric manifestation of systemic lupus erythematosus in children?
- A. Headaches
  - B. Seizures
  - C. Psychosis
  - D. Cognitive dysfunction
  - E. Chorea
- 57.** Cutaneous allodynia is most common in which headache type?
- A. Transformed migraine
  - B. Severe episodic tension-type headache
  - C. Chronic daily headache
  - D. Probable migraine
  - E. Episodic migraine
- 58.** Migraine is associated with:
- A. Major depressive disorder.
  - B. Bipolar disorder.
  - C. Panic disorder.
  - D. Social phobia.
  - E. All of the above

- 59.** What is the approximate lifetime prevalence of cluster headache?
- A. One in 100 people
  - B. One in 1,000 people
  - C. One in 10,000 people
  - D. One in 100,000 people
  - E. One in a million people
- 60.** Which of the following is associated with headache after childbirth?
- A. Cervicocephalic artery dissection
  - B. Reversible posterior leukoencephalopathy syndrome
  - C. Eclampsia
  - D. Reversible cerebral vasoconstriction syndrome
  - E. All of the above



# HEADACHE EPIDEMIOLOGY AND COMORBIDITY

## ANSWERS

**1. The answer is D.** There is an increased cardiovascular risk in migraineurs. In the Physicians' Health Study there was a 42% increase in myocardial infarction (MI) in healthy male physicians with migraine of any type. The type of migraine and their acuity were not specified in this study. In the Women's Health Study (WHS), an increased risk of any vascular event, including MI, was only apparent for women with active migraine with aura. After adjusting for age, 18 additional major cardiovascular disease (CVD) events were attributable to migraine with aura per 10,000 women per year. A past history of any type of migraine did not confer increased vascular risk. Triptan use does not increase cardiovascular risk, and migraine with aura is not a contraindication to their use in either men or women. (Diener, Kurth, & Dodick, *Curr Opin Neurol* 2007; Kurth Gaziano, Cook, et al., *JAMA* 2006)

**2. The answer is D.** Data from over a thousand patients with neuro-otological evaluation for a history of dizziness or vertigo found that 8% had benign paroxysmal positional vertigo (BPPV). A history of migraine was found in 21% of men and 43% of women with BPPV. The association may be related to the increased lifetime prevalence of BPPV in women (3.2%) as compared to men (1.6%). Vestibular neuronitis and labyrinthitis generally occur after a viral infection. (Von Brevern, Radtke, Lezius, et al., *J Neurol Neurosurg Psychiatry* 2007; Cohen, *J Neurol Neurosurg Psychiatry* 2007)

**3. The answer is E.** Virtually all of the listed migraine features, as well as pain exacerbated by activity and aura symptoms, supported the diagnosis of migraine using the nine-question ID Migraine diagnostic screener. However, the presence of nausea, disability, and photophobia together is the best predictor of the diagnosis of migraine. Of nine diagnostic screening questions, the three-item subset



of disability, nausea, and sensitivity to light had a sensitivity of 0.81 (95% CI, 0.77 to 0.85), a specificity of 0.75 (95% CI, 0.64 to 0.84), and positive predictive value of 0.93 (95% CI, 89.9 to 95.8). The presence of all three of these symptoms has a 93% probability of meeting the International Headache Society diagnostic criteria for migraine. (Lipton & Bigal, *Headache* 2007)

**4. The answer is C.** The Frequent Headache Epidemiology (FrHE) study identified specific risk factors associated with the development of chronic daily headache (CDH). Migraine, medication overuse, female gender, low socioeconomic status, head injury, attack frequency, obesity, life-stress, and snoring were statistically significant factors associated with the development of CDH. (Lipton & Bigal, *Headache* 2007)

**5. The answer is B.** Although there is an increased risk of MI in migraineurs, a specific link with coronary artery disease has not been shown. Patent foramen ovale (PFO), with or without an associated atrial septal aneurysm, and mitral valve prolapse are associated with migraine. The correlation is strongest with PFO, with an increased incidence of PFO in migraine patients and increased migraines in patients with PFO. The association is greatest with migraine with aura, as compared to migraine without aura. (Scher, Bigal, & Lipton, *Curr Opin Neurol* 2005)

**6. The answer is A.** Gastric stasis has been associated with migraine, with the assumption that delayed gastric emptying occurs only during the migraine attack. Gastric stasis explains why some, but not all, oral triptans demonstrate less rapid absorption during a headache. Gastric stasis may decrease the efficacy of oral medications used to treat headache pain. A study by Aurora et al, published in 2006, demonstrated that time to gastric emptying was delayed between, as well as during, migraine attacks. This suggests that migraineurs have abnormal autonomic function compared to nonmigraineurs. The absence of correlation between the clinical symptoms of nausea and gastric stasis indicates that nausea associated with migraine is a central process, rather than a consequence of gastric stasis. (Aurora, Kori, Barrodale, et al., *Headache* 2006)

**7. The answer is D.** Although the prevalence of PFO in patients with migraine without aura is approximately the same as controls (10–30%), the prevalence of PFO in patients with migraine with aura is significantly higher, in the range of 40–60%. A common genetic background may factor into the explanation of this unclear association. The role, if any, of the PFO in the pathogenesis of migraine with aura is unknown. The utility of PFO closure in migraine is being investigated. (Diener, Kurth, & Dodick, *Curr Opin Neurol* 2007)

**8. The answer is C.** Motion sickness occurs in about half of migraine patients, but only about 20% of patients with tension-type headaches (TTH). It is common in pediatric migraine patients, often presenting at a young age prior to the onset of migraine headaches. Motion sickness in young children may suggest a predisposition to developing migraine. Traveling in aircraft and trains is less likely to cause motion sickness than riding in cars, buses, and boats. Fixing vision on the horizon in the front seat and driving the car can decrease the sense of car sickness. Patients with migraine who have outgrown car sickness may admit to an inability to read in the car while someone else is driving. Many migraine patients are very uncomfortable when dragged on amusement park rides, especially ones with rapid circular motion. (Evans, Marcus, & Furman, *Headache* 2007)

**9. The answer is D.** In the United States, three large population studies, American Migraine Studies 1 and 2 and the American Migraine Prevalence and Prevention Study, have estimated the prevalence of migraine using established headache diagnostic criteria. The 1-year period prevalence of migraine in both men and women was 11.7–12.6%. In men, the prevalence was 5.6–6.5% and in women it was 17.1–18.2%. The prevalence of migraine has been stable over the past 15 years. (Silberstein, Lipton, & Dodick, *Wolff's Headache and Other Head Pain*, Chapter 4)

**10. The answer is A.** An increase risk of ischemic stroke has been found in patients with migraine, with the greatest and most consistent increase found in younger women who have migraine with aura. Relative risk estimates range from 3.8 to 8.4. However, the absolute risk of ischemic stroke is still very small; the estimated attributable risk ranges from 18 to 40 additional ischemic stroke cases per 100,000 women per year. Oral contraceptives and smoking increase the ischemic stroke risk for women with migraine with aura. (Diener, Kurth, & Dodick, *Curr Opin Neurol* 2007)

**11. The answer is B.** Depression, panic attacks, and generalized anxiety disorder (GAD) are associated with migraine, as well as other chronic pain disorders such as back pain, fibromyalgia, irritable bowel syndrome (IBS), and arthritis. The frequency of migraine attacks seems to correlate with increased association with depression and anxiety. (Scher, Bigal, & Lipton, *Curr Opin Neurol* 2005)

**12. The answer is B.** Chronic daily headache, a headache occurring more days than not, occurs in about 4% of the adult population and is associated with less education and lower income. It is more common in women and in those individuals who were previously married. Snoring, a body mass index (BMI) >30, stressful

life-events, musculoskeletal pain, and medication overuse are all correlated with CDH. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 2)

**13. The answer is C.** The prevalence of primary CDH in the United States is said to be 4%. Chronic daily headache is defined as headache occurring at least 15 days per month for at least three months. Chronic daily headache can be primary (not attributable to an underlying disorder) or secondary (attributable to an underlying disorder). Secondary CDH is rare compared to primary CHD. Chronic daily headache is approximately twice as common in adult women as in adult men. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 2)

**14. The answer is B.**

**15. The answer is C.** Age of incidence is the age at onset of symptoms. The peak age-range incidence of migraine without aura in males is 10–11 years. The peak age-range incidence of migraine without aura in females is 14–17 years. Peak age of first occurrence of migraine is younger in boys, as compared to girls. Age of onset of migraine with aura is younger than migraine without aura for both boys and girls. For migraine without aura the peak incidence is around 10–11 years for boys and around 14–17 years for girls. For migraine with aura the peak incidence is around 4–5 years for boys and around 12–13 years for girls. (Silberstein, Lipton, & Dodick. *Wolff's Headache and Other Head Pain*, Chapter 4)

**16. The answer is E.** Hypnic headaches occur at least 15 days per month, with pain that awakens the elderly individual from sleep. In a study by Evers and Goadsby, the average age of onset of the 71 individuals with hypnic headaches (more women than men) was  $63 \pm 10$  years. (Evers & Goadsby, *Neurology* 2003)

**17. The answer is E.** Migraine and vascular diseases are linked by more than just coincidental overlap. Migraine with aura is associated with an increased risk of ischemic stroke as well as cardiovascular disease (CVD). The relationship between migraine and CVD, however, is less well understood. The WHS was analyzed for correlation between migraine of different types and vascular events. Of 27,840 women initially free of CVD or angina, 18% reported any history of migraine. From the 3,610 women with active migraine, 39.7% reported migraine with aura. During a mean of 10 years of follow-up there were 251 ischemic strokes, 249 MIs, and 130 ischemic CVD deaths in the total cohort. After adjusting for age, 18 additional major CVD events were attributable to migraine with aura per 10,000 women per year. As compared with women with no migraine history, the hazard ratios (HRs) were 2.15 (95% confidence interval [CI], 1.58–2.92;  $p < .001$ ) for ma-

for CVD, 1.91 (95% CI, 1.17–3.10;  $p = .01$ ) for ischemic stroke, and 2.08 (95% CI, 1.30–3.31;  $p = .002$ ) for MI. Women with migraine with aura also had an increased risk of myocardial revascularization, angina, and CVD death. Increased risk was noted after approximately 6 years of follow-up. Women with active migraine without aura did not have any significantly increased risk of any CVD event or angina compared with women without any migraine history. Women who reported prior migraine had significantly increased risk of coronary revascularization and angina. The highest association between active migraine with aura and ischemic stroke was in women younger than age 50 and women with total cholesterol < 200 mg/dL. This study confirmed that women with migraine with aura have a greater risk of cardiovascular, as well as cerebrovascular, disease. Increased vascular risk remained even after controlling for the increase in risk factors seen in women with migraine with aura. The precise mechanisms to explain the link are currently unknown. (Kurth, Gaziano, Cook, et al., *JAMA* 2006)

**18. The answer is E.** The majority of patients with self-diagnosed sinus headaches have migraine or probable migraine headaches. Patients enrolled in the descriptive, clinical Sinus, Allergy and Migraine Study (SAMS) believed that they suffered from sinus headaches. However, a detailed history and examination of the 100 subjects with self-diagnosed sinus headaches revealed that they actually had migraine with or without aura (52%), headache associated with medication overuse (11%), probable migraine (23%), cluster headache (1%), hemicrania continua (1%), headache secondary to rhinosinusitis (3%), and nonclassifiable headaches (9%). Change in weather, seasons, and altitude, as well as exposure to allergens were frequent migraine triggers that were attributed to sinus headaches. Seventy-six percent of migraine subjects reported pain in the distribution of the second division of the trigeminal nerve (either unilateral or bilateral), and 62% experienced bilateral forehead and maxillary pain with their headaches. Symptoms that can be found with migraine headaches that contribute to confusion with so-called sinus headaches, include nasal congestion, eyelid edema, rhinorrhea, conjunctival injection, lacrimation, and ptosis. (Eross, Dodick, & Eross, *Headache* 2007)

**19. The answer is D.** Headaches and migraine are common in childhood, with 4–11% of children between the ages 5 and 15 years having headaches consistent with migraine. One to 3% of even younger children, ages 3–7 years, have migraines, with a slight male predominance. The impact of chronic headaches, including migraines in children, is significant, with missed school and social activities and compromised quality of life. The International Classification of Headache Disorders, 2nd Edition (ICHD-II) recognizes the shorter headache dura-

tion (1–72 hours) in children under age 15 years as compared to older children (2–72 hours). In some children with migraine, gastrointestinal (GI) symptoms, including nausea, intractable vomiting, and abdominal pain, may be more prominent than head pain. The head pain in migraine, generally unilateral in adults, is commonly bilateral in young children. Localization of the migraine head pain, relatively variable in adults, is usually fronto-temporal in children. Headaches persisting in an occipital location in a child should lead to investigation of a secondary headache etiology. (The International Classification of Headache Disorders, Second Edition (ICHD-II), *Cephalalgia* 2004; Battistella, Fiumana, Binelli, et al., *Cephalalgia* 2005)

**20. The answer is A.** In a study of 696 cases of adult community-acquired bacterial meningitis, *Streptococcus pneumoniae* was found in 51% of cases and *Neisseria meningitidis* was found in 37% of cases. Vaccination for *Haemophilus influenzae* has nearly eliminated this pathogen as a cause of community-acquired meningitis. *Listeria meningitis* may be associated with poor nutrition and alcoholism. *Staphylococcus aureus* meningitis may complicate neurosurgical procedures. (Van de Beek, de Gans, Spanjaard, et al., *N Engl J Med* 2004)

**21. The answer is D.** St. Paul was said to have suffered from bouts of unilateral headache and transient eye problems, consistent with migraine with aura. The flash of light that caused him to fall, followed by blindness and anorexia, may have been a visual aura. His recurring “thorn in the flesh,” which he interpreted as a message from Satan, may have been migraine pain, as this characterization has been reported by more contemporary migraineurs. St. Paul’s migraine symptoms may have precipitated his conversion from Judaism to Christianity, without any clear contemporary associations. The headache symptoms of the other listed saints are unknown. (Göbel, Isler, & Hasenfratz, *Cephalalgia* 1995; Jones, *Cephalalgia* 1999)

**22. The answer is D.** The evaluation of a child with headache in the emergency department should identify the less than 15% of children who may have a serious or life-threatening cause of head pain. However, over half of acute headaches in children may be due to viral upper respiratory or sinus infections. Head pain caused by migraine, head trauma, brain tumor, shunt failure, intracranial hemorrhage, or meningitis is less common. (Silberstein, Lipton, & Dodick, *Wolff’s Headache and Other Head Pain*, Chapter 27)

**23. The answer is E.** The Stroke Prevention in Young Women Study (SPYW), a population-based, case-control study published in *Stroke* in 2007, compared 386

women ages 15 to 49 years with first ischemic stroke and 614 age- and ethnicity-matched controls. The study found that probable migraine with visual aura was associated with an increased risk of stroke, particularly among women without other medical conditions associated with stroke. The SPYW found that women with probable migraine with visual aura had 1.5 greater odds of ischemic stroke (95% CI, 1.1 to 2.0); the risk was highest in those with no history of hypertension, diabetes, or myocardial infarction compared to women with no migraine. Smoking and oral contraceptive use markedly increased the risk of ischemic stroke. Women with probable migraine with visual aura who were current cigarette smokers and current users of oral contraceptives had 7.0-fold higher odds of stroke (95% CI, 1.3 to 22.8) than did women with probable migraine with visual aura who were nonsmokers and non-oral contraceptive users. All women, regardless of headache history, should be counseled not to smoke. The increase in the small absolute risk of stroke associated with oral contraception should be explained to a woman with active migraine with aura, so that she can balance her risk of an unwanted pregnancy (and its attendant vascular health risk) with her risk with oral contraception use and make the best contraceptive choice for herself. Low dose estrogen contraception is generally preferable; the recent studies on vascular risk were not analyzed based on the many different formulations of estrogen-containing contraceptive preparations (e.g. oral, transdermal, intravaginal) currently available. (MacClellan, Giles, Cole, et al., *Stroke* 2007)

**24. The answer is C.** A relationship between headaches and sleep disturbances has been found in both children and adults. Sleep disturbances are commonly associated with both TTH and migraine headaches in children and can be disturbing to the child and parents. Sleep disturbances in children with migraine include sleeping too little, insomnia, excessive daytime sleepiness, and snoring. Increased frequency and duration of migraine headaches predicts specific sleep disturbances, including sleep anxiety, parasomnias, and bedtime resistance. Children with more severe migraines have more severe sleep problems than do those children with milder headaches. Impaired sleep predicts behavior problems in children with migraine headaches. Children with migraine are prone to greater sleep and behavioral disturbances, including parasomnias, than are children without headache. (Miller, Palermo, Powers, et al., *Headache* 2003; Heng & Wirrell, *J Child Neurol* 2006)

**25. The answer is B.** Migraine and endometriosis (EM) are common conditions in women of reproductive age, and both are influenced by ovarian hormones. In a study that enrolled 171 women with migraine and 104 controls, EM was reported more commonly in migraineurs than in controls (22% vs. 9.6%,  $p < .01$ ).

The frequency of chronic headache was higher in migraineurs with EM compared to migraineurs without EM ( $p = .002$ ), and median headache-related disability scores were also higher in the EM group ( $p = .025$ ). Migraineurs with EM reported more menorrhagia, dysmenorrhea, and infertility as compared to the migraine cohort without EM and to nonheadache controls. Prevalence of EM was higher in women with migraine than in nonheadache controls. Migraineurs with EM have more frequent and disabling headaches, and are more likely to have other comorbid conditions affecting mood and pain, compared to migraineurs without EM. The other listed gynecological conditions have not been associated with migraine headaches. (Tietjen, Bushnell, Herial, et al. *Headache* 2007)

**26. The answer is B.** Multiple comorbid pain and mood disorders occur in migraineurs. A study of female migraine patients defined a group with depression, anxiety, and fibromyalgia. Compared to migraine patients with other medical conditions, including hypertension, hyperlipidemia, diabetes mellitus, and hypothyroidism, the group of migraine patients with depression, anxiety, and fibromyalgia had greater disability and lower quality of life. These patients more commonly reported sexual, physical, or emotional abuse. Although IBS has been associated with psychosocial stressors and a past history of abuse, the correlation between abuse and IBS in migraine patients is not clear. Tremor, seizures, and EM are associated with migraine headaches, but not a past history of abuse. (Tietjen, Herial, Hardgrove, et al. *Headache* 2007; Folks, *Curr Psychiatry Rep* 2004)

**27. The answer is E.** Obesity, anxiety, and depression are linked in migraineurs. In a population based study, Bigal et al. (2007) found that, among individuals with migraine, very frequent headaches (10–14 days/month) occurred in 7.4% of the overweight ( $p = .10$ ), 8.2% of the obese ( $p < .001$ ), and 10.4% of the morbidly obese ( $p < .0001$ ) individuals, compared with 6.5% of those with normal weight. Disability of migraine increased with increasing weight. The results indicated that obesity is an exacerbating factor for migraine, but not for other types of episodic headaches. Migraine and obesity are highly prevalent conditions in women, and are both independently linked to psychiatric conditions, such as depression and anxiety. The prevalence of obesity in a study of migraine patients (predominantly women) was 30%; only 38% of migraine patients had normal weight. Ongoing depression (42%) and anxiety (70%) were noted in the obese migraineurs. Obese migraineurs with anxiety and/or depression were more likely to have higher headache frequency and headache-related disability compared to normal-weight migraineurs without either condition. Compared to migraineurs with either ongoing depression or anxiety, migraineurs with both these conditions were more likely to have higher headache frequency and headache disability, with linkage



of these conditions to CDH. Idiopathic intracranial hypertension should also be considered in obese individuals with headaches, either as the main cause of chronic headaches or in addition to migraines. (Bigal, Tsang, Loder, et al., *Arch Intern Med* 2007; Tietjen, Peterlin, Brandes, et al., *Headache* 2007)

**28. The answer is B.** Menstruation is the most important trigger in increasing the risk of occurrence and persistence of headache and migraine in women. The PAMINA Study Group prospectively analyzed a wide spectrum of factors related to headache in 327 migraineurs who kept a comprehensive diary for 3 months. Menstruation had the most prominent effect, increasing the hazard of occurrence or persistence of headache and migraine by up to 96%. All other factors changed the hazard by <35%. The 2 days before menstruation, as well as muscle tension in the neck, psychic tension, tiredness, noise, and odors on days before headache onset all increased the risk of headache or migraine; whereas days off, a divorced marriage, relaxation after stress, and consumption of beer decreased the risk. However, abandoning one's job and marriage to relax and drink beer all day could bring on other types of headaches and problems. (Wöber, Brannath, Schmidt, et al., *Cephalalgia* 2007)

**29. The answer is A.** A study demonstrated a postdrome period, after relief of the head pain and associated symptoms, in 68% of migraine patients. The postdrome period generally lasts around 24 hours and is more often associated with a full-blown migraine attack. It is more common in females. The most common postdrome symptoms reported in a study of 827 migraineurs were tiredness (72%), head pain (33%), cognitive difficulties (12%), "hangover" sensation (11%), GI symptoms (8%), mood change (7%), and generalized weakness (6%). Patients with postdrome symptoms, as compared with patients without postdrome symptoms, have more migraine-associated symptoms. (Kelman, *Cephalalgia* 2006)

**30. The answer is E.** Premonitory symptoms (a prodrome) prior to a migraine headache are reported by about one-third of migraine patients. A study of 893 migraine patients found that the most common premonitory symptoms were tiredness, mood change, and GI symptoms. Patients with premonitory symptoms are different from patients without a prodrome; they have more headache triggers, including alcohol, hormones, light, hunger, perfume or noxious smells, stress, and weather changes. They report a longer duration of aura, a longer time between aura and headache, more auras without a headache, a longer time to peak pain of the headache, a longer time to respond to a triptan, a longer maximum duration of the headache, and more headache-associated nausea. Patients with premonitory symptoms are more likely to have a postdrome syndrome, which



is of longer duration. Whereas patients often accuse chocolate of triggering a migraine, chocolate craving may be a premonitory symptom. Chocolate, within reason, is all good, and dark chocolate can even be used as an adjunctive treatment for hypertension. (Kelman, *Headache* 2004)

**31. The answer is D.** The American Migraine Prevalence and Prevention Advisory Group published a study of migraineurs ( $n = 11,388$ ) who completed the Allodynia Symptom Checklist. The prevalence of allodynia among migraineurs was 63.2% and was associated with frequency, severity, disability, and associated symptoms of migraine. Severe cutaneous allodynia (CA) occurred in 20.4% of migraineurs, and was associated with migraine defining features (e.g., unilateral pain; throbbing pain; nausea), as well as illness duration, attack frequency, and disability. (Lipton, Bigal, Ashina, et al. *Ann Neurol* 2007)

**32. The answer is C.** Generalized anxiety disorder (GAD), a common comorbid disorder of headaches, is characterized by excessive, uncontrollable, irrational worry or anxiety occurring on more days than not over a 6-month period. It has a lifetime prevalence of 4–7%, generally beginning in young adulthood, although symptoms may start in childhood and adolescence. About 40% of patients have symptoms lasting >5 years. Generalized anxiety disorder is associated with functional impairment, with decreased vocational function and reduced quality of life. Patients with GAD, as high users of medical care, strain health care resources and frustrate health care providers. Benzodiazepines, venlafaxine, selective serotonin reuptake inhibitors, and cognitive-behavioral therapy may treat GAD. (Allgulander, Bandelow, Hollander, et al. *CNS Spectr* 2003)

**33. The answer is C.** James Boswell, a diarist best known as the biographer of Samuel Johnson, suffered from alcoholism and depression, but he did not recount severe headaches. Samuel Pepys was said to suffer from severe headaches as a young adult, curtailing the writing of his diaries. Virginia Woolf suffered from severe headaches, as well as severe depression, drowning herself at age 59 years. In her *Diary*, Ann Frank described “bad” to “terrifying” and “pounding” headache attacks, which were accompanied by vomiting. Her postpubescent headaches are consistent with migraines. Fyodor Dostoevsky had epilepsy since childhood, but he also suffered from severe headaches consistent with migraine. Many characters in his novels suffered from the neurologic conditions that he had experienced throughout his life. (de Almeida & Kowacs, *Cephalalgia* 2007)

**34. The answer is A.** Prevalence is the number or percentage of individuals with the disease in the population at a specific time. The most common headaches

in children include migraine or TTHs. The male predominance of migraine in younger children shifts to female predominance with adolescence. Recurrent headaches are very common in children, increasing with age. In children aged 7 years, the prevalence of recurrent headaches is in the range of 40–50%, increasing to the range of 60–80% by age 15 years. (Winner & Hershey, *Curr Pain Headache Rep* 2007)

**35. The answer is D.** Migraine headaches do not appear to increase the risk of subarachnoid hemorrhage (SAH). A multicenter, population-based, case-control study using cases of first-ever SAH during 1995–1998 and matched controls found that the frequency and characteristics of headaches were similar between the SAH and control groups. There was no evidence for an association between recurrent headaches and SAH. The SAH complications of rebleeding prior to aneurysmal clipping or coiling and hydrocephalus are not more likely to occur in patients with migraine headaches. However, the SAH complication of delayed ischemic neurological deficit (DIND) may be more common in patients with migraine. A small retrospective study using a telephone interview suggested that women younger than 60 years with migraine have a higher risk of developing DINDs after SAH than women without migraine. The prevalence of migraine was 47% in women with SAH with DIND, as compared to 25% in women with SAH without DIND ( $p < 0.05$ ; odds ratio: 2.68, confidence interval: 0.99–7.29). The correlation between DIND and migraine was independent of vascular risk factors. (Carter, Anderson, Jamrozik, et al. *J Clin Neurosci* 2005; Dreier, Kremer, & Lammers, *Eur J Neurol* 2007)

**36. The answer is E.** Multiple factors may impact the development of CDH by unclear mechanism. Some of the risk factors for CDH include low socioeconomic and educational status, habitual snoring, head injury, caffeine use, and current and childhood stressors. The Frequent Headache Epidemiology Study suggested that head and neck injury may account for approximately 15% of CDH cases, with the lifetime risk of CDH increasing with increasing number of injuries. In a population study of cases of CDH and controls, in comparison with episodic headache controls, CDH cases were more likely overall to have been high caffeine consumers before onset of CDH. The modest association was found in younger women with chronic episodic (as opposed to chronic continuous) headaches. (Silberstein, Lipton, & Dodick, *Wolff's Headache and Other Head Pain*, Chapter 4; Couch, Lipton, Stewart, et al., *Neurology* 2007; Scher, Stewart, & Lipton, *Neurology* 2004)

**37. The answer is D.** Fibromyalgia is a common non-articular pain syndrome, associated with CDH, which is diagnosed most often in middle-aged women. The

cause of fibromyalgia is unknown, and there is no specific laboratory diagnosis. It is diagnosed by the presence of at least 11 out of 18 specific tender points. Symptoms, which are present for more than 3 months, include chronic insomnia, fatigue, headache, generalized or focal stiffness but not arthritis, paresthesias, and anxiety. Treatment modalities for this syndrome include cognitive behavior therapy, exercise, physical therapy, and medication to treat the mood disorder, pain, and insomnia. (Chakrabarty & Zoorob, *Am Fam Physician* 2007)

**38. The answer is E.** Women with migraine headaches may note decreased frequency and severity of their headaches during pregnancy, especially in the second and third trimesters. However, a history of migraine may increase the vascular risk of pregnancy. Studies of pregnant women with migraine have revealed a significant association between migraine and conditions causing elevated blood pressure in pregnancy, such as preeclampsia and gestational hypertension. A review addressing the association between migraines and preeclampsia or gestational hypertension found eight out of 10 studies that reported a positive association between the syndromes. Eclampsia, a consequence of the ongoing untreated hypertension of preeclampsia with resultant seizures, may be associated with migraine. Migraine also appears to be a risk factor for ischemic stroke during pregnancy and the puerperium. (Adeney & Williams, *Headache* 2006; Allais, Castagnoli Gabellari, Airola, et al., *Neurol Sci* 2007)

**39. The answer is C.** Over 28 million Americans have chronic disabling migraine headaches, and most patients with a stable pattern of episodic, disabling headache, and a normal physical and neurologic examination have migraine headaches. In a prospective, open-label study, the initial headache diagnoses given to 1,203 patients by their physicians was compared to the headache diagnoses determined by expert evaluation of the patient's headache diaries. Overall, 94% of patients with an initial physician diagnosis of a primary headache disorder had International Headache Society (IHS)-defined migraine (76%) or probable migraine (18%) headache on the basis of their longitudinal diary data. Encouraging patients to keep a migraine diary is crucial in determining the cause of primary headaches. Although episodic tension-type headache (ETTH) may be the most common headache type experienced overall, patients with ETTH are less likely to seek medical care than are patients with episodic migraine headaches. Episodic TTHs are rarely disabling. Idiopathic intracranial hypertension (IIH) may cause disabling headaches but is most commonly diagnosed in overweight young women and is a relatively rare cause of long-term recurrent headaches. Patients with IIH generally have papilledema and they may have sixth nerve palsies. (Tepper, Dahlöf, Dowson, et al. *Headache* 2004)

**40. The answer is D.** Migraine may have a myriad of clinical manifestations. This woman appears to have probable migraine headache and nasal surgery, antibiotics, and allergy treatment will not give her sustained benefit. When migraine pain occurs in an area interpreted as “the sinuses,” the actual localization in a trigeminal nerve distribution may be overlooked. Nasal congestion, rhinorrhea, tearing, and other migraine symptoms may be construed as symptoms of a sinus infection or mechanical abnormality. A study to determine the prevalence of IHS-defined migraine without aura, migraine with aura, or migrainous disorder (probable migraine) in patients with a history of self-described or physician-diagnosed “sinus headache” screened 2,991 patients. The majority (88%) of these patients with “sinus headache” were diagnosed as migraine (80%) or probable migraine headache (8%). The most common symptoms that triggered the diagnosis of “sinus headache” were sinus-area pressure (84%), sinus-area pain (82%), and nasal congestion (63%). Patients with recurrent headaches with sinus-area symptoms, without documented fever or purulent nasal discharge, should be evaluated for migraine headaches. (Schreiber, Hutchinson, Webster, et al., *Arch Intern Med* 2004)

**41. The answer is B.** In a study of 1,207 patients with migraine headaches, 76% reported headache triggers, usually associated with a more severe migraine headache. The triggers included stress or stress relief (80%), hormonal changes in women (65%), hunger (57%), change in weather (53%), change in sleep (50%), smells (44%), neck pain (38%), light (38%), alcohol (38%), and smoke (36%). Other triggers include heat, food, exercise, and sexual activity. Although patients may be concerned that food is a migraine trigger, specific foods are generally not reliable or reproducible triggers, especially in the absence of other precipitants of headaches. A confluence of triggers, “a perfect storm” (e.g., staying out late during a thunderstorm to drink cheap red wine the night after the headache medicine board examination), may be needed to precipitate a migraine, whereas a single trigger might be insufficient. (Kelman, *Cephalalgia* 2007)

**42. The answer is A 2, B 1, C 4, D 3.** Incidence is defined as the rate at which new cases of a disease occur in a specific population. The incidence of migraine without aura peaks at a later age than does migraine with aura. The peak age at which migraine with aura occurs in boys is age 5 years at 6.6/1,000 person-years. Migraine without aura in boys has a peak incidence of 10/1,000 person-years at age 10–11 years. The onset of migraines peaks at a later age in girls, than in boys. The incidence of migraine with aura peaks between ages 12 and 13 years at 14.1/1,000 person-years in girls. However, the incidence of migraine without aura peaks in girls aged between 14 and 17 years at 18.9/1,000 person-years. (Winner & Hershey, *Curr Pain Headache Rep* 2007)

**43. The answer is E.** An association exists between chronic headaches, including migraines, and chronic GI symptoms, distinct from the GI symptoms occurring during the actual headache attack. The GI symptoms in headache-predisposed individuals may occur individually or in combination, such as with IBS. A questionnaire-based cross-sectional study (the Head-HUNT Study) studied the association between headache, including migraine, and GI symptoms in 43,782 individuals. A higher prevalence of headache was found in individuals with reflux (odds ratio [OR] 2.4, 95% CI, 2.2, 2.6), diarrhea (OR 2.4, 95% CI 2.1, 2.8), constipation (OR 2.1, 95% CI 1.9, 2.4), and nausea (OR 3.2, 95% CI 2.6, 3.8) as compared with individuals without these GI complaints. Complaints of GI symptoms were associated with nonmigrainous headache as well as migraine, and the association between headache and GI complaints increased markedly with increasing frequency of headaches. (Aamodt, Stovner, Hagen, et al., *Cephalalgia* 2008)

**44. The answer is A.** A case-control study of the comorbidity of migraine and restless legs syndrome (RLS) evaluated patients with IHS-diagnosed migraine and gender- and age-matched control subjects. The frequency of RLS was significantly higher in migraine patients than in control subjects (17.3% vs. 5.6%,  $p < 0.001$ ; OR 3.5, CI 2.2, 5.8). There was no significant association between migraine and depression (9.6% in migraine vs. 4.0% in control subjects,  $p = 0.190$ ) in this relatively small cohort study. Depression was more frequent in migraine patients with RLS (13.6%) than in migraine patients without RLS (8.7%). The authors found an association between RLS and migraine and a co-association with depression. A dysfunction of dopaminergic metabolism in migraine has been postulated to explain the association, although other dopamine-depletion movement disorders besides RLS are not linked with migraine headaches. (Rhode, Hösing, Happe, et al., *Cephalalgia* 2007)

**45. The answer is D.** Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by abdominal pain with change in bowel habits, in the absence of pathologic findings on evaluation. Patients may complain that the pain is relieved by defecation. The symptoms of IBS may include predominant or alternating constipation or diarrhea. Patients with IBS may have other stress- or mood-related disorders. A case cohort study using coding data from a large U.S. health plan found that people in the IBS cohort had a 40–80% higher prevalence of migraine, fibromyalgia, and depression. Magnesium is associated with diarrhea, but would not cause all this woman's symptoms. Celiac sprue or celiac disease is an inherited autoimmune disorder of the small bowel that generally presents in infancy but can be diagnosed in adulthood. It is characterized by chronic diarrhea, weight loss, and fatigue. Sprue can be treated by a gluten-free diet. Neurologic

associations include ataxia, myelopathy, and peripheral neuropathy. Although an association between celiac disease and migraine has been postulated based on anecdotal reports and a case-control study, with the suggestion that celiac treatment may decrease migraines, IBS remains the GI disorder most closely linked to migraine. (Cole, Rothman, Cabral, et al., *BMC Gastroenterol* 2006)

**46. The answer is C.** The association between migraine with aura and PFO is approximately three times greater than the association with migraine without aura. A composite of studies of PFO in patients with migraine found a greater prevalence of PFO associated with migraine with aura (54%) than associated with migraine without aura (16%). The prevalence of migraine with aura, but not migraine without aura, was similarly increased in patients with PFOs. In a study of young patients with cryptogenic stroke, migraine was more common in patients with PFO than in those without PFO. Although white matter lesions (WMLs) and PFO are increased in patients with migraine with aura, the Shunt Associated Migraine (SAM) study showed no correlation between the presence of WMLs on MRI and a PFO; and no specific headache characteristics were found to be associated with cardiac shunting. Although pulmonary arteriovenous malformations seem to be associated with migraine, another cause of a right-to-left shunt, an atrial septal defect, is not associated with migraine. The pathogenesis of the migraine with aura – PFO association is not clear but may be related to genetic co-localization. (Diener, Kurth, & Dodick, *Curr Opin Neurol* 2007) Adami A, Rossato G, Cerini R, Thijs VN, Pozzi-Mucelli R, Anzola GP, Del Sette M, Finocchi C, Meneghetti G, Zanferrari C; SAM Study Group. Right-to-left shunt does not increase white matter lesion load in migraine with aura patients. *Neurology*. 2008 Jul 8;71(2):101-7

**47. The answer is A.** Migraine is more common in Europe and the Americas as compared to Africa and Asia. In all geographic areas, migraine is more common in women than men, although the gender disparity is less in Africa as compared to North America. Migraine is less common in African Americans and Asians in the United States. This international variation is unexplained. (Silberstein, Lipton, & Dodick, *Wolff's Headache and Other Head Pain*, Chapter 4)

**48. The answer is D.** The BMI is calculated as weight in kilograms divided by height in meters squared. Categories of BMI are: underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), obese (30.0–34.9), and morbidly obese (>35.0). (Bigal, Tsang, Loder, et al., *Arch Intern Med* 2007)

**49. The answer is C.** Multiple studies have indicated a risk of ischemic CVD in women with migraine with aura. An analysis of the Women's Health Study

(WHS) noted the correlation between migraine with aura and vascular events. Of 27,840 women initially free of CVD or angina at initiation into the WHS, 18% reported any history of migraine. From the 3,610 women with active migraine, 39.7% reported migraine with aura. The women were followed for cardiovascular and cerebrovascular outcomes. There was an increased risk of ischemic stroke and CVD in women with active migraine with aura. Increased vascular risk was not found in women with migraine without aura. There was no increased risk of hemorrhagic stroke (subarachnoid hemorrhage or intracerebral hemorrhage) associated with migraine of any type. (Kurth, Gaziano, Cook, et al., *JAMA* 2006)

**50. The answer is A.** One could argue that the burden of the presidency is a major headache trigger and all presidents should have headaches. However Thomas Jefferson, Ulysses Grant, and Harry Truman are said to have had headaches. The other listed presidents had strokes, with less clear headache symptoms. Thomas Jefferson, author of the Declaration of Independence and founder of the University of Virginia, appeared to have suffered from migraine headaches. He died at age 83 years, presumably from dehydration due to dysentery. (Jones, *Cephalalgia* 1999)

**51. The answer is E.** Headaches in patients with systemic lupus erythematosus are very common. The most common headache type is migraine, which may affect up to half of lupus patients, both adults and children. They are associated with Raynaud's phenomenon,  $\beta_2$ -glycoprotein-I antibodies, active lupus disease, and depression. (Weder-Cisneros, Tellez-Zenteno, Cardiel, et al., *Cephalalgia* 2004; Appenzeller & Costallat, *Cephalalgia* 2004)

**52. The answer is B.** An association exists between migraine and ischemic cardiovascular and cerebrovascular events, but migraine is not a risk factor for SAH. A multicenter, population-based, case-control study using cases of first-ever SAH during 1995–1998 and matched controls in four study centers in Australia and New Zealand found that 206 of 432 (48%) cases and 236 of 473 (50%) controls had a history of headaches. The frequency and characteristics of headaches were similar between the two groups. No evidence was found for an association between recurrent headaches and SAH. There appears to be an association, albeit tenuous, between migraine and arterial dissection, but its pathophysiologic basis is not clear. (Carter, Anderson, Jamrozik, et al., *J Clin Neurosci* 2005; Weinberger, *Curr Cardiol Rep* 2007)

**53. The answer is E.** Tension-type headache (TTH) is the most common type of headache, but patients with ETTH consult with a doctor infrequently and the



diagnosis is made in less than a quarter of patients treated in a headache practice. Patients with TTH may self-diagnose and self-treat, often to excess, with over-the-counter medication. The lifetime prevalence is about 80%, with 3% of patients experiencing TTH for >15 days a month for more than 3 months (chronic TTH). The prevalence of TTH is higher in women, and declines with age in both genders. (Fumal & Schoenen, *Lancet Neurol* 2008)

**54. The answer is B.** A population-based study was conducted to examine the association between migraine and syncope-related autonomic nervous system symptoms. A systematic questionnaire and cardiovascular measurements addressed the prevalence of syncope, orthostatic intolerance, orthostatic hypotension, and the postural tachycardia syndrome in migraineurs and control subjects. Compared with control subjects, migraineurs had a higher lifetime prevalence of syncope (46 vs. 31%;  $p = 0.001$ ) and orthostatic intolerance (32 vs. 12%;  $p < 0.001$ ). Syncope was more common in women. There was an elevated prevalence of syncope and orthostatic intolerance in migraineurs without clear interictal signs of autonomic nervous system dysfunction. Elevated blood pressure response to stress, orthostatic hypotension, and resting tachycardia have not been shown to be more common in migraineurs. (Thijs, Kruit, van Buchem, et al., *Neurology* 2006)

**55. The answer is E.** Cutaneous allodynia is a painful skin sensation or discomfort induced by a non-noxious stimulus, that is a frequent complaint during prolonged migraine attacks. Cutaneous allodynia is experienced with sunburned skin where even the lightest touch is perceived as painful, a helpful analogy when explaining the phenomenon to those who have never experienced it. It is usually noted initially on the face ipsilateral to the migraine pain but can spread to the opposite side and involve the extremities as well. The Allodynia Symptom Checklist (ASC) was used to measure allodynia, as well as headache features, disability, and comorbidities in over 16,000 individuals who responded to a mail survey. Cutaneous allodynia was more common and more severe in patients with transformed migraine or migraine, as compared with other primary headache types. Among migraineurs, CA was associated with female gender, increased headache frequency, increased BMI, increased disability, and depression. However, a recently published report of twenty-five non-allodynic patients and 38 allodynic migraineurs studied with a 90-item self-report psychological symptom inventory, found no significant difference between the two groups in any area of the personality profile. (Bin, Ashina, Burstein, et al., *Neurology* 2008) Lovati C, D'Amico D, Brambilla A, Mariani C, Bussone G. Personality profile and allodynic migraine. *Neurol Sci.* 2008 May;29 Suppl 1:S152-4.



**56. The answer is A.** Neuropsychiatric manifestations, which often occur early in the disease, are found in about a quarter of children and adolescents with systemic lupus erythematosus. Headaches (66%), psychosis (36%), cognitive dysfunction (27%), and cerebrovascular disease (24%) are the most common neuropsychiatric manifestations; although seizures, chorea, and peripheral nerve disease are also common. Children may have multiple neuropsychiatric manifestations of the disease simultaneously and may suffer long-term damage from these disorders. (Benseler & Silverman, *Lupus* 2007)

**57. The answer is A.** The Allodynia Symptom Checklist (ASC) was used to measure allodynia, as well as headache features, disability, and comorbidities in over 16,000 individuals who responded to a mail survey. Prevalence of CA was significantly higher in patients with transformed migraine (TM, 68.3%) than with episodic migraine (63.2%,  $p < 0.01$ ). Cutaneous allodynia was reported less frequently in patients with probable migraine (42.6%), other CDHs (36.8%), and severe ETTH (36.7%). Female gender, increased headache frequency, increased BMI, headache-related disability, and depression increased the prevalence of CA. (Bigal, Ashina, Burstein, et al., *Neurology* 2008)

**58. The answer is E.** Migraine is associated with multiple psychiatric disorders, including major depressive disorder and posttraumatic stress disorder. In patients with psychiatric disease and migraine, the compounded disorders complicate disease management and lead to worsening health outcomes. A population-based study by Jette et al. (2008) found that major depressive disorder, bipolar disorder, panic disorder, and social phobia occurred more than twice as often in those with migraines, as compared with those without migraines. The lifetime prevalence of major depressive disorder in migraineurs was 18.8%, as compared to 9.8% in non-migraineurs. Health-related outcomes were worst in those with both migraines and a psychiatric disorder, and intermediate in those with either condition alone. (Jette, Patten, Williams, et al., *Headache* 2008)

**59. The answer is B.** Cluster headache is a male-predominant trigemino-autonomic cephalgia (TAC) with a low prevalence. A meta-analysis of population studies of cluster headache showed a lifetime prevalence of 124 per 100,000 [confidence interval (CI) 101, 151] and a 1-year prevalence of 53 per 100,000 (CI 26, 95). The overall male-to-female ratio was 4.3 but it was higher in chronic cluster headache (15.0) compared with episodic cluster headache (3.8). The ratio of episodic to chronic cluster headache was 6.0. The analysis revealed a relatively stable lifetime prevalence suggesting that about one in 1000 people suffers from cluster

headache. While cluster headaches are male predominant, they may be underdiagnosed in women. (Fischera, Marziniak, Gralow, et al., *Cephalalgia* 2008)

**60. The answer is E.** A study of cervicocephalic artery dissection (CAD) found that women with postpartum CAD often had coexisting conditions such as reversible cerebral vasoconstriction syndrome, reversible posterior leukoencephalopathy syndrome, and subarachnoid hemorrhage without signs of intracranial extension of CAD. The authors concluded that CAD and associated conditions should be considered in women with unusual headaches after childbirth. Eclampsia and pre-eclampsia, which can occur up to 6 weeks after delivery, may present with postpartum headaches as well. (Arnold, Camus-Jacqmin, Stapf, et al., *Stroke* 2008)

# 2

## HEADACHE ANATOMY AND PHYSIOLOGY QUESTIONS

- 61.** A study using positron emission tomography (PET) in patients with hemi-crania continua showed the most pronounced activation in which areas?
- A. Posterior hypothalamus and cingulate cortex
  - B. Posterior hypothalamus and posterior-lateral thalamus
  - C. Posterior hypothalamus and dorsal rostral pons
  - D. Anterior hypothalamus and ventrolateral midbrain
  - E. Anterior hypothalamus and pontomedullary junction
- 62.** What makes the trochlear nerve (CN IV) different from all other cranial nerves?
- A. It exits from the dorsal surface of the brainstem.
  - B. It is the smallest cranial nerve.
  - C. It is the only cranial nerve that decussates completely.
  - D. It has the longest intracranial course.
  - E. All of the above
- 63.** Which of the following describes the results of the CAMERA study of magnetic resonance imaging (MRI) lesions in migraineurs?
- A. Periventricular white matter lesions (WMLs) are more common in migraineurs without aura than in control individuals.
  - B. Patients with migraine have the same prevalence of cerebellar infarcts as do control individuals.
  - C. The prevalence of deep WMLs is increased in women with migraine without aura.
  - D. The prevalence of periventricular WMLs is increased in men with migraine with aura.
  - E. All of the above

- 64.** An increase in deposition of non-heme iron is seen in which brain region associated with chronic headaches?
- A. Dorsal raphe nucleus
  - B. Periaqueductal gray (PAG)
  - C. Trigeminal nucleus caudalis
  - D. Ventrolateral thalamus
  - E. All of the above
- 65.** Which of the following characteristics of evoked potentials is seen in patients with migraine?
- A. Lack of habituation
  - B. Decreased amplitude
  - C. Increased amplitude
  - D. Decreased latencies
  - E. Increased latencies
- 66.** Which is the *least* common gene linked to familial hemiplegic migraine (FHM)?
- A. SCN1A
  - B. NOTCH3
  - C. TREX1
  - D. CACNA1A
  - E. TP1A2
- 67.** Which of the following is the most important trigger of hemodialysis headache ?
- A. Calcitonin gene-related peptide (CGRP)
  - B. Substance P
  - C. Nitric oxide (NO)
  - D. Serotonin (5-HT)
  - E. Prostaglandins
- 68.** Ischemic optic neuropathy (ION) may be associated with:
- A. Hypertension.
  - B. Giant cell arteritis (GCA).
  - C. A surgical procedure.
  - D. Internal carotid artery dissection.
  - E. All of the above

**69.** A middle-aged woman complained of intermittent severe, stabbing right ear pain triggered when she put her finger in her right external auditory canal. What cranial nerve is most likely involved in her neuralgia?

- A. Maxillary division (CN V<sub>2</sub>) of the trigeminal nerve
- B. Mandibular division (CN V<sub>3</sub>) of the trigeminal nerve
- C. Facial nerve (CN VII)
- D. Glossopharyngeal nerve (CN IX)
- E. Vagal nerve (CN X)

**70.** Hypoperfusion during a migraine attack has been most consistently noted in which brain area?

- A. Frontal lobe
- B. Parietal lobe
- C. Occipital lobe
- D. Temporal lobe
- E. Brainstem

**71.** Match the symptom associated with dissection of the extracranial internal carotid artery with its associated anatomic location. Use each answer only once.

- |                          |                  |
|--------------------------|------------------|
| A. Dysgeusia             | 1. CN V          |
| B. Dysphagia             | 2. CN VII        |
| C. Tongue deviation      | 3. CNs IX, X, XI |
| D. Hemifacial numbness   | 4. CN XII        |
| E. Monocular visual loss | 5. CN II         |

**72.** Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) has been associated with mutations of which gene?

- A. CACNA1A
- B. ATP1A2
- C. SCN1A
- D. NOTCH3
- E. TREX1

**73.** A Horner's syndrome may result from a lesion in the:

- A. Hypothalamus.
- B. Medulla.
- C. Lung apex.
- D. Cavernous sinus.
- E. All of the above

74. Which of the following structures adheres most closely to the brain?
- A. Dura (periosteal layer)
  - B. Dural (meningeal layer)
  - C. Arachnoid
  - D. Pia
  - E. Venous sinuses
75. A subdural hematoma:
- A. Is generally associated with arterial hemorrhage.
  - B. Always needs surgical evacuation.
  - C. May be associated with metastatic cancer.
  - D. Appears as a lens-shaped collection crossing the midline
  - E. All of the above
76. Which of the following is a cause of headaches related to non-central nervous system (CNS) cancer?
- A. Cerebral venous thrombosis
  - B. Leptomeningeal tumor infiltration
  - C. Intracerebral hemorrhage
  - D. Fungal meningitis
  - E. All of the above
77. Increased frequency of tension-type headache (TTH) can lead to chronic tension-type headache (CTTH). Which of the following mechanisms appears the most likely to cause this chronification of TTH?
- A. Increased sensitivity to neurotransmitters such as substance P
  - B. Genetic predisposition to episodic tension-type headache (TTH)
  - C. Sensitization of central pain pathways to stimuli from pericranial myofascial tissues
  - D. An increase in inflammatory mediators in pericranial myofascial tissues
  - E. An increase in the number of myofascial trigger points

**78.** According to genetic studies of patient with sporadic hemiplegic migraine (SHM), which of the following is true?

- A. Sporadic hemiplegic migraine (SHM) is most frequently associated with a CACNA1A gene mutation.
- B. Sporadic hemiplegic migraine is most frequently associated with an ATP1A2 gene mutation.
- C. Sporadic hemiplegic migraine is most frequently associated with a SCN1A gene mutation.
- D. Sporadic hemiplegic migraine has never been associated any genetic mutation.
- E. Gene mutations associated with hemiplegic migraine have never been found in patients with nonhemiplegic migraine.

**79.** A 23-year-old woman with occasional migraine headaches is seen for her initial office visit. She is in excellent general health. While talking to her, you note that the iris of her right eye is a dark shade of blue, but the left iris is a lighter shade of blue. What finding on examination will give you the neurologic reason for her variation in eye color?

- A. Decreased visual acuity in her left eye
- B. Decreased pupil size in her left eye
- C. Ptosis of her right upper eyelid
- D. A café au lait spot on her left thigh
- E. Injection of her right conjunctiva

**80.** Hypnic headache is associated with which of the following?

- A. Nocturnal oxygen desaturation
- B. Rapid eye movement (REM) sleep
- C. Obstructive sleep apnea (OSA)
- D. Nocturnal hypertension
- E. All of the above

**81.** Serotonin is synthesized from which essential amino acid?

- A. Tryptophan
- B. Phenylalanine
- C. Lysine
- D. Leucine
- E. Threonine

- 82.** Which of the following statements best describes the pathophysiology of tension-type headache (TTH)?
- A. Pericranial muscle hardness and tenderness are increased even in the headache-free period in patients with tension-type headache (TTH).
  - B. Unlike with migraine headache, peripheral sensitization plays no role in the development of TTH.
  - C. Central pain processing appears similar in patients with episodic and chronic tension-type headache.
  - D. Consistent elevation of calcitonin gene-related peptide receptor (CGRP) levels have been found in the spinal fluid of patients with TTH.
  - E. Studies of nitric oxide (NO) inhibition indicate that NO does not have a role in central sensitization in chronic tension-type headache (CTTH).
- 83.** Menstrual migraine may be modulated by:
- A. Decreasing estrogen in the late luteal phase.
  - B. Fluctuation in plasma levels of prostaglandins during the menstrual cycle.
  - C. Suppression of serotonergic neurotransmitter systems in the late luteal phase.
  - D. Suppression of opiateergic neurotransmitter systems in the late luteal phase.
  - E. All of the above
- 84.** How frequently is the total cerebrospinal fluid (CSF) volume renewed?
- A. Every 2 hours
  - B. Every 6 hours
  - C. Every 12 hours
  - D. Every 24 hours
  - E. Every 48 hours
- 85.** Which of the following has been shown to be a genetic biomarker for migraine?
- A. SCN1A
  - B. MTHFR
  - C. CACNA1A
  - D. ATP1A2
  - E. All of the above



**86.** Manipulation of which of the following will most likely lead to a new treatment for acute migraine?

- A. Calcitonin gene-related peptide receptor (CGRP)
- B. Somatostatin receptor
- C. Nitric oxide synthase (NOS)
- D. Adenosine A<sub>1</sub> receptor
- E. Glutamate receptor

**87.** Decreased levels of which of the following may increase vascular risk in migraine patients?

- A. Microglial cells
- B. Fibroblasts
- C. Endothelial progenitor cells
- D. Astrocytes
- E. All of the above

**88.** Hypocretins are:

- A. Small people of limited intelligence.
- B. Neuropeptides synthesized exclusively in the hypothalamus.
- C. Neuropeptides synthesized exclusively in the pituitary.
- D. Neuropeptides synthesized in both the pituitary and the hypothalamus.
- E. Neuropeptides with exclusive projections to dopaminergic nuclei.

**89.** Where is the sensory nucleus of the trigeminal nerve located?

- A. Midbrain
- B. Pons
- C. Rostral medulla
- D. Cervicomedullary junction
- E. All of the above

**90.** The most common tumor in the cerebellopontine (CP) angle is:

- A. Cholesteatoma
- B. Metastatic lesion
- C. Vestibular schwannoma
- D. Meningioma
- E. Epidermoid

- 91.** Which cranial nerve runs through the parotid gland?
- A. CN V<sub>2</sub>
  - B. CN V<sub>3</sub>
  - C. CN VII
  - D. CN VIII
  - E. CN IX
- 92.** Serotonin (5-HT) is synthesized in which of the following brain structures?
- A. Accumbens nucleus
  - B. Suprachiasmatic nucleus
  - C. Raphe nuclei
  - D. Supraoptic nucleus
  - E. All of the above
- 93.** Otagia, or pain in the ear, can be due to an abnormality associated with which nerves?
- A. Upper cervical (C2 and C3) nerves
  - B. CN V<sub>3</sub>
  - C. CN VII
  - D. CN IX
  - E. All of the above
- 94.** Which of the following regions is activated in patients with short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)?
- A. Cingulate gyrus
  - B. Hypothalamus
  - C. Trigeminal nucleus caudalis
  - D. Dorsal raphe nucleus
  - E. Thalamus
- 95.** Hypersensitivity of migraine sufferers to dopamine has been proposed as an explanation of what migraine phenomenon?
- A. Premonitory symptoms of nausea and yawning.
  - B. Scintillating scotomata
  - C. Osmophobia
  - D. Throbbing pain
  - E. Post headache euphoria

- 96.** Which statement gives the best evidence for a role of serotonin (5-HT) in the pathogenesis of migraine?
- A. Triptans as selective serotonin (5-HT) antagonists are used to abort migraine headaches.
  - B. Medications used to abort migraines, but not migraine preventative medications, have serotonergic effects.
  - C. Cerebral vasoconstriction is mediated through the 5-HT<sub>1D</sub> receptor subtype on meningeal vessels.
  - D. Serotonin receptor subtypes 5-HT<sub>1D</sub> and 5-HT<sub>1F</sub> mediate neurogenic inflammation.
  - E. Ergot preparations used to treat migraine only interact with serotonergic receptors.
- 97.** During an attack of migraine without aura:
- A. Levels of a serotonin (5-HT) metabolite are decreased in the urine.
  - B. Levels of a 5-HT metabolite are increased in the urine.
  - C. Levels of a 5-HT metabolite are increased in the plasma.
  - D. Serotonin levels are decreased in the plasma.
  - E. Platelet serotonin levels are increased.
- 98.** Which statement best describes CGRP?
- A. Calcitonin gene-related peptide (CGRP) is distributed in the central nervous system (CNS) but is not present in the peripheral nervous system.
  - B. Calcitonin gene-related peptide dilates cranial blood vessels.
  - C. Plasma levels of CGRP increase with treatment with triptans, corresponding with migraine relief.
  - D. Activation of CGRP receptors in humans decreases the pain of a migraine headache.
  - E. All of the above
- 99.** Cortical spreading depression (CSD) is characterized by:
- A. A decrease in intracellular sodium (Na<sup>+</sup>) and calcium (Ca<sup>2+</sup>).
  - B. An increase in membrane resistance.
  - C. An increase in extracellular potassium (K<sup>+</sup>) concentration.
  - D. A rapid propagation (20–50 mm/minute) of depolarization across major sulci.
  - E. All of the above

**100.** Interictal changes, including increased cortical thickness, have been found in which brain region of patients with migraine?

- A. Supplementary motor cortex
- B. Hippocampus
- C. Somatosensory cortex
- D. Caudate nucleus
- E. Corpus callosum

**101.** Idiopathic intracranial hypertension (IIH) may be attributed to which of the following factors?

- A. Venous outflow obstruction
- B. Increased cerebral blood volume
- C. Excessive spinal fluid production
- D. Compromised spinal fluid resorption
- E. All of the above

**102.** Visual loss in giant cell arteritis (GCA) may be caused by:

- A. Anterior ischemic optic neuropathy
- B. Cilioretinal artery occlusion
- C. Central retinal artery occlusion
- D. Occipital lobe infarction
- E. All of the above

**103.** Which area of the brain has shown anatomic change using imaging studies in patients with migraine?

- A. Cingulate cortex
- B. Periaqueductal gray matter (PAG)
- C. Subcortical white matter
- D. Cerebellum
- E. All of the above

**104.** Adiponectin:

- A. Is secreted by adipose tissue.
- B. Has anti-inflammatory properties.
- C. Inhibits the development of insulin resistance.
- D. May play a role in the development of chronic migraine.
- E. All of the above

**105.** Neuroimaging techniques indicate activation of which of the following structures in patients with trigeminal autonomic cephalalgias (TACs)?

- A. Nucleus raphe magnus
- B. Hypothalamus
- C. Periaqueductal gray (PAG) matter
- D. Nucleus tractus solitaries
- E. Trigeminal spinal nucleus

**106.** Which of the following neurotransmitters plays a critical role in CSD?

- A. Dopamine
- B. Acetylcholine
- C. Serotonin (5-HT)
- D. Glutamate
- E. Substance P

**107.** Which of the following has been linked to hemodialysis headaches?

- A. High serum phosphorus levels
- B. Low serum magnesium levels
- C. High serum potassium levels
- D. Low serum sodium levels
- E. High serum bicarbonate levels

**108.** Mutations of the TREX1 gene are associated with:

- A. Systemic lupus erythematosus (SLE)
- B. Aicardi-Goutieres syndrome
- C. Familial chilblain lupus
- D. Retinal vasculopathy with cerebral leukodystrophy
- E. All of the above

**109.** Match the disorder associated with migraine with its associated gene. Use each answer only once.

- |   |            |
|---|------------|
| A. Familial hemiplegic migraine type 1 (FHM1)   | 1. CACNA1A |
| B. Familial hemiplegic migraine type 2 (FHM2)   | 2. TREX1   |
| C. Familial hemiplegic migraine type 3 (FHM3)   | 3. SCN1A   |
| D. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) | 4. ATP1A2  |
| E. Retinal vasculopathy with cerebral leukodystrophy (RVCL)   | 5. NOTCH3  |

**110.** Symptoms from injury of which cranial nerve are seen most often in patients with spontaneous dissection of the extracranial internal carotid artery?

- A. CN III
- B. CN V
- C. CN VII
- D. CN XI
- E. CN XII

**111.** Match the cranial neuralgia with its affected cranial nerve. Use each answer only once, more than once, or not at all.

- |                                |                            |
|--------------------------------|----------------------------|
| A. Nervus intermedia neuralgia | 1. First division of CN V  |
| B. Nasociliary neuralgia       | 2. Second division of CN V |
| C. Supraorbital neuralgia      | 3. Third division of CN V  |
| D. Infraorbital neuralgia      | 4. CN VII                  |
| E. Lingual neuralgia           | 5. CN VIII                 |

**112.** Which is the most common vasoactive peptide released within the trigemino-vascular system with stimulation of the trigeminal ganglia?

- A. Vasoactive intestinal peptide
- B. Calcitonin gene-related peptide (CGRP)
- C. Substance P
- D. Neuropeptide Y
- E. Nitric oxide synthase (NOS)

**113.** Which gene is associated with FHM, medication-responsive episodic ataxia, and spinocerebellar ataxia?

- A. SCN1A
- B. NOTCH3
- C. TREX1
- D. CACNA1A
- E. ATP1A2

**114.** Match each cranial nerve with the foramen through which it traverses the skull. Each answer may be used once, more than once, or not at all.

- |   |                             |
|---|-----------------------------|
| A. Trigeminal nerve – ophthalmic division<br>(CN V <sub>1</sub> ) | 1. Foramen rotundum         |
| B. Trigeminal nerve – maxillary division<br>(CN V <sub>2</sub> )  | 2. Foramen ovale            |
| C. Trigeminal nerve – mandibular division<br>(CN V <sub>3</sub> ) | 3. Stylomastoid foramen     |
| D. Facial nerve (CN VII)  | 4. Jugular foramen          |
| E. Glossopharyngeal nerve (CN IX)                                 | 5. Superior orbital fissure |

**115.** Which of the following innervates the right orbicularis oculi muscles?

- The bilateral corticobulbar tracts
- The right corticobulbar tract
- The left corticobulbar tract
- The bilateral motor nuclei of VII
- The left motor nucleus of VII

**116.** Which of the following structures does *not* run through the cavernous sinus?

- Ophthalmic nerve (CN V<sub>1</sub>)
- Maxillary nerve (CN V<sub>2</sub>)
- Facial nerve (CN VII)
- Internal carotid artery
- Trochlear nerve (CN IV)

**117.** A variant of which of the following genes may indicate increased risk for migraine?

- Prothrombin G20210A Gene
- Factor V Leiden
- Methylenetetrahydrofolate reductase gene
- Protein Z gene
- PROS1 gene

**118.** Which of the following is seen frequently on the interictal electroencephalogram (EEG) of patients with migraine?

- Left temporal slowing
- Increased photic driving response
- Suppression of  $\alpha$  rhythm
- Periodic lateralized epileptiform discharges (PLEDs)
- All of the above

**119.** Which of the following is a clinically useful CSF biomarker for primary headache disorders?

- A. Tumor necrosis factor (TNF)- $\alpha$
- B. Somatostatin
- C. Substance P
- D. Calcitonin gene-related peptide (CGRP)
- E. None of the above

**120.** Which brain area has been found to be abnormal in MRI studies of patients with migraine headaches?

- A. Frontal lobes
- B. Brainstem
- C. Subcortical areas
- D. Cerebellum
- E. All of the above

**121.** Direct mechanical stimulation of which of the following brain regions is associated with production of migraine-like headaches?

- A. Hypothalamus
- B. Periaqueductal gray (PAG)
- C. Posterior cingulate cortex
- D. Occipital cortex
- E. All of the above

**122.** What is the rate of CSD of Leão?

- A. 0.5–2 mm per minute
- B. 3–4 mm per minute
- C. 6–8 mm per minute
- D. 10–12 mm per minute
- E. 13–15 mm per minute

**123.** According to the CAMERA study, incidental infarct-like MRI lesions are most commonly found in which area of the brain?

- A. Frontal cortex
- B. Occipital cortex
- C. Parietal cortex
- D. Cerebellum
- E. Brainstem



**124.** Which of the following is a potential mechanism for topiramate in blocking neuronal hyperexcitability?

- A. Potentiation of  $\gamma$ -aminobutyric acid (GABA)
- B. Blockade of AMPA and kainate receptors
- C. Blockage of voltage-dependent sodium channels
- D. Blockage of calcium channels
- E. All of the above

**125.** A 58-year-old woman developed brief, lancinating episodes of pain in the throat, radiating to the left side of her neck around the angle of her mandible. She describes that the pain could be triggered by swallowing or sticking out her tongue. What nerve is causing her pain?

- A. CN V<sub>2</sub>
- B. CN V<sub>3</sub>
- C. CN VII
- D. CN IX
- E. CN X

**126.** The tongue is innervated by multiple cranial nerves. Match the tongue function with the correct cranial nerve. Each answer may be used once, more than once, or not at all.

- |   |           |
|---|-----------|
| A. General sensation to the anterior two-thirds | 1. CN V   |
| B. General sensation to the posterior one-third | 2. CN VII |
| C. Taste to the anterior two-thirds             | 3. CN IX  |
| D. Taste to the posterior one-third             | 4. CN XI  |
| E. Motor control                                | 5. CN XII |

**127.** The convergence hypothesis:

- A. Supposes that most sinus headaches are migraine headaches.
- B. Postulates a shared pathophysiological mechanism in a migraineur with multiple primary headache types.
- C. Assumes that menstrual and episodic migraine have a similar pathophysiological mechanism.
- D. Dictates that patients with episodic migraine will develop chronic migraine.
- E. All of the above

**128.** A pain syndrome, which may involve the face, can develop after a stroke in the vascular territory of which vessel?

- A. Anterior cerebral artery
- B. Middle cerebral artery
- C. Internal carotid artery
- D. External carotid artery
- E. Basilar artery

**129.** Which of the following is *not* directly associated with hypothalamic dysfunction?

- A. Chronic migraine headaches
- B. Gelastic seizures
- C. Multiple sclerosis (MS)
- D. Narcolepsy
- E. Hemicrania continua

**130.** Which is the only cranial nerve that emerges from the dorsal brainstem?

- A. Oculomotor nerve (CN III)
- B. Trochlear nerve (CN IV)
- C. Trigeminal nerve (CN V)
- D. Abducens nerve (CN VI)
- E. Facial nerve (CN VII)

**131.** Which hypothalamic nucleus plays a key role in the sleep–wake cycle?

- A. Paraventricular nucleus
- B. Suprachiasmatic nucleus
- C. Supraoptic nucleus
- D. Lateral preoptic nucleus
- E. Arcuate nucleus

**132.** Which neurotransmitter is most closely associated with vomiting?

- A. Noradrenaline
- B. Calcitonin gene-related peptide (CGRP)
- C. Acetylcholine (ACh)
- D. Substance P
- E. Vasoactive intestinal peptide

**133.** A 30-year-old woman complains of mild headaches, left-sided numbness for 2 weeks, and double vision starting 3 days ago. On examination, she has decreased sensation to light touch and pin-prick in her left face, arm, and leg. On right gaze, she is unable to move past midline with her left eye, and she develops horizontal nystagmus in the right eye. Eye movement to the left and convergence are normal. Where is her brainstem lesion?

- A. Left medial longitudinal fasciculus
- B. Right medial longitudinal fasciculus
- C. Left superior colliculus
- D. Right paramedian pontine reticular formation
- E. Left paramedian pontine reticular formation

**134.** The MRIs of migraineurs may show:

- A. Cerebellar infarct-like lesions
- B. Supratentorial periventricular white matter lesions (WMLs)
- C. Supratentorial deep subcortical WMLs
- D. Pontine lesions
- E. All of the above

**135.** Levels of which neuropeptide are increased in cranial venous outflow during the pain of migraine, cluster headache, and trigeminal neuralgia?

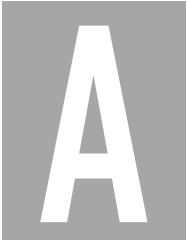
- A. Neuropeptide Y
- B. Vasoactive intestinal peptide
- C. Calcitonin gene-related peptide (CGRP)
- D. Substance P
- E. All of the above

**136.** Which area of the brain showed a significant volumetric decrease on MRI in migraineurs as compared to healthy controls?

- A. Calcarine cortex
- B. Cingulate cortex
- C. Pons
- D. Corpus callosum
- E. Prefrontal cortex

**137.** Which cranial nerve supplies sensation to the external auditory meatus and the tympanic membrane?

- A. CN V
- B. CN VII
- C. CN IX
- D. CN X
- E. All of the above



# HEADACHE ANATOMY AND PHYSIOLOGY

## ANSWERS

**61. The answer is C.** Hemicrania continua is a strictly unilateral, continuous headache of moderate intensity pain, with superimposed intermittent episodes of severe pain. These indomethacin-responsive headaches are accompanied by trigeminal autonomic features and migrainous symptoms. Seven patients with hemicrania continua who were studied using positron emission tomography (PET), showed significant activation of the contralateral posterior hypothalamus and ipsilateral dorsal rostral pons. Also noted were activation of the ipsilateral ventrolateral midbrain, with extension to the red nucleus and the substantia nigra, and of the bilateral pontomedullary junction. Hypothalamic activation has also been seen in patients with trigeminal autonomic cephalalgias (TACs; cluster headache (CH), paroxysmal hemicrania (PH), short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing/cranial autonomic features [SUNCT/SUNA]) and migraine headaches. This study illustrated that hemicranias continua, which is not classified as a TAC, shares pathophysiological mechanisms with TACs and migraine. (Matharu, Cohen, McGonigle, et al. *Headache* 2004)

**62. The answer is E.** Although the trochlear nerve (CN IV) is the cranial nerve with the fewest neurons, it has the longest intracranial course after it exits from the dorsal surface of the midbrain. The nerve curves around the cerebral peduncle to emerge between the posterior cerebral artery and the superior cerebellar artery. After coursing through the cavernous sinus (along with CNs III, V<sub>1</sub>, V<sub>2</sub>, and VI), CN IV enters the orbit through the superior orbital fissure, running along the roof of the orbit to innervate the superior oblique muscle. (Wilson-Pauwels, Akesson, & Stewart, *Cranial Nerves*, 1988)

**63. The answer is C.** CAMERA, a cross-sectional prevalence study, used brain magnetic resonance imaging (MRI) to screen for infarcts and periventricular and deep white matter lesions (WMLs) in migraineurs with and without aura. Patients

with migraine had a higher prevalence of cerebellar infarcts than did controls; the highest risk was in patients with migraine with aura, with one or more attacks per month (odds ratio [OR], 15.8; 95% confidence interval [CI], 1.8–140). The prevalence of deep WMLs was increased in women with migraine as compared to controls. This increased risk for deep WMLs in women was similar in women with migraine with or without aura, and was higher in migraineurs with increased attack frequency. The prevalence of deep WMLs was not different between male controls and male migraineurs. No correlation was seen between periventricular WMLs and migraine, irrespective of gender or migraine frequency or subtype. Analysis of migraineurs with deep white matter lesions has found no correlation with the presence of PFO. (Kruit, van Buchem, Hofman, et al. *JAMA* 2004)

**64. The answer is B.** The periaqueductal gray (PAG) modulates trigeminovascular nociception. Welch et al. studied iron homeostasis in the midbrain of patients with episodic migraine (EM) and with chronic daily headache (CDH). High-resolution magnetic resonance techniques were used to measure non-heme iron in tissues by transverse relaxation rates. Iron homeostasis in the PAG was impaired in the EM and CDH groups, correlating with frequency of headaches. The degree of iron deposition correlated with length of headache suffering. The findings that headaches can be precipitated by a lesion in the PAG and that iron deposition in the PAG correlates with headache chronicity suggest that the PAG may modulate migraine attacks by dysfunctional control of the trigeminovascular nociceptive system. (Welch, Nagesh, Aurora, et al., *Headache* 2001; Cutrer & Black, *Headache* 2006)

**65. The answer is A.** Information processing, as measured by visual and auditory evoked responses, is abnormal in migraineurs who show lack of interictal habituation. Habituation may be a protective mechanism to conserve energy and to prevent the brain from experiencing sensory overload. This habituation pattern may be a familial trait marker that can be used to predict migraine risk. Interictal lack of habituation has been found on blink response (a trigeminofacial brainstem reflex) on electromyogram. Latencies and amplitudes on evoked response testing are not reliably abnormal in patients with migraine. (Gantenbein & Sándor, *Headache* 2006)

**66. The answer is A.** The SCN1A gene encodes the  $\alpha_1$  subunit of neuronal voltage-gated sodium ( $\text{Na}_v1.1$ ) channels involved in the generation and propagation of action potentials. Multiple SCN1A gene mutations have been associated with different types of epilepsy syndromes. The SCN1A gene mutation, which is associated with familial hemiplegic migraine (FHM) type 3, is the least common FMH-associated gene mutation. Mutations of the CACNA1A and the ATP1A2

genes are associated with FHM types 1 and 2 respectively. Patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) have a mutation in the NOTCH3 gene. The TREX1 gene mutation is linked to retinal vasculopathy with cerebral leukodystrophy. (Van den Maagdenberg, Haan, Terwindt, et al., *Curr Opin Neurol* 2007)

**67. The answer is C.** Although calcitonin gene-related peptide, substance P, serotonin (5-HT), and prostaglandins are some of the multiple endogenous agents that mediate neurogenic inflammation in primary headache, and possibly hemodialysis headache, bradykinin modulation of nitric oxide (NO) synthesis is thought to play an important role in its triggering. Nitric oxide is increased in the plasma of patients with a hemodialysis headache, which may be mechanistically similar to an NO donor headache. (Antonizzi & Corrado, *Curr Pain Headache Rep* 2007)

**68. The answer is E.** Ischemic optic neuropathy (ION) produces monocular visual loss due to an infarction of the anterior, or, less commonly posterior, segment of the optic nerve. ION is usually due to disease of small perforating arteries in older individuals, who may have traditional vascular risk factors, including hypertension, diabetes, hyperlipidemia, or thrombophilias. Other causes of ION include large-vessel internal carotid artery disease due to atherosclerosis, arteritis, or dissection. Posterior ION may be nonarteritic, arteritic (giant cell arteritis [GCA] in older patients), or associated with systemic surgery. Patients with anterior ION experience subacute painless visual loss with an afferent pupillary defect and a swollen optic nerve head. Posterior (retrobulbar) ION is characterized by vision loss with a normal fundoscopic examination initially, followed by optic nerve atrophy. (Fontal, Kerrison, Garcia, et al., *Semin Neurol* 2007)

**69. The answer is C.** Nervus intermedius neuralgia is a neuropathic pain in the distribution of the sensory branch of the facial nerve (CN VII). The intermittent, excruciating, lancinating pain of nervus intermedius neuralgia is localized deep in the external auditory canal. Due to its close anatomic proximity, temporomandibular dysfunction should be considered in a patient with external auditory canal pain. (Figueiredo, Vazquez-Delgado, Okeson, et al., *Cranio* 2007)

**70. The answer is C.** Cerebral perfusion studies during the migraine aura have shown variable results, but the most consistent area of involvement has been the occipital cortex. Reductions in regional cerebral blood flow (rCBF) in the occipital cortex have been found in xenon inhalation studies of migraineurs with aura. The mild reduction in rCBF (oligemia) was less than the reduction in rCBF as-

sociated with ischemia. Perfusion-weighted magnetic resonance imaging studies of migraine with aura have shown inconsistent reduction of rCBF in the occipital cortex. A PET study of a patient with a spontaneous migraine headache with only transient blurring of vision showed bilateral spreading hypoperfusion beginning in the visual association cortex (Brodmann areas 18 and 19). The occipital activation due to cortical spreading depression (CSD) may play a role in migraine without typical visual aura. (Wood, Jacoboni, & Mazziotta, *N Engl J Med* 1994; Cutrer & Black, *Headache* 2006)

**71. The answer is A 2, B 3, C 4, D 1, E 5.** Cranial nerve palsies, with injury due to mechanical or ischemic mechanisms, can occur in over 10% of patients with dissection of the extracranial internal carotid artery. Disruption of lower cranial nerves, specifically cranial nerves IX, X, XI (dysphagia, hoarseness), and XII (tongue deviation), is the most common cranial nerve syndrome associated with internal carotid artery dissection. Ischemic optic neuropathy (optic nerve ischemia) and Horner's syndrome (postganglionic oculo-sympathetic paresis) can also occur with internal carotid artery dissection. Dysgeusia, an alteration of taste sensation, is due to a lesion of the chorda tympani nerve, a branch of cranial nerve VII, which supplies taste to the anterior two-thirds of the tongue. (Mokri, Silbert, Schievink, et al., *Neurology* 1996)

**72. The answer is D.** Patients with CADASIL have a mutation in the NOTCH3 gene, which encodes for a receptor involved in the functioning of vascular smooth muscle cells in small arteries and arterioles. Familial hemiplegic migraine is a genetically heterogeneous migraine disorder associated with mutations in the CACNA1A (FHM1), ATP1A2 (FHM2), and SCN1A (FHM3) genes. TREX1 is involved in the cellular response to oxidative stress, and has been identified as the causal gene for autosomal dominant retinal vasculopathy with cerebral leukodystrophy (RVCL). Migraine and Raynaud's phenomenon have been associated with RVCL. (Stam, van den Maagdenberg, Haan, et al., *Curr Opin Neurol* 2008)

**73. The answer is E.** Horner's syndrome, or oculosympathetic paresis, results from disruption of the sympathetic innervation of the eye and presents with miosis, ptosis, and often facial anhidrosis (lack of sweating) on the affected side. First-order neurons descend from the dorsolateral hypothalamus to the midbrain; they pass anterolaterally through to the medulla, close to the spinothalamic tract and vestibular nucleus (lateral medullary syndrome). The first-order neurons synapse in the lower cervical spinal cord. The second-order neurons exit the spinal cord at the C8 to T2 roots to form the inferior (in proximity to the lung apex) and middle cervical ganglia. The preganglionic sympathetic trunk fibers synapse in the supe-



rior cervical ganglion, located near the bifurcation of the common carotid artery. The third-order neurons form a sympathetic plexus, the internal carotid nerve, with branches that lie within the cavernous sinus. The third-order neurons innervate the blood vessels, pupil, muscles of the lid, and lacrimal glands of the eye. A Horner's syndrome may be congenital (associated with heterochromia) or acquired. A new onset Horner's syndrome and acute head and/or neck pain may indicate a TAC (hypothalamic mediated) or cervical internal carotid artery dissection. (George, Haydar, & Adams, *Clin Radiol* 2008)

**74. The answer is D.** The dura, the outermost meningeal layer covering the brain, is adherent to the inner table of the skull. The periosteal and meningeal layers of the dura separate to accommodate the venous sinuses. The leptomeninges are made up of outer (arachnoid) and inner (pia) layers. The arachnoid layer is attached to the dura; the pial layer is intimately adherent to the surface of the brain. Cerebrospinal fluid (CSF) flows beneath the arachnoid layer; the arachnoid layer, which is attached to the dura, does not dip down into sulci of the brain. (Gartner & Patestas, *Textbook of Neuroanatomy*, 2006)

**75. The answer is C.** Subdural hematomas are acute, subacute, or chronic collections of blood that generally accumulates after traumatic rupture of bridging veins. Depending of the age of the blood, they are hyper-, hypo-, or isodense crescent-shaped collections on computed tomography (CT) scanning that do not cross the falx of the brain. Small chronic subdural hematomas are found not infrequently on neuroimaging of elderly individuals who are prone to falls or on chronic anticoagulation; surgical evacuation may not be required. Metastatic disease to the dura may hemorrhage, causing nontraumatic, spontaneous subdural hematomas in the setting of cancer. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging*, 2004)

**76. The answer is E.** Headache in a patient with cancer may have many causes. An acquired thrombophilia in patients with solid tumors can result in cerebral venous thrombosis that may present with a headache, followed by seizures or focal neurologic deficits from venous infarction and intracerebral hemorrhage. Cancer patients may bleed spontaneously into the brain or its coverings due to a systemic blood dyscrasia related to the cancer or its therapy. Cancer patients may hemorrhage into a metastatic or primary tumor in the brain, skull, dura, or leptomeninges. Spinal fluid analysis and an enhanced MRI of the brain and spine may diagnose leptomeningeal metastatic or infectious disease. Opportunistic infections, especially fungal infections, can complicate cancer or its treatment. (Rogers, *Neurol Clin* 2003)

**77. The answer is C.** The pathogenesis of tension-type headache (TTH) is multifactorial and poorly understood. Pericranial myofascial mechanisms appear important in episodic tension-type headache (ETTH), whereas sensitization of central pain pathways appear to factor into chronic tension-type headache (CTTH). Although neurotransmitters, such as calcitonin-gene-related peptide (CGRP), substance P, and 5-HT, are implicated in the activation of the trigeminovascular system leading to migraine headaches, their role in the evolution from ETTH to CTTH is not clear. Genetic studies indicate a genetic influence for CTTH, but not for ETTH; however, genetic predilection does not appear to influence risk of progression from ETTH to CTTH. Although myofascial factors come into play in ETTH, muscular inflammation does not appear important in the pathogenesis of CTTH. Active myofascial trigger points (hyperirritable spots in skeletal muscle) are associated with both TTH and CTTH, but do not appear to be related to the chronification of TTH. (Fumal & Schoenen, *Lancet Neurol* 2008)

**78. The answer is B.** Familial hemiplegic migraine is a genetically heterogeneous migraine disorder associated with mutations in the CACNA1A (FHM1), ATP1A2 (FHM2), and SCN1A (FHM3) genes. Approximately 15% of patients with sporadic hemiplegic migraine (SHM) have a functional mutation of an FHM-associated gene. Sporadic hemiplegic migraine has been most commonly associated with the ATP1A2 mutations. Mutations of genes associated with FHM have also been found in FHM family members who have nonhemiplegic typical migraine with and without aura. Nonhemiplegic migraine, SHM, and FHM appear to be part a continuum with a shared pathogenetic mechanism. (De Vries, Haan, Frants, et al., *Headache* 2006; Stam, van den Maagdenberg, Haan, et al., *Curr Opin Neurol* 2008)

**79. The answer is B.** This woman has an incidental finding that is unrelated to her migraine headaches. The lighter iris color on the left, with decreased pupil size (miosis) more noticeable in the dark and an upper eyelid ptosis, indicate a congenital Horner's syndrome (oculosympathetic paresis). Melanocytes in the superficial stroma of the iris are sympathetically innervated and congenital denervation or denervation in infancy leads to heterochromia. The lighter-colored iris is on the side of the disruption of the sympathetic fibers as they course through two synapses (first-, second-, and third-order neurons) from the hypothalamus to the eye. If the oculospmpathetic paresis with heterochromia is longstanding in an adult, as determined by photographs, there is less concern about determining its cause. Children with a presumed congenital Horner's syndrome with heterochromia should be evaluated for an underlying lesion, although a Horner's syndrome may occur after forceps delivery. (Gesundheit & Greenberg, *N Engl J Med* 2005)

**80. The answer is B.** Hypnic headache appears to be a chronobiological disorder, with elderly patients experiencing headache at the same time of night. The onset of hypnic headache attacks is associated with rapid eye movement (REM) sleep, as determined by polysomnography. The headache does not seem to be associated with nocturnal oxygen desaturation or hypertension. Although sleep apnea maybe associated with headache on awakening, the elderly men and women who experience hypnic headaches generally do not have obstructive sleep apnea. (Evans & Goadsby, *Neurology* 2003)

**81. The answer is A.** Serotonin (5-hydroxytryptamine; 5-HT) is synthesized to 5-hydroxytryptophan from tryptophan through the rate-limiting enzyme tryptophan hydroxylase (TPH), which exists in two isoforms. Then, 5-hydroxytryptophan is decarboxylated by L-amino acid decarboxylase into 5-HT. The TPH2 isoform is brain specific and is exclusively expressed in neurons located within the brainstem raphe nucleus, with projections throughout the brain. Serotonin is degraded by monoamine oxidase (MAO) into its primary metabolite, 5-hydroxyindoleacetic acid (5-HIAA). The caution about the use of MAO inhibitors in combination with serotonergic medications is due to the possibility of inducing a symptomatic excess of serotonin. (Hamel, *Cephalalgia* 2007)

**82. The answer is A.** Increased pain sensitivity in the pericranial region of patients with TTH may be partially due to peripheral sensitization of nociceptors in myofascial tissues. Patients with CTTH are more sensitive to stimuli applied to cephalic and extracephalic regions than are patients with ETTH. General pain sensitivity in the central nervous system (CNS) is increased in patients with CTTH, whereas the central pain processing seems to be normal in patients with ETTH. No consistent elevation of CSF or plasma levels of CGRP has been noted in patients with TTH. Sensitization of pain pathways is associated with activation of NO synthase (NOS) and generation of NO. Inhibition of NO in CTTH has shown reduction in headache intensity and decreased muscle hardness and tenderness. (Ashina, Bendtsen, & Ashina, *Curr Pain Headache Rep* 2005)

**83. The answer is E.** Putative mechanisms for menstrual migraine are complex and multifactorial. Decreased plasma estrogen, but not progesterone, in the late luteal phase of the menstrual cycle increases the risk of menstrual migraine. Other mechanisms for menstrual migraine are less well understood. Suppression of serotonergic and opiategic neurotransmitter systems, which are regulators of trigeminal pain pathways, during the late luteal and early follicular phases may increase the risk of migraine during this part of the cycle. Elevated plasma levels

of prostaglandins during menstruation may also contribute to the onset of menstrual migraine. (Newman, *Headache* 2007)

**84. The answer is B.** The total CSF volume is renewed about four times per day in humans. The rate of turnover of CSF declines with age, in part due to the declining ability of the choroid plexus to form CSF. (Johanson, Duncan, Klinge, et al., *Cerebrospinal Fluid Res* 2008)

**85. The answer is E.** Genetic biomarkers for migraine are genetic variations (mutations or polymorphisms) that can predict migraine susceptibility, disease outcome, or response to acute or preventative headache treatment. Mutations in three different genes known to be responsible for FHM (CACNA1A, ATP1A2, and SCN1A for FHM 1, 2, 3 respectively) and the MTHFR C677T polymorphism in migraine with aura are genetic biomarkers that have been replicated in clinical studies of patients with migraine. However, many contender genetic biomarkers for migraine have not showed linkage with repeated investigation. (De Vries, Haan, Frants, et al., *Headache* 2006)

**86. The answer is A.** Early results of parenteral and oral CGRP antagonists in the treatment of acute migraine are encouraging, and CGRP antagonists are projected to be an acute treatment of migraine without vascular risk. The benefits from treating acute migraine with NOS blockers, glutamate blockade, and adenosine A<sub>1</sub> receptor agonists are still theoretical. A somatostatin agonist has shown benefit, preliminarily, in patients with CH. (Goadsby, *Curr Opin Neurol* 2005)

**87. The answer is C.** Migraine carries an increased risk for cardiovascular and cerebrovascular diseases that cannot be explained by traditional vascular risk factors. The circulating endothelial progenitor cell (EPC) number is a surrogate biologic marker of vascular function, and diminished EPC counts are associated with increased vascular risk. EPCs circulate in peripheral blood and are capable of proliferating and differentiating into endothelial cells. They play a role in neovascularization and in endothelial repair after atherosclerotic injury. A study investigating abnormalities in EPC levels and functions in migraine patients found that circulating EPC numbers and function were reduced in migraine patients, as compared to patients with TTH and controls. EPC levels can be added to the other intriguing links between migraine and vascular risk. (Lee, Chu, Jung, et al., *Neurology* 2008; Elkind, *Neurology* 2008)

**88. The answer is B.** Hypocretins (orexins) are neuropeptides synthesized by neurons located exclusively in the hypothalamus. Hypocretin-containing neu-

rons project throughout the CNS to monoaminergic and serotonergic brainstem centers. The hypocretin system may be involved in pain modulation in the CNS, and is involved in physiological processes such as feeding, arousal, and reward. There may be a pathophysiological role for the hypocretin neuronal system in CH and chronic migraine. (Rainero, De Martino, & Pinessi, *Expert Rev Neurother* 2008)

**89. The answer is E.** The motor nucleus of trigeminal nerve is located in the mid pons. The sensory nucleus of the trigeminal nerve is the largest cranial nerve nucleus and extends caudally from the midbrain to the second cervical segment of the spinal cord. It has three subnuclei: the mesencephalic nucleus, the pontine trigeminal nucleus, and the nucleus of the spinal tract of the trigeminal nerve. The three divisions of the trigeminal nerve join at the trigeminal ganglion, with the sensory root entering the midlateral pons. The first-order neurons synapse with the second-order neurons, whose cell bodies make up the trigeminal sensory nuclei. Second-order neurons project within the brainstem and crossed cortical (trigeminothalamic tract) regions. Third-order neurons in the thalamus (including in the ventral posterior nucleus) project through the internal capsule to cortical regions. (Gartner & Patestas, *Textbook of Neuroanatomy*, 2006)

**90. The answer is C.** All the tumors listed can be found in the cerebellopontine (CP) angle, but the most common pathologic CP angle lesion is the relatively slow growing vestibular schwannoma arising from cranial nerve VIII. Initial symptoms include vertigo, tinnitus, and deafness. The tumor may eventually involve cranial nerve VII in the internal auditory canal, at which point facial weakness develops. Signs of cerebellar involvement due to direct compression and of increased intracranial pressure due to obstruction of CSF outflow may develop as the tumor expands. Very rarely, a schwannoma can expand abruptly due to hemorrhage within the tumor. (Bonneville, Savatovsky, & Chiras, *Eur Radiol* 2007)

**91. The answer is C.** The facial nerve (CN VII) emerges through the skull in the stylomastoid foramen, passing through the parotid gland, before it branches to innervate muscles of facial expression. The parotid gland is at the angle of the jaw, inferior and anterior to the ear. Although unilateral facial weakness due a lower motor neuron lesion of the facial nerve is usually due to an idiopathic Bell's palsy, an expanding neoplasm or other lesion in the parotid gland may produce ipsilateral facial weakness. Secretion of saliva by the parotid gland is controlled by parasympathetic fibers of the inferior salivatory nucleus of the glossopharyngeal nerve (CN IX). Despite innervation of the parotid itself by other cranial nerves, only the facial nerve runs through the gland. (Veillon, Taboada, Eid, et al., *Neuroimaging Clin N Am* 2008)

**92. The answer is C.** The serotonergic system from the brainstem raphe nuclei has been implicated in migraine pathophysiology. 5-Hydroxytryptamine (5-HT) or serotonin is synthesized from the essential amino acid tryptophan. The brain-specific isoform of the rate limiting enzyme tryptophan hydroxylase (TPH) is exclusively expressed in neurons located within the raphe nuclei that send projections throughout the brain. Changes in 5-HT metabolism during and between migraine attacks and the clinical response to migraine medications that manipulate serotonergic receptors suggest that migraine is a consequence of a central neurochemical imbalance in which a low 5-HT state facilitates activation of the trigeminovascular nociceptive pathway, as induced by CSD. The accumbens nucleus, located near the head of the caudate, synthesizes  $\gamma$ -aminobutyric acid (GABA). Vasopressin is synthesized in the hypothalamic supraoptic and supra-chiasmatic nuclei. (Hamel, *Cephalalgia* 2007)

**93. The answer is E.** The sensation of the ear is served by the second and third cervical nerves (great auricular nerve), the auriculotemporal branch of the mandibular nerve (CN V<sub>3</sub>), and branches of the facial nerve (CN VII), the glossopharyngeal nerve (CN IX), and the vagus nerve (CN X). (Gartner & Patesta, *Textbook of Neuroanatomy* 2006)

**94. The answer is B.** All the listed regions are involved in the pathophysiology of headaches; however, the posterior hypothalamus is activated in functional imaging studies of primary SUNCT. The hypothalamus may be a central generator for primary TACs. Activation of the hypothalamus has been found in TACs, including CH, PH, and SUNCT. The hypothalamic activation in SUNCT may be ipsilateral to the pain or may be bilateral. (Cohen, *Cephalalgia* 2007)

**95. The answer is A.** Dopamine may be involved in the modulation of trigeminovascular transmission, and appears to play a role in premonitory symptoms, especially yawning and nausea. Dopamine may also contribute to hypotension during migraine. Migraine sufferers appear to be hypersensitive to dopamine agonists, with increased yawning, nausea, vomiting, dizziness, and sweating. Dopamine D<sub>2</sub> antagonists are antiemetics used in the treatment of migraine-associated symptoms. Data indicating a role for dopamine in the induction of head pain are conflicting. The role of dopamine in the pathophysiology of migraine is not as strong as for other neurotransmitters, including serotonin, NO, and CGRP. (Akerman & Goadsby, *Cephalalgia* 2007)

**96. The answer is D.** Serotonin (5-HT) and its receptors play a major role in the pathophysiology of headaches. Cerebral vasoconstriction is mediated through the

5-HT<sub>1B</sub> receptor subtype on meningeal vessels. Agonistic activity of the 5-HT<sub>1D</sub> and 5-HT<sub>1F</sub> receptors leads to inhibition of vasogenic peptide release, neurogenic inflammation, and firing of trigeminal afferents. Triptans, selective serotonin (5-HT<sub>1B/1D</sub>) agonists, are used to abort migraine headaches. Ergots, including ergotamine and dihydroergotamine, used to abort migraine headaches via serotonergic agonist effects, also interact with noradrenergic and dopaminergic receptors. Medications used to abort migraines and migraine preventative medications both have serotonergic effects. (Schwedt, *Cephalalgia* 2007)

**97. The answer is B.** Serotonin and its receptors are implicated in the pathophysiology of multiple headache types. Serotonin (5-HT) is generally an inhibitory neurotransmitter that is broken down by monoamine oxidase to make 5-hydroxyindolacetic acid (5-HIAA). Levels of 5-HT and 5-HIAA are altered in subjects during a migraine without aura, with an increase in 5-HT and a decrease in 5-HIAA in the plasma. The concentration of the metabolite 5-HIAA in the urine is increased during a migraine attack. Platelets are the main repository of 5-HT in the blood, with reduction of platelet serotonin levels during a migraine without aura. (Schwedt, *Cephalalgia* 2007)

**98. The answer is B.** Calcitonin gene-related peptide is a 37-amino acid neuropeptide that has an important role in migraine pathophysiology. It is distributed in both the central and the peripheral nervous systems, and is widely expressed on trigeminal nerve endings. Stimulation of the trigeminal ganglion results in release of CGRP, a potent cerebral vasodilator. Plasma levels of CGRP increase during a migraine attack and decrease with triptan treatment, corresponding with migraine relief. Blockade of CGRP receptors in humans decreases the pain of a migraine headache, and CGRP antagonists show promise as an abortive treatment of migraine, without vasoconstrictive properties. (Doods, Arndt, Rudolf, et al., *Trends Pharmacol Sci* 2007)

**99. The answer is C.** With the initiation of neuronal depolarization, voltage-sensitive calcium (Ca<sup>2+</sup>) channels open, and the presynaptic Ca<sup>2+</sup> influx increases glutamate release into the synaptic cleft. An increase in extracellular potassium (K<sup>+</sup>) and glutamate concentration initiate CSD. Glutamate binds to its postsynaptic receptor with termination of the depolarization. The propagation velocity of CSD is on the order of 2–5 mm per minute, with a pattern of vasodilation followed by vasoconstriction. The phenomenon of spreading depression is not unique to the cortex and has been reported in other cerebral structures including the cerebellum. (Moskowitz, *Headache* 2007; Sanchez Del Rio, Reuter, & Moskowitz, *Curr Opin Neurol* 2006)



**100. The answer is C.** A case-control cohort study measuring cortical thickness of the somatosensory cortex (SSC) of patients with migraine with and without aura, found that migraineurs had, on average, increased thickness in the caudal SSC, where the trigeminal area, including head and face, is somatotopically represented. The SSC plays a role in somatosensory processing of pain. Thickening in the SSC correlated with diffusion abnormalities observed in the subcortical trigeminal somatosensory pathway of the same migraine cohort. The authors of the study opined that repetitive migraine attacks were related to neuroplastic changes in cortical and subcortical structures of the trigeminal somatosensory system. (DaSilva, Granziera, Snyder, et al., *Neurology* 2007)

**101. The answer is E.** All the listed factors are considered as possible etiologies for idiopathic intracranial hypertension (IIH). Venous sinus hypertension increases CSF pressure, possibly through an increased resistance to CSF absorption due to an insufficiently high driving pressure gradient from the subarachnoid space to the venous system. Studies evaluating an increase in cerebral blood volume have revealed variable results. Overproduction of CSF is an attractive theory to explain IIH; but normal or decreased ventricular size seen on MRI does not appear consistent with this hypothesis. An abnormally increased spinal fluid outflow resistance has been demonstrated in IIH. (Skau, Brennum, Gjerris, et al., *Cephalalgia* 2006)

**102. The answer is E.** The most common serious complication of GCA in elderly individuals is vision loss, which can be monocular, binocular, or hemianopic. Monocular vision loss may be due to anterior ION, cilioretinal artery occlusion, central retinal artery occlusion, and posterior ION. The posterior ciliary arteries are most commonly involved with monocular visual loss. Occipital lobe infarction from vertebral artery disease with GCA may occasionally cause hemianopic visual deficits. (Hall & Balcer, *Curr Treat Opt Neurol* 2004)

**103. The answer is E.** Magnetic resonance imaging studies clearly indicate the anatomic toll that migraine headaches take on the brain. Nonheme iron deposition in the periaqueductal grey, as well as a decreased size of the cingulate cortex, has been reported in the brains of migraineurs. Subcortical (deep) WMLs and infarct-like lesions in the cerebellum are more prominent in the MRIs of migraineurs, as compared to control patients. Migraineurs have been found to have increased thickness in the caudal SSC, where the trigeminal area, including head and face, is somatotopically represented. The MRIs of migraineurs may show sulcal prominence and decreased gyral size out of proportion to age. (Cutter & Black, *Headache* 2006)



**104. The answer is E.** Adiponectin, an adipocytokine secreted by adipose tissue, may inhibit insulin resistance, dyslipidemia, and atherosclerosis. Despite being produced by adipose tissue, adiponectin is decreased in obesity. Adiponectin exhibits anti-inflammatory properties, with inhibition of interleukins and with induction of anti-inflammatory cytokines. Adiponectin levels are inversely correlated with C-reactive protein (CRP), tumor necrosis factor (TNF)- $\alpha$ , and interleukin (IL)-6 levels. A possible correlation between CRP, TNF- $\alpha$ , and IL-6 and migraine attacks may indicate a correlation between migraine and adiponectin. Insulin sensitivity is impaired in migraine, and obesity is a risk factor for the transformation from episodic to chronic migraine. (Peterline, Bigal, Tepper, et al., *Cephalalgia* 2007)

**105. The answer is B.** Trigeminal autonomic cephalgias (TACs) are characterized by unilateral trigeminal distribution pain accompanied by ipsilateral cranial autonomic symptoms. The TACs include CH, PH, and SUNCT/SUNCA. Structural and functional neuroimaging supports a role for hypothalamic dysfunction in all TACs. The strongest hypothalamic correlation is with CH. The exact anatomic location of hypothalamic activation with different TACs, as determined by neuroimaging studies, is variable. Many pain-modulating structures have connections to the hypothalamus, including the structures listed as alternative choices, through multiple putative pathways. The orexinergic system has projections from orexin- (hypocretin-) containing cells in the posterolateral hypothalamus to multiple areas in the neuroaxis. Somatostatinergic pathways and opioidergic mechanisms have also been suggested to explain the role of the hypothalamus in the generation of TAC pain and dysautonomia. (Matharu & May, *Curr Pain Headache Rep* 2008)

**106. The answer is D.** The excitatory amino acid neurotransmitter glutamate and the N-methyl-D-aspartate (NMDA) receptor are critical in the initiation, propagation and inhibition of CSD. Glutamate applied to the cortex can initiate spreading depression, and antagonism of the NMDA receptor can block CSD. The beneficial effect of magnesium in the acute and chronic treatment of headache may relate to its antagonistic effect on the NMDA receptor. The depolarization of glutaminergic neurons leads to the opening of presynaptic P/Q-type  $Ca^{2+}$  channels. Glutamate is released, with increase in its extracellular concentration, by the presynaptic  $Ca^{2+}$  influx at the initiation of CSD. Glutamate diffuses across the synaptic cleft and binds to its postsynaptic receptors, initiating a postsynaptic  $Ca^{2+}$  influx. Astrocytes remove glutamate from the synaptic cleft via a membrane-bound glutamate transporter, terminating synaptic activity. (Moskowitz, *Headache* 2007)

**107. The answer is B.** The etiology of hemodialysis headache (HDH) is unclear, with risk factors including elevated blood pressure, decreased serum osmolality, sodium loss, and high blood urea nitrogen level. Serum magnesium (Mg) levels were decreased in a study of patients with HDH. Both the mean pre- and postdialysis serum Mg levels in the HDH group were significantly lower than the corresponding levels in the control group ( $p = .05$  and  $p = .02$ , respectively). The mean predialysis serum sodium level in the HDH group was higher than in the control group ( $p = .003$ ). Low serum Mg and high sodium levels may be risk factors for HDH. Magnesium supplementation may help patients with HDH with low serum Mg levels. (Goksel, Torun, Karaca, et al., *Headache* 2006)

**108. The answer is E.** TREX1 is involved in the cellular response to oxidative stress, but the mechanism by which mutations in this gene produces multiple clinical diseases is not known. Heterozygous C-terminal frameshift mutations in TREX1, which encodes a 3'-5' exonuclease, have been identified in families with autosomal dominant retinal vasculopathy with cerebral leukodystrophy (RVCL), a microvascular endotheliopathy with middle-age onset that is associated with migraine and Raynaud's phenomenon. Aicardi-Goutieres syndrome and familial chilblain lupus (ulcerating acral skin lesions in children) have all been associated with mutations of the TREX1 gene. Aicardi-Goutieres syndrome is a genetically and clinically heterogeneous pediatric encephalopathy with cerebral atrophy, chronic CSF lymphocytosis, and basal ganglia calcification. Interferon- $\alpha$  is elevated in the spinal fluid. TREX1 mutations are also associated with other disorders with elevated interferon- $\alpha$ , including systemic lupus erythematosus (SLE) and Sjögren's syndrome. (Richards, van den Maagdenberg, Jen, et al., *Nat Genet* 2007; Stam, van den Maagdenberg, Haan, et al., *Curr Opin Neurol* 2008)

**109. The answer is A 1, B 4, C 3, D 5, E 2.** Patients with CADASIL have a mutation in the NOTCH3 gene, which encodes for a receptor involved in the functioning of vascular smooth muscle cells in small arteries and arterioles. Migraine is a prominent, and often presenting, symptom in patients with CADASIL, who also develop psychiatric disease and ischemic stroke. Familial hemiplegic migraine (FHM) is a genetically heterogeneous migraine disorder associated with mutations in the CACNA1A (FHM1), ATP1A2 (FHM2), and SCN1A (FHM3) genes. TREX1 is involved in the cellular response to oxidative stress, but the mechanism by which mutations in the gene produce clinical disease is not known. TREX1 has been identified as the causal gene for autosomal dominant RVCL. Migraine and Raynaud's phenomenon have been associated with RVCL. (Stam, van den Maagdenberg, Haan, et al., *Curr Opin Neurol* 2008; Sanchez-Del Rio, Reuter, & Moskowitz, *Curr Opin Neurol* 2006)

**110. The answer is E.** Cranial nerve palsies due to mechanical or ischemic mechanisms can occur in over 10% of patients with spontaneous dissection of the extracranial internal carotid artery. A cranial nerve palsy may be the only symptom of the dissection; however, most patients have head, face, or neck pain. If the arterial dissection leads to local clot formation, transient or fixed neurologic deficits from cerebral thromboembolic events may occur. A syndrome of lower cranial nerve palsies (with invariable involvement of cranial nerve XII) is the most common cranial nerve abnormality. Palsies of cranial nerves III, V, VII (chorda tympani), and VIII, as well as ION and Horner's syndrome can occur with spontaneous internal carotid artery dissection. (Mokri, Silbert, Schievink, et al., *Neurology* 1996)

**111. The answer is A 4, B 1, C 1, D 2, E 3.** The nervus intermedia, a branch of the facial nerve (CN VII), supplies sensation from the skin of the external ear and an area behind the ear. The nasociliary nerve branches from the ophthalmic division (CN V<sub>1</sub>) of the trigeminal nerve, with sensation supplied from the medial skin of the eyelids and to the nose. The supraorbital nerve runs from the forehead and scalp and joins the supratrochlear nerve, which together form the frontal nerve, which is a branch of the ophthalmic division (CN V<sub>1</sub>) of the trigeminal nerve. Cutaneous branches from the upper lip, medial cheek, and side of the nose form the infraorbital nerve, a branch of the maxillary division (CN V<sub>2</sub>) of the trigeminal nerve. The lingual nerve, a branch of the mandibular division (CN V<sub>3</sub>) of the trigeminal nerve, carries general sensation from the anterior two thirds of the tongue. (Wilson-Pauwels, Akesson, & Stewart, *Cranial Nerves*, 1988)

**112. The answer is B.** About 40% of the trigeminal neurons projecting to the meninges contain CGRP. A smaller number of neurons contain substance P (18%), NOS (15%), and other substances such as vasoactive intestinal peptide and neuropeptide Y. The importance of CGRP has led to intensive investigation of CGRP receptor antagonists in the abortive treatment of migraine headache, with encouraging initial results. A CGRP receptor antagonist does not have the vasoconstricting properties of triptans and ergotamines, but the efficacy of a CGRP receptor antagonist as compared to traditional acute treatment with serotonin agonists is still unclear. (Moskowitz, *Headache* 2007)

**113. The answer is D.** The CACNA1A gene encodes the pore-forming  $\alpha_{1A}$  subunit of Ca<sub>v</sub>2.1 (P/Q-type) voltage-gated neuronal calcium channels. Multiple CACNA1A mutations have been associated with a range of clinical phenotypes, including FHM type 1, episodic ataxia type 2, and spinocerebellar ataxia type 6. Other clinical manifestations of this gene mutation include different types of mental retardation, epilepsy, and ataxia, as well as coma after minor head trauma.

A CACNA1A mutation is associated with episodic ataxia responsive to acetazolamide or valproic acid. (Van den Maagdenberg, Haan, Terwindt, et al., *Curr Opin Neurol* 2007)

**114. The answer is A 5, B 1, C 2, D 3, E 4.** The trigeminal nerve emerges from the midlateral surface of the pons with a large sensory root (CN V<sub>1</sub>, V<sub>2</sub>, V<sub>3</sub>) and a smaller motor root (CN V<sub>3</sub>) to course anteriorly, dividing into three major divisions. The ophthalmic division (CN V<sub>1</sub>) runs through the cavernous sinus before it exits the skull most superiorly through the superior orbital fissure, branching into the lacrimal, frontal, and nasociliary nerves. The maxillary division (CN V<sub>2</sub>) exits the skull through the foramen rotundum, branching into the zygomatic, infraorbital, and pterygopalatine branches. The mandibular division (CN V<sub>3</sub>) exits through the foramen ovale to form both sensory (buccal, auriculotemporal, lingual, inferior alveolar) and motor (pterygoid, masseteric) branches. The facial nerve (CN VII) arises at the junction of the pons and medulla, and courses through internal auditory canal in the petrous part of the temporal bone, emerging from the skull through the stylomastoid foramen. The glossopharyngeal nerve (CN IX) emerges from the medulla, between the olive and the inferior cerebellar peduncle. Rootlets of CN IX converge and exit the skull through the jugular foramen. (Wilson-Pauwels, Akesson, & Stewart, *Cranial Nerves*, 1988)

**115. The answer is A.** Muscles of upper facial expression (including the orbicularis oculi and frontalis) are innervated through the bilateral corticobulbar tracts that pass through the posterior limbs of the internal capsules to the ipsilateral motor nucleus of VII. The muscles of lower facial expression are innervated by the contralateral corticobulbar tract projecting to the ipsilateral motor nucleus of VII. Facial weakness due to an upper motor neuron lesion such as a stroke or brain tumor will generally show relative sparing of the muscles of the eyelid and forehead, which have bilateral cortical innervation. A lower motor neuron lesion of the facial nerve, such as a Bell's palsy, produces paresis of both the upper and lower face. (Gartner & Patestas, *Textbook of Neuroanatomy* 2006)

**116. The answer is C.** The internal carotid artery, and cranial nerves III, IV, V<sub>1</sub>, V<sub>2</sub>, and VI all pass through this venous space between the sphenoid and temporal bones. Cranial nerves V<sub>3</sub> and VII do *not* pass through the cavernous sinus, so facial weakness is not a symptom of infection, thrombosis, or inflammation of the cavernous sinus. The internal carotid artery courses through this venous structure. Rupture of an aneurysm of the intracavernous carotid artery produces a carotid-cavernous fistula with a painful, pulsating, injected eye. (Gartner & Patestas, *Textbook of Neuroanatomy* 2006)

**117. The answer is C.** All the listed genes are associated with thrombosis risk, but there appears to be an association between migraine and C677T polymorphism of the methylenetetrahydrofolate reductase (MTHFR) gene. The C677T polymorphism of the key gene involved in homocysteine metabolism reduces enzymatic capability by 50% and causes hyperhomocysteinemia. A meta-analysis of published studies evaluating the link between the gene and migraine noted an association between the MTHFR TT genotype and migraine with aura. (Rubino, Ferrero, Rainero, et al., *Cephalalgia* 2007)

**118. The answer is B.** The “headache” or “H” response is the increased sensitivity to photic stimulation that can occur on an interictal electroencephalogram (EEG) in patients with migraine headaches. Suppression of  $\alpha$  rhythm has been described in patients with and without migraine during the attack, but the other listed EEG findings are not due to migraine headaches. (Gantenbein & Sandor, *Headache* 2006)

**119. The answer is E.** A myriad of markers have been assayed in the CSF of patients with primary headaches, but none has been consistently and exclusively identified as a clinically useful biomarker for migraine or other primary headaches. Interictal elevations of substances including glutamine, tryptophan, and GABA may hold future promise. (Harrington, *Headache* 2006; Loder, Harrington, Cutrer, et al., *Headache* 2006)

**120. The answer is E.** Migraine sufferers may have a progressive brain disease with an increased risk of subcortical white matter hyperintensities (WMH) as a function of increasing attack frequency. A study with MRI and optimized voxel-based morphometry identified sites of MRI lesions in 28 patients with migraine compared with control subjects. Preferential sites of brain abnormalities, including WMH, in migraineurs were in the frontal lobes, brainstem, and the cerebellum. Cerebellar infarcts may be seen on the MRI of migraineurs. Both attack frequency and disease duration correlated with brain lesions in migraine. However, the lesions do not appear to correlate with the presence of a PFO. (Schmitz, Admiraal-Behloul, Arkink, et al., *Headache* 2008)

**121. The answer is B.** The PAG modulates trigeminovascular nociception with a role in the production of migraine. Spontaneous hemorrhage, electrode implantation, and demyelination in the PAG have all been associated with migraine-like headaches, which are usually contralateral to the lesion. Impairment of iron homeostasis in the PAG with increased nonheme iron deposition has been found in patients with headaches. (Cutrer & Black, *Headache* 2006)

**122. The answer is B.** In 1944, Leão published a study of spreading depression in the cerebral cortex at a rate of 3–4 mm per minute. The rate of CSD, hyperexcitation following suppression, mirrors the rate of progression of the migraine visual aura, as described by Lashley in the early 1940s. Functional imaging studies indicate that the alteration in cerebral blood flow noted during the migraine aura is a consequence of the changes in metabolic demand of the cortical neurons as the depression spreads in a posterior to anterior direction along the cortex. (Leão, *J Neurophysiol* 1944)

**123. The answer is D.** Patients with migraine are at significantly increased risk of silent infarct-like lesions in the vertebrobasilar territory of the brain, especially in the cerebellum. The CAMERA study found that the lesions, which are often round or oval-shaped with a mean size of 7 mm, were most frequently located in the vascular border zone location in the cerebellum. These border zone lesions were more common in migraineurs with aura than in migraineurs without aura or in non-headache controls. The migraineurs with the infratentorial lesions were generally older but did not have more cardiovascular risk factors. (Kruit, Launer, Ferrari, et al., *Brain* 2005)

**124. The answer is E.** The mechanisms by which topiramate blocks neuronal hyperexcitability in patients with frequent headache are still incompletely understood, but the headache-preventative medication appears to reduce neuronal hyperexcitability by acting on mechanisms of phosphorylation. Proposed mechanisms include blockage of voltage-dependent of Na<sup>+</sup> channels, blockage of calcium channels, potentiation of GABA at some subtypes of GABA receptors, and antagonism of the AMPA and kainate (non-NMDA) glutamate receptors. (Ramadan, *Headache* 2007)

**125. The answer is D.** This woman has a glossopharyngeal neuralgia, characterized by dysphagia and unilateral deep throat pain radiating to the ear and worsened by swallowing. General sensation of pain, temperature, and touch from the posterior third of the tongue and the upper pharynx is carried by sensory axons of CN IX, with cell bodies in the superior or inferior glossopharyngeal ganglia. Eagle's syndrome, with pain in the head and neck due to neurovascular compression by an elongated styloid process, may be cause of glossopharyngeal neuralgia. (Rozen, *Neurol Clin* 2004)

**126. The answer is A 1, B 3, C 2, D 3, E 5.** Sensory input from the tongue is divided into the general sensations of pain, temperature, and touch and the special visceral sense of taste. General sensation from the anterior two-thirds of

the tongue is from fibers in the lingual branch of the mandibular division of the trigeminal nerve (CN V<sub>3</sub>). The glossopharyngeal nerve (CN IX) includes fibers for the general sensation in the posterior one-third of the tongue, as well as the upper pharynx and middle ear. The chorda tympani branch of the facial nerve (CN VII) supplies fibers for taste to the anterior two-thirds of the tongue; taste to the posterior one-third is supplied by the glossopharyngeal and vagus nerves (CN IX, X). The hypoglossal nerve (CN XII) supplies the intrinsic muscles of the tongue. (Gartner & Patestas, *Textbook of Neuroanatomy*, 2006)

**127. The answer is B.** The convergence hypothesis postulates a shared pathophysiologic mechanism to explain the spectrum of primary headache types experienced by patients with migraine headaches. The genesis for the hypothesis was the observation by Cady et al. that migraineurs experienced relief treating nonmigraine headaches with subcutaneous sumatriptan. In the Spectrum Study, patients with migraine experienced relief from both migrainous headaches and TTH with sumatriptan. (Cady, *Headache* 2007)

**128. The answer is E.** The poststroke pain syndrome described a century ago by the French neurologists Dejerine and Roussy occurs after a thalamic infarct due to posterior circulation disease or embolization. Other components of the Dejerine-Roussy syndrome include sensory deficits, hemiparesis, ataxia, and choreoathetosis. The thalamic pain syndrome of Dejerine-Roussy is produced preferentially by right diencephalic lesions. The right hemisphere may be specialized for monitoring somatic states, including mediating pain. A literature review of Dejerine-Roussy syndrome indicated that the right laterality predominance was greater among men than women. Pain onset was within the first week post-stroke in over a third of patients. A quarter of patients with a geniculothalamic artery territory stroke develop spontaneous post-infarct pain. (Nasreddine & Saver, *Neurology* 1997)

**129. The answer is C.** The hypothalamus is involved in the pathophysiology of primary headaches including TACs, hemicranias continua, and chronic migraine headaches. Gelastic or laughing seizures are often associated with hypothalamic hamartomas. A selective loss of hypocretin- (orexin-) producing neurons in the perifornical hypothalamus is found in narcolepsy with cataplexy. Multiple sclerosis (MS) is not directly related to hypothalamic dysfunction. (Holland & Goadsby, *Headache* 2007)

**130. The answer is B.** The trochlear nerve emerges from its nucleus in the tegmentum of the midbrain at the level of the inferior colliculus; it then decussates



with superior medullary velum to exit from the midbrain on its dorsal surface. It courses through the lateral wall of the cavernous sinus to enter the orbit through the superior orbital fissure. It only innervates one extraocular muscle, the superior oblique, which causes the globe to intort, moving inferiorly and laterally. (Gartner & Patestas, *Textbook of Neuroanatomy* 2006)

**131. The answer is B.** The hypothalamus modulates body rhythms and metabolic function, and plays role in the pathophysiology of primary headaches. The suprachiasmatic nucleus (SCN) in the anterior hypothalamus functions as a master circadian pacemaker, controlling the sleep–wake cycle and coordinating circadian rhythms. Neuropeptides produced in the SCN include vasopressin and vasoactive intestinal peptide. (Holland & Goadsby, *Headache* 2007)

**132. The answer is D.** Substance P (SP)-neurokinin-1 (NK1) receptor pathways are involved in the pathophysiology of emesis and depression. It is a potent vasodilator mediated by endothelial release of NO. Substance P is involved in central and peripheral pain transmission; however, although SP antagonists have shown beneficial results in treatment of depression and nausea, their antinociceptive properties have been disappointing. Aprepitant is a SP antagonist used for chemotherapy-induced nausea and vomiting. (Hargreaves, *J Clin Psychiatry* 2002)

**133. The answer is A.** This woman has a left internuclear ophthalmoplegia (INO) due to a lesion of the left medial longitudinal fasciculus (MLF) on the same side as the eye with the medial rectus weakness. She is unable to adduct her eye on the side of the lesion and has contralateral abducting nystagmus. The MLF lesion blocks the transmission of information from the contralateral conjugate gaze center in the lower pons (paramedian pontine reticular formation) from ascending to the ipsilateral CN III nucleus. A young woman with an INO and other focal neurologic deficits is very likely to have MS. An INO, which can be unilateral or bilateral, in an older individual with vascular risk factors is usually due to an ischemic brainstem stroke. (Frohman, Galetta, Fox, et al., *Neurology* 2008)

**134. The answer is E.** Magnetic resonance imaging studies have indicated that migraineurs are at increased risk of cerebellar infarcts and supratentorial WMLs. In the CAMERA study, infratentorial hyperintensities on MRI were identified in 13 of 295 (4.4%) migraineurs and in 1 of 140 (0.7%) controls ( $P=0.04$ ). Most hyperintensities were in the bilateral dorsal basis pontis. Migraineurs with infratentorial hyperintensities were also likely to have supratentorial WMLs. While periventricular (as opposed to deep white matter) lesions are found on the MRI of migraineurs, their prevalence is the same as on the MRIs of non-headache



controls. A hemodynamic ischemic pathogenesis for these lesions is postulated, but unproven. (Kruit, Launer, Ferrari, et al., *Stroke* 2006)

**135. The answer is C.** Levels of the neuronal signal substance CGRP are increased during the pain of primary headaches. Studies sampling cranial venous outflow from the external jugular vein have shown elevated levels of CGRP with attacks of migraine with and without aura, trigeminal neuralgia, CH, and chronic paroxysmal headache. Venous levels of the parasympathetic neurotransmitter, vasoactive intestinal peptide, are increased during attacks of CH and chronic paroxysmal headache. (Edvinsson, *Headache* 2006)

**136. The answer is B.** In a study comparing MRI and voxel-based morphometry of the brain in migraineurs and healthy controls, a significant decrease of gray matter was observed in the cingulate cortex (an area associated with the transmission of pain), but not in areas specific for migraine, such as the brainstem. A relative decrease in the cingulate cortex has been found in chronic pain states, such as chronic phantom pain and chronic back pain. This change in migraine patients may be related to frequent nociceptive input, and may supply yet another justification for the aggressive prevention of headache pain. (Schmidt-Wilcke, Gänssbauer, Neuner, et al., *Cephalalgia* 2008)

**137. The answer is E.** Sensation from the external auditory meatus and the external surface of the tympanic membrane is carried by the auriculotemporal branch of the mandibular nerve (CN V<sub>3</sub>), the auricular branch of CN X, and a branch of CN VII. Sensation from the internal surface of the tympanic membrane is carried by a branch of the glossopharyngeal nerve (CN IX). (Wilson-Pauwels, Akesson, & Stewart, *Cranial Nerves*, 1988)

# 3

## HEADACHE CLASSIFICATION AND DIAGNOSIS QUESTIONS

**138.** Diagnostic criteria from the International Classification of Headache Disorders, Second Edition (ICHD-II) for medication-overuse headache (MOH) generally requires that a headache be present for more than 15 days a month, with intake of the acute medication for  $\geq 10$  days a month on a regular basis for  $\geq 3$  months. This is true for all the listed medications *except*:

- A. Ergotamine
- B. Triptans
- C. Opioid medications
- D. Simple analgesics
- E. Combination medications

**139.** What of the following best describes the attack frequency of paroxysmal hemicrania ?

- A. An attack once a week
- B. One attack every other day to eight per day
- C. One to 40 attacks a day
- D. Three to 200 attacks a day
- E. Ten to 500 attacks a day

**140.** Which factor has the greatest impact on the development of a headache after lumbar puncture?

- A. Volume of spinal fluid removed
- B. Duration of bed rest after lumbar puncture
- C. Hydration after lumbar puncture
- D. Position of patient during the procedure
- E. Needle size

**141.** Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA):

- A. Are characteristically responsive to indomethacin.
- B. Generally have refractory periods between triggering of attacks.
- C. Characteristically have pain in the jaw and teeth.
- D. Are more common in men than women.
- E. Are not found in patients with migraine.

**142.** Which of the following is characteristic of a retinal migraine?

- A. Monocular scintillations
- B. Monocular blindness
- C. Monocular scotoma
- D. Migraine during the visual symptoms
- E. All of the above

**143.** Which statement best describes a headache after lumbar puncture?

- A. A post lumbar puncture headache (PLPH) is always a benign complication of the procedure.
- B. The headache is characteristically worse while upright, improving when recumbent.
- C. Replacing the stylet before withdrawing the needle increases the risk of headache.
- D. The magnetic resonance imaging (MRI) is characteristically normal with a severe PLPH.
- E. The headache pain begins immediately after the procedure.

**144.** The end of which holiday is traditionally associated with a headache by sundown?

- A. Christmas
- B. Easter
- C. Purim
- D. Yom Kippur
- E. St. Patrick's Day

**145.** Medication-overuse headaches:

- A. Are not associated with triptan use.
- B. Are caused most frequently by combination analgesics.
- C. Are distinguished from chronic tension-type headaches (CTTH) by the pain characteristics alone.
- D. Can be caused by analgesic overuse in nonmigraineurs.
- E. Do not develop in migraine sufferers with nonheadache pain.

**146.** Who is most likely to develop a headache after lumbar puncture?

- A. An overweight 50-year-old woman
- B. A 6-year-old boy
- C. A thin 25-year-old woman
- D. A 30-year-old man with a concussion
- E. A 10-year-old girl

**147.** Match the granulomatous vasculitis with its most likely patient. Use each answer only once.

- |                               |   |
|-------------------------------|---|
| A. Takayasu's arteritis       | 1. 50-year-old man with nasal polyps and asthma |
| B. Giant cell arteritis (GCA) | 2. 70-year-old woman with malaise and headaches |
| C. Wegner's granulomatosis    | 3. 30-year-old woman with malaise and headaches |
| D. Churg-Strauss syndrome     | 4. 50-year-old man with nose bleeds and a cough |

**148.** Cluster headache (CH) and SUNCT/SUNA syndrome have similar properties. The following are similarities between the two headache types *except*:

- A. Both are male predominant primary headaches.
- B. Both are unresponsive to indomethacin.
- C. Both have excruciating unilateral pain.
- D. Both have nocturnal attacks.
- E. Both are associated with autonomic symptoms.

**149.** A 35-year-old woman from New York City flew to a mountaintop hotel in Alta, Utah for a wedding. Although most of the wedding guests wanted to go skiing, she was obese and had asthma, so she decided to spend the next day in the spa. The sauna was so relaxing that she felt sluggish and dizzy, and then she developed a moderate-intensity dull frontal bilateral headache with nausea. As she tried to get up to go to the pool to cool down, she fell to the floor of the sauna where she was found, lethargic but oriented, by the spa attendant. A neurologist happened to have just finished a massage at the spa and was asked to take a look at her. What should the neurologist do to help this woman?

- A. She should reassure the woman that she is dehydrated, give her some water with lemon, and help her back to her room.
- B. She should give the woman the triptan sample that a prepared neurologist always keeps in her purse.
- C. She should put the woman in her car and drive her down the mountain.
- D. She should arrange transportation to the local emergency department, where the woman should be given oxygen and acetazolamide.
- E. She should give the woman her card and tell her to call the office the next day.

**150.** Which of the following best describes hemiplegic migraine?

- A. Motor deficit is the only manifestation of the aura.
- B. Hemiplegic migraine always has an autosomal dominant inheritance.
- C. Hemiplegic migraine is rarely confused with ischemic stroke.
- D. Attacks of hemiplegic migraine may occur in children as young as 5 years.
- E.  $\beta$ -Blockers are routinely used for prevention of hemiplegic migraine.

**151.** Headaches are linked with Raynaud's phenomenon in which of the following disorders?

- A. Fibromyalgia syndrome
- B. Systemic lupus erythematosus (SLE)
- C. Rheumatoid arthritis (RA)
- D. Scleroderma
- E. Irritable bowel syndrome (IBS)

**152.** Migraine is most strongly associated with an increased risk of:

- A. Hemorrhagic stroke.
- B. Myocardial infarction (MI).
- C. Ischemic stroke.
- D. Cerebral vasospasm.
- E. Intracerebral hemorrhage.

**153.** A 35-year-old woman with a low-grade astrocytoma underwent resection and radiation therapy. Five years later, she began having transient episodes of right-sided weakness and speech difficulty, not resolving with antiplatelet or anti-epilepsy drugs. She also noted new-onset headaches and intermittent confusion. Several months later, she developed a right hemiparesis with an MRI showing enhancement of the cortical ribbon in the left parietal region. The hemiparesis and MRI lesion resolved in 3 weeks. What is the most likely explanation for this woman's symptoms?

- A. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)
- B. Mitochondrial encephalopathy lactic acidosis and stroke-like symptoms (MELAS)
- C. Familial hemiplegic migraine (FHM)
- D. Stroke-like migraine attacks after radiation therapy (SMART)
- E. Reversible cerebral vasoconstriction syndrome

**154.** The period of recurrent neurological symptoms with transient neurological deficits associated with pseudomigraine with lymphocytic pleocytosis [also known as headache with neurological deficits and cerebrospinal fluid (CSF) lymphocytosis (HaNDL)] is characteristically:

- A. One week.
- B. One month.
- C. Three months.
- D. One year.
- E. Three years.

**155.** Which of the following features of a pediatric headache may not be consistent with migraine?

- A. Short duration (1–72 hours) of pain
- B. Bifrontal location of pain
- C. Occipital location of pain
- D. Nausea
- E. Anorexia

**156.** Which of the following statements best describes primary angiitis of the central nervous system (PACNS)?

- A. Primary angiitis of the central nervous system (PACNS) generally presents with headaches and focal neurological deficits due to infarcts.
- B. Fever, weight loss, and malaise are common symptoms of PACNS.
- C. A pathognomonic abnormality is seen on MRI scan of the brain.
- D. Brain biopsy is rarely needed for diagnosis.
- E. PACNS can be ruled out by normal catheter angiography.

**157.** Transient global amnesia (TGA):

- A. Is never associated with a headache.
- B. Produces a characteristic abnormality on electroencephalography.
- C. Is much more common in people with traditional vascular risk factors.
- D. May be related to a transient disturbance of hippocampal CA-1 neurons.
- E. Causes long-term neurocognitive deficits.

**158.** Which of the following locations of intracerebral hemorrhage is most commonly associated with cerebral amyloid angiopathy?

- A. Putaminal hemorrhage
- B. Lobar hemorrhage
- C. Cerebellar hemorrhage
- D. Intraventricular hemorrhage
- E. Pontine hemorrhage

**159.** Arteriovenous malformations (AVMs):

- A. Are congenital lesions.
- B. Commonly cause headaches.
- C. Are most often symptomatic in the sixth or seventh decade.
- D. Present with seizures as the most common and serious symptom.
- E. Are not a cause of hemorrhagic stroke in children.

**160.** The most common presenting clinical manifestation of cavernous malformation (angiomas) is:

- A. Hemorrhage.
- B. Seizures.
- C. Focal neurologic deficits.
- D. Headaches.
- E. Ischemic stroke.

- 161.** Patients with Ehlers-Danlos syndrome are at risk for headaches due to:
- A. Cerebral vasculitis.
  - B. Cerebral arterial thrombosis.
  - C. Cerebral venous thrombosis.
  - D. Subarachnoid hemorrhage (SAH).
  - E. All of the above
- 162.** Medication-overuse headache in cluster headache (CH) patients:
- A. Does not exist.
  - B. Occurs only with opioid use.
  - C. Occurs more often in CH patients with a personal or family history of migraine.
  - D. Is described as an increased frequency of the characteristic CH.
  - E. Can be successfully treated in only a rare patient.
- 163.** Osmophobia:
- A. Is rarely reported by patients with migraine headaches.
  - B. Is never reported in cluster headache (CH) patients.
  - C. Is associated with both migraine and episodic tension-type headaches (ETTH).
  - D. Is sensitivity to scents, food smells, and cigarette smoke.
  - E. Is not reported by children with headaches.
- 164.** Which animal is associated with a headache that characteristically occurs in the morning?
- A. Armadillo
  - B. Turtle
  - C. Giraffe
  - D. Skunk
  - E. Possum
- 165.** Persistent craniofacial pain after craniotomy:
- A. Is usually related to an underlying post-operative anatomic abnormality.
  - B. Is associated with anxiety and depression.
  - C. Rarely lasts a year after surgery.
  - D. Is only seen with posterior fossa lesions.
  - E. Is only seen in patients with preoperative headaches.



**166.** Barotrauma-related headaches:

- A. Can be due to elevator flights in skyscrapers.
- B. Are noted on every flight in susceptible individuals.
- C. Are a type of trigeminal autonomic cephalgia.
- D. May be related to pressure activation of receptors within ethmoid sinuses.
- E. Occur commonly with hot-air balloon rides in Denver.

**167.** Which of the following statements best describes SUNCT syndrome?

- A. The syndrome is a common, female predominant primary headache disorder.
- B. The pain of short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is usually maximal in the  $V_3$  division of the trigeminal nerve.
- C. The attacks of pain generally last about 5–240 seconds.
- D. The attacks of pain generally alternate sides.
- E. The syndrome is responsive to indomethacin.

**168.** A 52-year-old woman describes 10 months of a coaster-sized headache over her right parietal region. The pain is a mild to moderate aching sensation that is almost always present to some degree, never switching sides or changing location. The area is described as sensitive to touch, and she does not like to brush her hair on the right side. Nausea, vomiting, photophobia, phonophobia, and autonomic features are not denied. She is postmenopausal, with a past history of menstrual headaches and currently has mild untreated depression. Which of the following etiologies for headache best describes her symptoms?

- A. Giant cell arteritis (GCA)
- B. Tension-type headache (TTH)
- C. Nummular headache
- D. Migraine
- E. Cluster headache (CH)

**169.** A 48-year-old woman reported sharp stabbing and burning pain in the left ear radiating to her zygoma and temple area. The pain lasted up to several hours, occurring several times a week. She grew her previously short hair long to cover up her ear after several people teased her about her intermittently red left ear, which was present with or without the ipsilateral ear pain. When she moved from Arizona to Alaska, the episodes became more frequent. Which term best describes these headaches?

- A. Red ear syndrome
- B. Long hair syndrome
- C. Cold weather syndrome
- D. Perimenopausal headache syndrome
- E. Self-image syndrome

**170.** Which of the following conditions is most usually associated with headaches caused by spontaneous intracranial hypotension?

- A. Diabetes
- B. Chiari I malformation
- C. Sickle cell disease
- D. Marfan syndrome
- E. Migraine headaches

**171.** Which of the following is a childhood periodic syndrome that may be a precursor to migraine headaches?

- A. Attention deficit disorder
- B. Cyclic vomiting syndrome
- C. Growing pains
- D. Dyslexia
- E. All of the above

**172.** Which of the following statements best describes chronic daily headache (CDH)?

- A. Chronic daily headache (CDH) is defined as a headache occurring every single day.
- B. Chronic daily headache is always a primary headache disorder.
- C. The most common CDHs are cluster headaches (CHs) and transformed migraine.
- D. Chronic daily headache is more common in male hedge fund managers than in waitresses.
- E. Patients with CDH and medication overuse have a worse prognosis than CDH patients who do not overuse acute headache medication.

- 173.** Which of the following statements best describes headaches and sleep?
- A. Snoring is correlated with frequent morning headaches.
  - B. The use of continuous positive pressure airway pressure (CPAP) in patients with obstructive sleep apnea (OSA) does not improve frequent morning headaches.
  - C. Gender predilection for OSA mirrors gender predilection for migraine headaches.
  - D. Obstructive sleep apnea is a known trigger for migraine headaches.
  - E. Patients with migraine have the same incidence of sleep disorders as an age-matched population without migraine.
174. When are migraine headaches most likely to occur?
- A. Between 4 AM and 9 AM
  - B. In the late morning
  - C. Between noon and 5 PM
  - D. In the early evening
  - E. Late at night
- 175.** Which of the following best describes headaches associated with triptan overuse?
- A. Medication-overuse headaches (MOHs) caused by triptans develop faster than MOHs associated with use of combination analgesics.
  - B. Withdrawal from triptan overuse is more difficult and prolonged than withdrawal from combination analgesic overuse.
  - C. The MOH associated with triptan overuse is always a tension-type daily headache.
  - D. The MOH associated with triptan overuse occurs with higher doses than with other analgesics.
  - E. Restriction of triptan use to no more than four doses a week will avoid MOH.

**176.** Which of these statements best describes a headache associated with an ischemic stroke?

- A. A headache is more commonly associated with posterior than anterior circulation ischemia.
- B. A headache is more commonly associated with lacunar than nonlacunar infarcts.
- C. A headache is more commonly associated with cardioembolic than atherothrombotic stroke.
- D. A severity of the headache always correlates with the size of the infarction.
- E. Headache rarely occurs associated with ischemic stroke.

**177.** Match the patient with the most likely chronic headache diagnosis.

- |   |  |
|---|--|
| A. 60-year-old woman with a holocephalic headache awakening her from sleep              | 1. Low-cerebrospinal fluid volume headache   |
| B. 50-year-old man with multiple 30-second attacks of periorbital pain with tearing     | 2. Medication overuse headache (MOH)   |
| C. 25-year-old woman with frequent migraines taking 15 triptan doses a month            | 3. Hypnic headache   |
| D. 42-year-old woman with severe unilateral periorbital pain responsive to indomethacin | 4. Hemicrania continua   |
| E. 31-year-old woman with headache present on standing, relieved with lying down        | 5. Short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing syndrome (SUNCT) |

**178.** Which of the following best characterizes the pain of hemicrania continua?

- A. Unilateral without side-shift
- B. Pain-free periods of up to several weeks
- C. Mild intensity without exacerbation
- D. Associated with contralateral nasal congestion
- E. Never associated with nausea, vomiting, photophobia, and phonophobia

**179.** Which of the following can accompany the headache of idiopathic intracranial hypertension (IIH)?

- A. Transient visual obscurations
- B. Pain on eye movement
- C. Tinnitus
- D. Horizontal diplopia
- E. All of the above

**180.** Which of the following statements best describes the diagnosis of cervicogenic headache?

- A. Consensus about the diagnosis of cervicogenic headache has led to defined and established headache criteria.
- B. Epidemiological data clearly defines the prevalence of cervicogenic headache.
- C. The diagnosis of cervicogenic headache, as defined by the ICHD-II, can be made without demonstrable neck pathology.
- D. The ICHD-II diagnosis of cervicogenic headache dictates that the pain be abolished by cervical blockade or that the pain resolves after treatment of the causative disorder or lesion.
- E. According to clinical trials, a radiological lesion in the cervical spine is identified more often patients with cervicogenic headaches, as compared to control patients.

**181.** Headache accompanied by bilateral neck pain:

- A. Indicates the diagnosis of cervicogenic headache.
- B. Is consistent with the diagnosis with migraine.
- C. Generally correlates with an anatomic neck lesion on radiological testing.
- D. Has been proven to respond to radiofrequency radiolysis.
- E. Is inconsistent with the diagnosis of tension-type headache (TTH).

**182.** Which of the following is a necessary diagnostic criterion for migraine without aura?

- A. Headache attack lasting 4–72 hours
- B. Unilateral location
- C. Throbbing pain
- D. Moderate or severe pain intensity
- E. Osmophobia

**183.** In a large cohort of adult patients with community-acquired bacterial meningitis, approximately what percentage of patients presented with the classic triad of fever, stiff neck, and change in mental status?

- A. <5%
- B. 20%
- C. 40%
- D. 60%
- E. >80%

**184.** Which of the following are similarities between trigeminal neuralgia and SUNCT/SUNA syndrome?

- A. Both produce pain primarily confined to a periorbital region
- B. Both are responsive to indomethacin
- C. Both rarely have nocturnal attacks
- D. Both are associated with autonomic symptoms
- E. All of the above

**185.** Contact point headache:

- A. Is attributed to the contact between first- and second-order neurons in the trigeminovascular system.
- B. May occur due to contact between the septum and the middle nasal turbinate.
- C. Is not a specific headache type by ICHD-II criteria.
- D. Is specifically treated with oral analgesics.
- E. All of the above

**186.** Which of the following statements best describes hemicrania continua?

- A. The ICHD-II criteria for hemicrania continua requires unilateral pain without side-shift, but some similar headaches are bilateral.
- B. About half of cases of hemicrania continua respond to indomethacin.
- C. “Jabs and jolts” are pathognomonic for hemicrania continua.
- D. Migrainous features do not occur in hemicrania continua.
- E. Hemicrania continua is the same headache as chronic paroxysmal hemicrania.

**187.** Which of the following is found in patients with IHH?

- A. Papilledema
- B. An enlarged blind spot
- C. Visual field defect
- D. Sixth-nerve palsy
- E. All of the above

**188.** Autonomic symptoms (lacrimation, nasal congestion, ptosis, miosis) are absent in which of the following primary headaches?

- A. Hemicrania continua
- B. Chronic paroxysmal hemicrania
- C. Cluster headache (CH)
- D. Short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome
- E. None of the above

**189.** Which statement best describes a thunderclap headache (TCH)?

- A. A thunderclap headache (TCH) is a headache of very severe intensity that comes on over 5 minutes.
- B. A TCH cannot be classified as a primary headache.
- C. The most common secondary cause of TCH is subarachnoid hemorrhage (SAH).
- D. A TCH is almost always due to underlying vascular disease.
- E. A TCH should be evaluated with conventional angiography.

**190.** Which of the following is most often associated with secondary cough headache?

- A. Chiari type I malformation
- B. Unruptured cerebral aneurysm
- C. Noncommunicating hydrocephalus
- D. Arachnoid cyst of the temporal lobe
- E. Chronic subdural hematoma

**191.** A 50-year-old woman complained of continuous, moderate- to severe-intensity pain around her left ear, radiating to her temple, zygoma, and head of her mandible. She had tenderness in front of her left ear, and pressure in the area worsened the pain. She reported that she was able to eat and brush her teeth without significant exacerbation of her pain. She denied any autonomic symptoms associated with her pain. MRI studies of the brain and cervical spine were normal. What is the most likely diagnosis?

- A. Auriculotemporal neuralgia
- B. Trigeminal neuralgia
- C. Cervicogenic headache
- D. Hemicrania continua
- E. Paroxysmal hemicrania

**192.** SUNCT is best distinguished from trigeminal neuralgia by which attack characteristic?

- A. Refractory period
- B. Location of pain
- C. Duration of pain
- D. Frequency of attacks of pain
- E. Gender of patient

**193.** Headache attributed to either acute or chronic hypoxia is defined as occurring associated with what partial pressure of oxygen in arterial blood ( $\text{PaO}_2$ ) level?

- A. <90 mm Hg
- B. <80 mm Hg
- C. <70 mm Hg
- D. <60 mm Hg
- E. <50 mm Hg

**194.** Headaches that develop during scuba diving are most commonly due to:

- A. Migraine triggered by the dive.
- B. Decompression sickness.
- C. Carbon monoxide (CO) intoxication.
- D. Hypercapnia with  $\text{PaCO}_2 > 50$  mm Hg.
- E. Beach bar hangover.



**195.** Which of the following statements best describes pseudomigraine with temporary neurological symptoms and lymphocytic pleocytosis, which is also known as headache with neurological deficits and CSF lymphocytosis (HaNDL)?

- A. Visual symptoms occur more frequently than sensory symptoms.
- B. Neurological deficits persist between attacks.
- C. Spinal fluid protein is rarely elevated.
- D. A viral-like illness may precede the onset of symptoms.
- E. Patients are more likely to be female.

**196.** Which of the following statements best describes SUNCT syndrome?

- A. Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNCT) may be a subset of short-lasting unilateral neuralgiform headache attacks with cranial autonomic features (SUNA).
- B. SUNCT is an indomethacin responsive trigeminal autonomic cephalgia.
- C. SUNCT is easily treated with preventative medications.
- D. SUNCT is associated with activation of a pontine nucleus.
- E. All of the above

**197.** Which statement best describes headache in pregnancy and the postpartum period?

- A. Headaches during pregnancy and the postpartum period are rare, afflicting less than 10% of women.
- B. Headaches in pregnant or postpartum women with a past history of headaches are usually migraine headaches.
- C. A secondary headache is a rare cause of a new-onset headache during pregnancy or the postpartum period.
- D. Migraine headaches worsen as pregnancy progresses.
- E. Headaches are rare after pregnancy in the setting of hormonal changes and sleep deprivation.

**198.** In a pregnant woman with the new onset of severe headache, which of the following is true?

- A. Since headaches are very rare during pregnancy, a severe headache indicates serious pathology.
- B. Imaging of the brain should not be performed unless there is a motor or cranial nerve deficit on neurological examination.
- C. Imaging of the brain should be considered even if the neurological examination is normal.
- D. Migraine is the most common cause of new-onset headache in a woman without any pregestational history of headaches.
- E. Computed tomography (CT) scanning of the brain of pregnant women should never be performed because of radiation risk to the fetus.

**199.** Which rank order, from shortest to longest, best describes the duration of attacks of trigeminal autonomic cephalalgias?

- A. Cluster headache; paroxysmal hemicrania; SUNCT
- B. SUNCT; cluster headache; paroxysmal hemicrania
- C. Paroxysmal hemicrania; cluster headache; SUNCT
- D. SUNCT; paroxysmal hemicrania; cluster headache
- E. Cluster headache; SUNCT; paroxysmal hemicrania

**200.** Which is the most critical aspect of the headache history when a patient presents with suspected subarachnoid hemorrhage (SAH)?

- A. Severity of the headache
- B. Presence of neck pain
- C. Age of the patient
- D. Acuity of the headache onset
- E. Patient's prior headache history

**201.** Which of the following is considered to be a childhood periodic syndrome with symptoms that are recurrent and periodic in nature and are associated with migraine or a family history of migraine?

- A. Cyclic vomiting
- B. Abdominal migraine
- C. Benign paroxysmal vertigo
- D. Paroxysmal torticollis
- E. All of the above

**202.** Headaches associated with sexual activity (HSA):

- A. Almost always indicate the presence of a leaking cerebral aneurysm.
- B. Generally occur only once, despite continued sexual activity.
- C. Are usually mild, causing minimal patient anxiety.
- D. Have a poor prognosis, generally resulting in conversion to celibacy.
- E. Generally have a benign etiology.

**203.** A 34-year-old woman without any prior neurologic history developed a headache a day after vaginal delivery with epidural anesthesia. The headache persisted despite treatment with a nonsteroidal anti-inflammatory drug (NSAID), and a neurology consultation was requested. Before the neurologist could evaluate the patient, she was found unresponsive with clonic movements. A few minutes later, she was responsive but with mild left-sided weakness. What is a likely cause of her postpartum seizure and weakness?

- A. Subdural hematoma
- B. Cerebral venous thrombosis
- C. Ischemic stroke
- D. Subarachnoid hemorrhage (SAH)
- E. Any of the above

**204.** Which congenital cutaneous vascular syndrome is characterized by a facial port-wine stain?

- A. Neurofibromatosis
- B. Osler-Weber-Rendu Disease
- C. Ehlers Danlos Syndrome
- D. Sturge-Weber Syndrome
- E. Marfan Syndrome

**205.** Pregnant women with migraine headaches:

- A. Generally note improvement of headaches in the second and third trimesters.
- B. May note worsening of headaches during pregnancy.
- C. Generally note worsening of headaches postpartum.
- D. Are at increased risk of maternal complications of pregnancy.
- E. All of the above

**206.** Several hours after running the New York marathon in 4.5 hours, a young woman complained of a headache of increasing severity. She became progressively more lethargic before being brought to your emergency department. She has no significant past medical history and is on no medications except oral contraceptives. A contrasted computed tomography (CT) scan shows an empty delta sign. Which test should be part of her evaluation?

- A. Activated protein C resistance (Factor V Leiden mutation)
- B. Transesophageal echocardiogram
- C. Liver function tests
- D. Anticardiolipin antibody level
- E. Holter monitor

**207.** Familial hemiplegic migraine type 1 (FHM1):

- A. Is rarely associated with permanent cerebellar symptoms.
- B. Generally consists of reversible motor weakness without other neurological symptoms.
- C. Affects women more frequently than men.
- D. Has been associated with a mutation of the CACNA1A gene encoding a subunit of a voltage-dependent neuronal calcium channel.
- E. Is an inherited autosomal recessive migraine subtype.

**208.** How long does a CH attack last?

- A. <1 second to 120 seconds
- B. 5–240 seconds
- C. 2–30 minutes
- D. 15–180 minutes
- E. None of the above

**209.** A 75-year-old man with a history of hypertension and atrial fibrillation on therapeutic warfarin presented to the emergency department with the sudden onset of headache, dizziness, nausea, and vomiting. The CT scan was read as showing no hemorrhage or ischemia. His examination appeared unremarkable until he got up from lying on the stretcher to go to the bathroom and fell to the floor. What would be the most appropriate next step?

- A. Send the patient home with an antiemetic and instructions to call the family doctor within the next 2–3 days.
- B. Obtain an MRI of the brain and a magnetic resonance angiograph (MRA) of the brain and neck vessels.
- C. Admit the patient to the hospital with acute onset of vertigo and order nursing checks every 6 hours.
- D. Do an immediate lumbar puncture to rule out subarachnoid hemorrhage (SAH).
- E. Obtain a carotid ultrasound in the emergency department.

**210.** Which of the following is a clinical characteristic of MOH?

- A. The headaches occur on the majority of days of the month for over three months.
- B. The patient's threshold for head pain appears to be low.
- C. Withdrawal symptoms may occur with abrupt discontinuation of acute medication.
- D. Prophylactic medications are ineffective if the acute medication continues to be used excessively.
- E. All of the above

**211.** Which of the following is *not* a symptom of acute migrainous vertigo ?

- A. Nystagmus
- B. Gait imbalance
- C. Hearing loss
- D. Ocular motor deficits
- E. Vertigo

**212.** A 72-year-old woman called her internist to report that she had the new onset of a dull headache, without nausea or vomiting, involving her entire head. She was discharged from the hospital a day ago after suffering a mild stroke. She was put on some new medications, which she listed for her doctor. Which medication is most likely to be responsible for her headaches?

- A. Aspirin and extended-release dipyridamole (Aggrenox<sup>®</sup>)
- B. Atorvastatin (Lipitor<sup>®</sup>)
- C. Amlodipine (Norvasc<sup>®</sup>)
- D. Metoprolol (Lopressor<sup>®</sup>)
- E. Hydrochlorothiazide

**213.** Which headache diagnosis is associated with vision loss?

- A. Headache, neurological deficits, and cerebrospinal fluid lymphocytosis (HaNDL)
- B. Idiopathic intracranial hypertension (IIH)
- C. Migraine with aura
- D. Retinal migraine
- E. All of the above

**214.** Which of the following symptoms is most commonly noted in patients with HaNDL?

- A. Aphasia
- B. Sensory loss
- C. Changes in vision
- D. Gait ataxia
- E. Ophthalmoplegia

**215.** Which patient may have IIH?

- A. A 40-year-old woman, weighing 280 pounds, with an opening pressure of 238 mm H<sub>2</sub>O on lumbar puncture.
- B. A 20-year-old woman, weighing 130 pounds, with an opening pressure of 190 mm H<sub>2</sub>O on lumbar puncture.
- C. A 37-year-old man with chronic headaches and sagittal sinus thrombosis on magnetic resonance venogram (MRV).
- D. A 28-year-old man with double vision and a new-onset diffuse daily headache.
- E. All of the above

**216.** Pulsatile tinnitus is commonly reported by patients with:

- A. Acoustic neuroma.
- B. Idiopathic intracranial hypertension (IIH).
- C. Cluster headaches (CH).
- D. Chiari type I malformation.
- E. All of the above

**217.** Which of the following is *not* a childhood periodic syndrome that may be a precursor to migraine?

- A. Cyclic vomiting
- B. Abdominal migraine
- C. Benign positional vertigo
- D. Selective mutism
- E. All of the above

**218.** A 53-year-old neurology department chair came to the office of a colleague because of strange behavior for 4 days. He complained of a moderately severe holocephalic headache but was unable to relate any other symptoms due to his lethargy and confusion. He was oriented to name and hospital, but had difficulty stating the date. He could not retain the names of three objects, and he was inattentive with word finding difficulty. His neurological examination was otherwise nonfocal. An emergency CT scan of the brain with and without contrast was normal. An electroencephalogram (EEG) showed left greater than right temporal slowing with periodic lateralizing epileptiform discharges. Which of the following tests is now most urgent?

- A. An MRI scan of the brain
- B. A cerebral angiography
- C. A lumbar puncture
- D. An electrocardiogram
- E. A nerve conduction study

**219.** Basilar-type migraine is associated with which of the following symptoms?

- A. Tinnitus
- B. Vertigo
- C. Dysarthria
- D. Ataxia
- E. All of the above

- 220.** Which gene on chromosome 19 is associated with familial hemiplegic migraine type 1?
- A. SCN1A
  - B. CACNA1A
  - C. ATP1A2
  - D. All of the above
  - E. None of the above
- 221.** Trigeminal autonomic cephalgias (TACs) include:
- A. Cluster headache (CH)
  - B. Paroxysmal hemicrania
  - C. Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA)
  - D. Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)
  - E. All of the above
- 222.** A sentinel headache:
- A. Rarely occurs prior to a subarachnoid hemorrhage (SAH).
  - B. Occurs prior to intracerebral hemorrhage.
  - C. Indicates an increased risk of rebleeding after SAH.
  - D. Is always due to aneurysmal leakage.
  - E. All of the above
- 223.** The highest relapse rate after withdrawal of treatment is associated with which acute headache medication that causes MOH?
- A. Triptans
  - B. Combination medications
  - C. Simple analgesics
  - D. Ergotamine
  - E. Opioids



**224.** A 55-year-old woman reported severe right-sided throbbing headaches after resection of a right acoustic neuroma 4 months ago. The tumor presented with hearing loss and tinnitus. The headaches are not positional, and she denies any autonomic symptoms including rhinorrhea. Headaches were rare prior to surgery, but now she needs narcotic analgesics for pain relief. Her neurological examination is normal but she appears anxious. What do you suggest?

- A. Cisternography
- B. Revision of her skull defect
- C. Referral to a psychiatrist
- D. Use of a headache preventative medication
- E. Liberal use of narcotics

**225.** Which of the following diseases is most closely associated with headaches?

- A. Systemic lupus erythematosus (SLE)
- B. Rheumatoid arthritis (RA)
- C. Hypothyroidism
- D. Sarcoidosis
- E. Multiple sclerosis (MS)

**226.** Which of the following neurological disorders is associated with antiphospholipid antibodies?

- A. Ischemic stroke
- B. Seizures
- C. Headache
- D. Demyelinating disease
- E. All of the above

**227.** Which of the following correlates most closely with cognitive decline in CADASIL?

- A. Frequency of headaches
- B. Severity of headaches
- C. Length of time from diagnosis of depression
- D. Ischemic changes on neuroimaging studies
- E. Family history of CADASIL

**228.** A 35-year-old woman with a history of depression describes an unpleasant sensation of her head “exploding,” occurring when falling asleep, but rarely while awake. Some of these episodes, which occur almost every week, are accompanied by flashing lights. What treatment do you suggest?

- A. Clomipramine (Anafranil)
- B. Melatonin
- C. Lithium
- D. Lamotrigine (Lamictal)
- E. Lorazepam (Ativan)

**229.** Which headache syndrome is associated with sleep?

- A. Exploding head syndrome
- B. Hypnic headaches
- C. Cluster headaches (CH)
- D. Turtle headaches
- E. All of the above

**230.** A 23-year-old woman presented to the emergency department complaining of 1 week of blurred vision and diffuse moderately severe headaches. She denied any prior visual problems or headaches. On examination, she had a blood pressure of 146/94 and a body mass index (BMI) of 33. She had a visual acuity of 20/60 OD and 20/80 OS. Her left eye did not fully abduct on lateral gaze, with inducible double vision. Her blind spots were enlarged bilaterally on visual field testing. Bilateral papilledema was noted on funduscopic evaluation. Which is the most likely diagnosis?

- A. Posterior reversible encephalopathy syndrome (PRES)
- B. Idiopathic intracranial hypertension (IIH)
- C. Pituitary apoplexy
- D. Subarachnoid hemorrhage (SAH)
- E. Susac syndrome

**231.** A 40-year-old man noted the sudden onset of bilateral posterior head pain radiating frontally. Despite the absence of a history of prior headaches, he did not seek medical help until the head persisted for 3 days, at which time he consulted with his primary care doctor. His doctor sent him for a CT scan, which showed blood in the suprasellar cistern. No aneurysm was seen on CT angiography. What is the most likely cause of this man's headache?

- A. A subdural hemorrhage
- B. Venous hemorrhage
- C. A vertebral artery aneurysm
- D. A basilar artery dissection
- E. Pituitary apoplexy

**232.** A 59-year-old woman with a remote history of breast cancer complained of intense stabbing pain in her left ear. Her neurological examination was normal, and no lesions were noted in her external auditory canal, tongue, or face. Her tympanic membrane and external auditory were normal. What is the most likely diagnosis?

- A. Trigeminal neuralgia
- B. Nervus intermedius neuralgia
- C. Ramsey-Hunt syndrome
- D. Otitis externa
- E. Temporomandibular joint metastatic disease

**233.** The most common transient neurological deficit associated with pseudotumor cerebri with lymphocytic pleocytosis is characteristically:

- A. Visual changes.
- B. Changes in sensation.
- C. Motor deficits.
- D. Aphasic.
- E. Vertiginous symptoms.

**234.** A 55-year-old woman complains of an intense continuous burning sensation in her mouth and tongue for several years. She reports an alteration in her sense of taste. She has a history of depression treated with a tricyclic antidepressant. Surgical history is unremarkable except for recent radial keratotomy. Multiple evaluations by dentists and otorhinolaryngologists were normal. She notes dry eyes, and an appointment with a rheumatologist was scheduled. What diagnosis is most likely?

- A. Burning mouth syndrome (BMS)
- B. Sjögren's syndrome
- C. Medication side effect
- D. Glossopharyngeal neuralgia
- E. Anxiety

**235.** Which of the following can be a manifestation of multiple sclerosis (MS)?

- A. Unilateral upper facial paresis
- B. Unilateral hearing loss
- C. Trigeminal neuralgia
- D. Sixth-nerve palsy
- E. All of the above

**236.** Which of the following is characteristic of reversible cerebral vasoconstriction syndromes?

- A. Thunderclap headache (TCH)
- B. Depressed level of consciousness
- C. Male gender
- D. Lymphocytic pleocytosis
- E. All of the above

**237.** Match the syndrome associated with a headache with its description. Each answer is used only once.

- |                          |  |
|--------------------------|--|
| A. Call-Fleming syndrome | 1. Urticaria and arthritis                       |
| B. Caroli's triad        | 2. Reversible cerebral vasoconstriction syndrome |
| C. Raeder's syndrome     | 3. Painful ophthalmoparesis                      |
| D. Tolosa-Hunt syndrome  | 4. Periocular pain and oculosympathetic paresis  |

**238.** Which of the following may produce a postpartum headache?

- A. Migraine
- B. Sheehan's syndrome
- C. Preeclampsia
- D. Cerebral venous thrombosis (CVT)
- E. All of the above

**239.** A 28-year-old man was undergoing arterial embolization for intractable epistaxis when he developed a severe headache and left-sided weakness. His general examination was remarkable for multiple tiny red skin lesions. What disorder does this man have?

- A. Neurofibromatosis
- B. Ehlers-Danlos syndrome
- C. Sturge-Weber syndrome
- D. Osler-Weber-Rendu disease
- E. Marfan syndrome

**240.** Which of the following are similarities between chronic paroxysmal hemicrania (CPH) and SUNCT syndrome?

- A. Both are male-predominant primary headaches.
- B. Both are unresponsive to indomethacin.
- C. The duration of both attacks generally overlap.
- D. Both may produce severe periorbital pain.
- E. All of the above

**241.** Which of the following is a characteristic of a migraine aura?

- A. Positive visual features
- B. Positive sensory features
- C. Dysphasic speech disturbance
- D. Gradual onset of symptoms
- E. All of the above

**242.** Which of the following is true of cyclic vomiting?

- A. Vomiting during attacks occur at least four times an hour for at least 1 hour.
- B. Nausea and vomiting last from 1 hour to 5 days.
- C. The child is symptom-free between attacks.
- D. Cyclic vomiting may be a precursor of migraine.
- E. All of the above

- 243.** Which of the following is an ICHD-II criteria for TTH?
- A. Headache duration from 30 minutes to 7 hours
  - B. Nausea and vomiting
  - C. Both photophobia and phonophobia
  - D. Aggravation by routine physical activities
  - E. All of the above
- 244.** Which of the following is *not* included in the ICHD-II criteria for CH?
- A. Conjunctival injection
  - B. Eyelid edema
  - C. Nasal congestion
  - D. Facial swelling
  - E. Sense of restlessness
- 245.** Basilar-type migraine:
- A. Is a migraine type clearly distinct from migraine with aura.
  - B. Is not associated with bilateral symptoms.
  - C. Has an autosomal dominant inheritance
  - D. Is more common in children
  - E. All of the above
- 246.** What is the most common headache type in patients with systemic lupus erythematosus (SLE)?
- A. Tension-type headaches (TTH)
  - B. Migraine headaches
  - C. Idiopathic intracranial hypertension (IIH)
  - D. Cluster headaches (CH)
  - E. Paroxysmal hemicrania
- 247.** Hypnic headache is generally associated with which of the following?
- A. Headaches occurring at least 15 times per month for at least a month
  - B. Attack duration of 10–180 minutes
  - C. Rapid eye movement (REM) sleep
  - D. Therapeutic response to lithium
  - E. All of the above

**248.** The Pott puffy tumor is a complication of:

- A. Otitis media
- B. Frontal sinusitis
- C. Occipital skull fracture
- D. Carotid cavernous fistula
- E. All of the above

**249.** Positional headaches are associated with which anatomic lesion?

- A. Sphenoid wing meningioma
- B. Chiari type I malformation
- C. Cervical syrinx
- D. Colloid cyst of the third ventricle
- E. All of the above

**250.** New daily persistent headache (NDPH):

- A. Is easily treated.
- B. Defines a specific primary headache type.
- C. Is a male-predominant headache.
- D. Is characterized by the acuity of its onset.
- E. All of the above

**251.** A 60-year-old man with a history of hypertension and cigarette smoking presented to the emergency room with the sudden onset of a bifrontal headache, along with nausea, vomiting, and dizziness. The neurology resident calls you to report that the patient's CT scan is negative, but she is still concerned that the man had a stroke. What type of stroke is this man most likely to have?

- A. A thalamic infarct
- B. A cerebellar infarct
- C. A pontine infarct
- D. A parietal lobe infarct
- E. A medullary infarct

**252.** Cluster headache and trigeminal neuralgia are similar in:

- A. Gender predilection.
- B. Age of onset.
- C. Presence of autonomic symptoms.
- D. Pain severity.
- E. Pain location.

- 253.** What is the most common cause of pulsatile tinnitus in young women?
- A. Carotid fibromuscular dysplasia
  - B. Carotid cavernous fistula
  - C. Dural arterio-venous fistula
  - D. Idiopathic intracranial hypertension (IIH)
  - E. Palatal myoclonus
- 254.** Which of the following can complicate spontaneous intracranial hypotension (SIH) and cause neurological disability?
- A. Arterial dissection
  - B. Intracerebral hemorrhage
  - C. Subdural hematoma
  - D. Cerebellar tonsillar herniation
  - E. All of the above
- 255.** Patients with Ehlers-Danlos syndrome are at risk for headaches due to:
- A. Cerebral vasculitis
  - B. Cerebral arterial thrombosis
  - C. Cerebral venous thrombosis
  - D. Subarachnoid hemorrhage (SAH)
  - E. All of the above
- 256.** A 68-year-old woman developed inability to close her right eye and a pain in her right ear. On examination, she had peripheral facial weakness and lesions in the external auditory canal. Where is the source of this syndrome?
- A. Trigeminal ganglion
  - B. Geniculate ganglion
  - C. Otic ganglion
  - D. Anterior horn cells
  - E. The right external carotid artery
- 257.** Retinal migraine is most common in:
- A. Men over age 60 years.
  - B. Women without a headache history.
  - C. Young women.
  - D. Postmenopausal women.
  - E. Children under age 10.



**258.** What is the most common headache type?

- A. Medication-overuse headache (MOH)
- B. Tension-type headache (TTH)
- C. Migraine without aura
- D. Migraine with aura
- E. Cervicogenic headache

**259.** Match the encephalitis diagnosis with a clue in the patient's travel history. Use each clue only once.

- |                                 |  |
|---------------------------------|--|
| A. Cerebral malaria             | 1. A mosquito bite in urban Indonesia            |
| B. Leptospirosis                | 2. A mosquito bite in the plains of East Africa  |
| C. Lymphocytic choriomeningitis | 3. Mucking out a barn in the Hamptons            |
| D. Lyme disease                 | 4. Hiking the Appalachian trail in Connecticut   |
| E. Dengue                       | 5. Swimming in a fresh water pond in East Africa |

**260.** A 51-year-old woman with a history of migraine headaches notes a patch of numbness on the right side of her chin for about 2 weeks. Which of the following diagnostic tests is most likely to give the specific diagnosis?

- A. Transthoracic echocardiogram
- B. Holter monitor
- C. Mammography
- D. Cervical spine MRI scan
- E. Electrolyte panel

**261.** Which of the following inherited disorders, which may be associated with headaches, is linked to chromosome 9?

- A. Mitochondrial encephalomyopathy with lactic acidosis and strokelike episodes (MELAS)
- B. CADASIL
- C. Myoclonic epilepsy with ragged-red fibers (MERRF)
- D. Occipitotemporal lobe epilepsy associated with migraine with visual aura
- E. All of the above

**262.** A 25-year-old woman with a history of migraine headaches, developed a new persistent daily headache for about 2 weeks. The pain, which was of varying intensity, involved her entire head. She was fired from her job as an administrative assistant when her employer found her taking off her clothes and sunbathing in the office waiting room window. Her family brought her into your emergency department because of her new odd behavior. She is encephalopathic with a profound memory disturbance, but has no focal motor or sensory abnormalities. Her MRI appears unremarkable. Your very astute resident listed the following possible diagnoses. You tell your resident that you think she will be cured by surgery. What do you think her diagnosis is?

- A. Herpes encephalitis
- B. Hashimoto's encephalopathy
- C. PACNS
- D. Paraneoplastic limbic encephalitis
- E. Whipple's disease

**263.** Ramsay-Hunt syndrome overlaps with which of the following disorders?

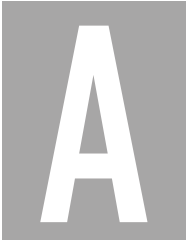
- A. Bell's palsy
- B. Tolosa-Hunt syndrome
- C. Trigeminal neuralgia
- D. Paroxysmal hemicrania
- E. Guillain-Barré syndrome

**264.** According to the specific ICHD-II diagnostic criteria, tension-type headache (TTH) is never associated with:

- A. Nausea
- B. Vomiting
- C. Photophobia
- D. Phonophobia
- E. All of the above

**265.** Cluster headaches are characteristically triggered by:

- A. Alcohol consumption
- B. Shaving
- C. Brushing teeth
- D. Eating
- E. All of the above



# HEADACHE CLASSIFICATION AND DIAGNOSIS

## ANSWERS

**138. The answer is D.** According to the International Classification of Headache Disorders, Second Edition (ICHD-II), expert opinion rather than formal evidence suggests that use of simple analgesics used for more than 15 days a month for at least 3 months is needed to induce analgesic-overuse headache. The other listed medications induce overuse headache after  $\geq 10$  days of use a month on a regular basis. (ICHD-II, *Cephalalgia* 2004)

**139. The answer is C.** Paroxysmal hemicrania attacks occur at a frequency of about one to 40 a day. Cluster headache (CH) attacks occur on alternate days or up to eight times a day. Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) attacks occur from about 3 to 200 times a day. (Cohen, Matharu, & Goadsby, *Headache* 2007)

**140. The answer is E.** The amount of cerebrospinal fluid (CSF) leakage increases with increased size of the dural tear and of the needle. The incidence of headache is 70% if the needle size is between 16- and 19-gauge, but only 12% if the needle size is between 24- and 27-gauge. Factors that do not influence the incidence of headache after lumbar puncture include volume of spinal fluid removed, duration of bed rest, improving hydration, patient position, or opening pressure. (Ahmed, Jayawarma, & Jude, *Postgrad Med J* 2006)

**141. The answer is D.** SUNCT and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) are rare, male-predominant, primary headache syndromes, classified as trigeminal autonomic cephalgias (TACs). The pain of SUNCT or SUNA occurs in multiple areas including orbital/retro-orbital, supraorbital, or temporal regions; the side, top, or back of head; second and third trigeminal divisions; or the teeth, neck, or ear. However, the pain is most characteristically around the eye. Most patients have no refractory period between triggering of attacks and are not agitated during the attacks of pain. Cu-

taneous stimuli-triggered attacks occur in SUNCT patients more than in SUNA patients. Patients may have a history of migraine or a family history of migraine. Patients with SUNCT have conjunctival injection and tearing; whereas, patients with SUNA have other cranial autonomic symptoms including nasal blockage, rhinorrhea, eyelid edema, facial sweating/flushing, and ear flushing. Unlike some other TACs, the pain of SUNCT and SUNA is not responsive to indomethacin. (Cohen, *Cephalalgia* 2007; Cohen, Matharu, & Goadsby, *Brain* 2006)

**142. The answer is E.** The ICHD-II diagnostic criteria for retinal migraine include monocular scintillations, blindness, or scotoma. The headache begins during the visual symptoms or follows them within 60 minutes. The ophthalmologic examination between attacks is normal. (ICHD-II, *Cephalalgia* 2004)

**143. The answer is B.** A post lumbar puncture headache (PLPH) generally begins within 24–48 hours after a dural puncture with bilateral dull or throbbing pain that is characteristically positional, worse while upright and with head movement. The headache is also called a post dural puncture headache, however cervical punctures are rarely performed. Sixth cranial nerve palsies (unilateral or bilateral) may rarely be seen with a lumbar puncture headache. Although a PLPH is generally benign, resolving within a few days after the puncture, symptomatic unilateral or bilateral subdural hematomas (SDH) may rarely complicate a lumbar puncture. Magnetic resonance imaging (MRI) of the brain may show diffuse enhancement of the pachymeninges, sagging of the brain, and obliteration of the basal cisterns. Needle size and design, direction of the bevel, number of lumbar puncture attempts, and replacement of the stylet all factor into the development of headache after lumbar puncture. (Ahmed, Jayawarma, & Jude, *Postgrad Med J* 2006)

**144. The answer is D.** The stress of any holiday can lead to a headache, but the all-day fast of the holiest day of the Jewish calendar is traditionally associated with a headache. A “Yom Kippur headache” is common after the High Holy Day fast from sundown to sundown. Fasting is a major trigger for migraines and is associated with headaches in individuals with a prior history of headache. Dehydration and caffeine withdrawal are also headache triggers associated with fasting. The mandated alcohol consumption of Purim and St. Patrick’s Day may also be associated with an alcohol-induced headache the day after the holiday. (ICHD-II, *Cephalalgia* 2004)

**145. The answer is B.** All drugs, including triptans, used for the treatment of the acute pain of a headache can result in medication overuse headache (MOH)

in patients with primary headache disorder. The description of the pain of MOH is not diagnostic; the diagnosis of MOH is made after withdrawal from the medication results in resolution of the headache. Combination analgesics containing butalbital, caffeine, aspirin, and acetaminophen are the most common culprits; however, triptan overuse can result in MOH. Although access to triptans is generally controlled by cost issues, overuse of triptans may eventually surpass overuse of combination medications in causing MOH. Medication overuse headaches are distinguished from chronic tension-type headaches (CTTH) and other chronic primary headache types by the use of analgesic medication for 10–15 days a month, depending on the medication, and the improvement in headaches after medication withdrawal. Chronic overuse of analgesics for nonheadache conditions does not cause increased headaches in nonmigraineurs. Migraine sufferers who consume analgesics for nonheadache conditions are at greater risk than nonmigraineurs to develop MOH. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 11 2006)

**146. The answer is C.** A PLPH occurs more often in young adults, especially in the 18–30 year age group. Young women with a lower body mass index (BMI) and pregnant women have the highest risk of developing headaches after lumbar puncture. (Ahmed, Jayawarma, & Jude, *Postgrad Med J* 2006)

**147. The answer is A 3, B 2, C 4, D 1.** Takayasu's arteritis characteristically affects young women who present with nonspecific systemic symptoms including fatigue and headaches. Syncope may occur with posterior circulation disease. They develop inflammatory changes in the aorta and its main branches, with bruits, decreased peripheral pulses and asymmetric blood pressures. Women with giant cell arteritis (GCA) are older when they present with nonspecific systemic symptoms followed by inflammatory changes of medium- and large-sized cranial vessels. Patients with GCA, who characteristically have temporal headaches, are at risk for monocular visual loss. Wegner's granulomatosis consists of necrotizing granulomatous changes in the upper and lower respiratory tract and pulmonary vessels, as well as necrotizing glomerulitis. Patients present with nonspecific symptoms, and upper airway and pulmonary symptoms. Patients with Churg-Strauss syndrome, a rare systemic necrotizing granulomatous vasculitis, have a history of allergic rhinitis with nasal polyps, asthma, eosinophilia, and elevated levels of IgE. (Marquez et al., *Curr Rheum Rep* 2003)

**148. The answer is D.** Cluster headache and SUNCT/SUNA syndrome are both TACs that are associated with severe unilateral pain with autonomic symptoms. Neither headache type is responsive to indomethacin. Although women can suf-

fer from both of these primary headaches, they are both more common in men. Nocturnal attacks are very common with CHs, but not with SUNCT/SUNA. Cluster headache attacks are of longer duration and occur less frequently than the attacks of SUNCT/SUNA. Patients with an attack of cluster, but not SUNCT/SUNA, pain are characteristically agitated. (Pareja, Caminero, & Sjaastad, *CNS Drugs* 2002)

**149. The answer is D.** This woman has a high-altitude headache (HAH) with some mild symptoms of acute mountain sickness (AMS). She rapidly ascended to 3,000 meters with risk factors of residence near sea level, dehydration, obesity, and a pulmonary condition. Her headache was consistent with HAH, developing within 24 hours after ascent. In AMS, the HAH is accompanied by gastrointestinal symptoms, insomnia, dizziness, and fatigue. Mild symptoms of AMS are generally self-limiting, but progressive symptoms can be life-threatening with the development of high-altitude cerebral edema, the serious but uncommon end-stage of AMS. Other less likely etiologies of her symptoms should be ruled out. Rehydration or a triptan is not adequate treatment for symptoms of AMS. Descent can be a treatment for HAH and mild AHS, but the neurologist needed to get dressed for the rehearsal dinner since she was a member of the wedding party. Headaches can be treated with acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs), but for AMS progressing to brain edema treatment includes oxygen, acetazolamide, and steroids. (Queiroz & Rapoport, *Curr Pain Headache Rep* 2007)

**150. The answer is D.** Hemiplegic migraine is a rare migraine subtype that presents with acute neurologic signs and symptoms indistinguishable from ischemic stroke. Its focal neurologic manifestations may persist for hours to days. Sensory, visual, or aphasic symptoms occur along with the characteristic motor aura. Although the mean age of onset is in the teens, some children may begin to have auras followed by headaches as young as toddlers. Adults, who had hemiplegic migraine in childhood, may eventually develop migraine headaches that are no longer associated with focal neurological deficits. Hemiplegic migraine can be sporadic or inherited in an autosomal dominant pattern. Familial hemiplegic migraine (FHM) has been mapped to specific genes, including a mutation of a P/Q voltage-gated calcium ( $\text{Ca}^2$ ) channel (CACNA1A) gene on chromosome 19p13 in the first, most common subtype of FHM. Although triptans, ergotamines, and  $\beta$ -blockers are generally proscribed in hemiplegic migraine, the risk with their use is poorly characterized. (Black, *Semin Neurol* 2006)

**151. The answer is B.** In Raynaud's phenomenon, vasospasm of the digital arteries causes pallor with cyanosis, alternating with rubor occurring spontaneously

or triggered by cold or emotion. It can be idiopathic or secondary to diseases or conditions such as scleroderma and systemic lupus erythematosus (SLE). Symptoms of Raynaud's phenomenon are generally mild and are commonly noted by patients with migraine headache. Severe symptoms may result in digital ischemia leading to amputation. Headaches are very common in lupus patients and are associated with Raynaud's phenomenon and  $\beta_2$ -glycoprotein-1 antibodies. Scleroderma is not particularly associated with headaches. The other listed diseases are not specifically associated with the combination of headaches and Raynaud's phenomenon. (Pope, *Drugs* 2007; Weder-Cisneros, Teliez-Zenteno, Cardiel, et al., *Cephalalgia* 2004)

**152. The answer is C.** Patients with migraine headaches, especially migraine with aura, have an increased incidence of ischemic stroke. In women aged less than 45 years, risk of stroke increased threefold associated with migraine without aura and sixfold in women with migraine with aura. The increased risk may be related to platelet aggregation, vasoreactivity of extracerebral vessels, or an increased incidence of patent foramen ovale (PFO). There may be an increased incidence of myocardial infarction (MI) in migraine patients, but the relationship is less clear than with ischemic stroke. Hemorrhagic stroke is not clearly associated with migraine headaches. Although changes in blood vessel diameter may play a role in migraine headaches, it is primarily a neurovascular disorder modulated by brainstem nuclei. Migraine is not associated with clinically evident cerebral vasospasm. (Olesen, Goadsby, Ramadan, et al., *Headaches*, Chapter 64, 2005)

**153. The answer is D.** The listed disorders all cause transient spells with MRI abnormalities that may be temporary or permanent. However this presentation is most consistent with stroke-like migraine attacks after radiation therapy (SMART), a newly recognized syndrome that occurs as a delayed consequence of cerebral irradiation. Patients with SMART have prolonged, reversible neurologic signs and symptoms including confusion, visual changes, hemi-motor and sensory deficits, aphasia, seizures, and headaches. Transient, diffuse, unilateral cortical enhancement of cerebral gyri in the area of irradiation is seen on MRI. (Black et al., *Cephalalgia* 2006)

**154. The answer is C.** Pseudomigraine with lymphocytic pleocytosis is a syndrome, more common in men, with temporary neurological deficits, moderate to severe headache, and occasional fever. The neurological deficits, which are most commonly sensory loss and aphasia, last 5 hours on average and occur episodically over a period of up to 3 months. Motor deficits may occur, but migraine-like visual changes are uncommon. Between attacks patients are normal, without

neurological complaints or deficits. In the ICDH-II classification, this syndrome is called headache with neurological deficits and CSF lymphocytosis (HaNDL). (Pascual & Valle, *Curr Pain Headache Rep* 2003)

**155. The answer is C.** The pain of pediatric headaches is often of shorter duration than adult migraine. The localization is predominantly bilateral, often frontotemporal. If the pain of a pediatric headache is purely occipital, the child should be imaged with an MRI scan to rule out a posterior fossa mass lesion. The child may have difficulty expressing the difference between nausea and anorexia; both are consistent with pediatric migraine. (Winner & Hershey, *Curr Pain Headache Rep* 2007)

**156. The answer is A.** Primary angiitis of the central nervous system (PACNS) generally presents with headaches followed by focal neurological deficits. It is rarely accompanied by fever, weight loss, or malaise. Catheter angiography shows beading, occlusion, or luminal irregularity in 60–80% of patients with PACNS. Since PACNS predominantly involves small vessels, up to 40% of patients may have negative angiography. MRI abnormalities include ischemic lesions, leptomeningeal enhancement, hemorrhage, mass lesion, or diffuse white matter disease. The MRI and spinal fluid may be nondiagnostic in PACNS, and brain biopsy may be needed for pathological diagnosis. Treatment is generally intravenous to oral steroids, often with the addition of other immunosuppressive therapy. (West, *Curr Rheum Rep* 2003)

**157. The answer is D.** An older adult with transient global amnesia (TGA) suddenly develops selective retrograde and anterograde amnesia, lasting generally less than 24 hours. The event may occur after sudden severe stress, physical exertion, or sexual activity (often with unaccustomed partners). Recovery of memory is complete, except for the period of time of the amnesic event. Attacks are differentiated from seizures or transient ischemic attacks (TIAs) by their longer duration and the specificity of the memory deficit in the absence of alteration in consciousness or focal neurologic symptoms. An individual is unlikely to have a repeat attack, although one can occur rarely. A headache may be noted during the episode, and migraine has been suggested as one potential cause of TGA. Speculation about the pathogenesis of TGA also includes cerebral venous congestion. Although focal ischemia may factor into the etiology of TGA, patients generally lack the traditional vascular risk factors such as hypertension and hypercholesterolemia. TGA does not increase risk of ischemic stroke. TGA is a benign short-lived memory disorder, related to transient disturbance of hippocampal CA-1 neurons, without structural and neuropsychological sequelae. (Bartsch et al., *Brain* 2006; Roach, *Arch Neurol* 2006)



**158. The answer is B.** Cerebral amyloid angiopathy is a neurodegenerative vasculopathic disorder generally diagnosed in demented elderly individuals. The  $\beta$ -amyloid peptide deposition in cerebral blood vessels increases the patients' risk of hemorrhages, which are characteristically lobar. Basal ganglia (putaminal) and cerebellar hemorrhages are most often related to hypertension. Brainstem hemorrhages may be due to hypertension or underlying lesions, such as cavernous malformations or arteriovenous malformations (AVMs). Intraventricular hemorrhage, like subarachnoid hemorrhage, is most often caused by a ruptured intracranial aneurysm. (Atterns, *Acta Neuropathol* 2005)

**159. The answer is A.** Arteriovenous malformations are congenital, not developmental, lesions. These lesions most often become symptomatic during the second to fourth decades, although symptoms can occur in children or in the elderly. Hemorrhage from an AVM is the most common cause of intracerebral hemorrhage in children. Seizures are a common problem in children and adults with AVM, but the most serious complications are related to cerebral hemorrhage due to AVM rupture. In general, unruptured AVMs are incidental findings on imaging studies in patients with headache and are uncommon etiologic causes of headache. Treatments of AVMs include embolization, stereotactic radiosurgery, and neurosurgical excision. Treatment may not be possible for some AVMS in eloquent areas. Grading systems can be used to determine risk of hemorrhage. (Choi & Mohr, *Lancet Neurol* 2005)

**160. The answer is B.** Cavernous malformations are generally asymptomatic collections of blood-filled vascular spaces. They may develop over time as acquired lesions. They may be sporadic or familial, and are often incidental findings on brain, brainstem, and spinal cord imaging studies. The presentation of cavernous angiomas may be associated with seizures, focal neurologic deficits due to hemorrhage, and headaches. Their main clinical presentation is seizures. Hemorrhage is the rare presenting problem of most patients with cavernous angiomas. Cavernous malformations are generally unrelated to the headaches that precipitated the imaging study. (Rivera, Willinsky, & Porter, *Neuroimag Clin N Am* 2003)

**161. The answer is D.** Ehlers-Danlos syndrome type IV, the vascular type, results from mutations in the gene for type III procollagen (COL3A1). Patients with Ehlers-Danlos syndrome type IV have abnormal elastic tissue and are at risk for cerebral aneurysms and arterial dissections. They may present with a sudden-onset severe headache due to aneurysmal subarachnoid hemorrhage (SAH). They do not have increased risk of either vasculitis or inflammatory disease, nor do

they have any propensity for arterial or venous thrombosis. They may suffer ischemic strokes due to intracranial or extracranial cerebral arterial dissection. (Pepin, Schwarze, Superti-Furga, et al., *N Engl J Med* 2000)

**162. The answer is C.** Cluster headache patients were felt to be particularly resistant to MOH; however, CH patients can develop MOH. In a retrospective study of 17 patients (13 men, four women) with episodic and chronic CH, MOH was associated with overuse of simple analgesics, caffeine, opioids, ergotamine, and triptans. The MOH in CH patients was not a characteristic CH but was a bilateral, dull, and featureless daily headache, or was associated with nausea, exacerbation with head movement, or throbbing pain. All the patients had either a personal history of migraine or family history of migraine or unspecified headaches. Medication withdrawal was successful in 13 out of the 17 CH patients with MOH. (Paemeleire, Bahra, Evers, et al., *Neurology* 2006)

**163. The answer is D.** Intolerance to smell, especially perfumes and smoke, is often reported by children and adults with migraine. Osmophobia may also be reported rarely by CH patients. In a study of osmophobia in patients with the diagnoses of migraine and tension-type headache (TTH), about 40% of patients with migraine reported osmophobia during the attacks but none of the TTH patients reported sensitivity to smells during their headaches. Scents, food smells, and cigarette smoke were the most frequent offending odors reported by osmophobic migraineurs. Although sensitivity to smell may be reported during the migraine headache, even between headaches, migraineurs tend to be intolerant of cigar smokers and department store perfume spritzers. (Zanchin, Dainese, Trucco, et al., *Cephalalgia* 2007)

**164. The answer is B.** Turtle headaches are generalized or bifrontal, short-lived headaches noted on awakening as the person sticks his head, turtle-like, out from under the covers. They are associated with sleeping with covers over the head and appear to be related to hypercapnia, producing increased cerebral blood flow, with concomitant hypoxia. (Poceta, *Curr Pain Headache Rep* 2003)

**165. The answer is B.** Chronic headaches related to the surgery occur commonly in patients after craniotomies in multiple locations, including for resection of posterior fossa tumors and both anterior and posterior circulation aneurysms. Most acute and chronic post craniotomy headaches have no underlying anatomic correlate and may be related to a disturbance of dural nociceptive receptors. Persistent postoperative headache is more common in women and is associated with depression and anxiety. In a study of headaches after acoustic neuroma resec-

tion, three-quarters of the patients with new postoperative headaches had the headaches persist for at least a year after surgery. Female gender, lack of previous headache, and small acoustic neuroma size predicted development of chronic postoperative headache. (Rimaaja, Haanpaa, Blomstedt, et al., *Cephalalgia* 2007; Rocha-Filho, Gherpelli, de Siqueira, et al., *Cephalalgia* 2007)

**166. The answer is D.** Intermittent but recurrent, severe, short-lasting, unilateral, periorbital headaches, presumably due to sinus barotraumas, can be caused by changes in airplane cabin pressure. The most severe pain of these headaches lasts from 15–20 minutes, occurring in some, but not all, flights in susceptible individuals who may be smokers. The headaches tend to occur during landing, especially at seaside airports. Subclinical congestion and inflammation in the ethmoid sinus and middle turbinate mucosa, with a vacuum effect triggering ethmoid nerves branches of the trigeminal nerve and nociceptors on the anterior ethmoid artery, may be an explanation for the attacks. (Berilgen & Mungen, *Cephalalgia* 2006)

**167. The answer is C.** The SUNCT syndrome is a rare, male-predominant primary headache disorder. The pain is severe, maximal in the  $V_1$  division of the trigeminal nerve. The attacks of pain generally last 5–240 seconds, and are typically unilateral and side-locked. The syndrome is often refractory to treatment, but some efficacy has been noted with lamotrigine, topiramate, gabapentin, steroids, and intravenous lidocaine. This is not a syndrome characteristically responsive to indomethacin. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 8, 2005)

**168. The answer is C.** This woman's description of a round, constant area of pain and sensitivity best fits with nummular headache, a round or oval area of mild to severe head pain. The pain is continuous, but periods of spontaneous remission may last weeks to months. A distortion of sensation is commonly noted in the area of the pain, but symptoms that accompany migraine headaches are generally absent. The patient's relatively young age and the location of the pain are not consistent with GCA. The pattern and the location of the pain are not characteristic of CH or TTH. The pain characteristics and lack of accompanying symptoms make migraine headaches unlikely in this woman. (Grosberg, Solomon, & Lipton, *Curr Pain Headache Rep* 2007)

**169. The answer is A.** This woman has the descriptive red ear syndrome, with recurrent attacks of unilateral ear pain associated with erythema. The attacks of ear pain are spontaneous or provoked by stimulation such as touch, change in temperature, exertion, or neck movement. Although multiple putative etiologies

have been proposed for this syndrome, described by Lance as an “auriculo-autonomic cephalalgia,” no specific cause has been determined for this headache type that may be associated with migraines. Many treatments have been attempted, and some relief has been noted with ibuprofen. No medical therapy has been consistently beneficial in these patients. (Purdy & Dodick, *Curr Pain Headache Rep* 2007)

**170. The answer is D.** Evidence of an underlying generalized connective tissue disorder is found in about two-thirds of patients with spontaneous spinal fluids leaks. About one in five patients with spontaneous spinal fluids leaks have subtle isolated skeletal manifestations of Marfan syndrome, such as tall stature, arachnodactyly, highly arched palate and hypermobile joints, without the genetic defect associated with the syndrome. Other disorders associated with spontaneous intracranial hypotension (SIH) include Marfan syndrome with fibrillin-1 (FBN1) gene mutation, Ehlers-Danlos syndrome, and autosomal dominant polycystic kidney disease. (Schievink, *JAMA* 2006)

**171. The answer is B.** The childhood periodic syndromes that appear to be precursors to migraine headaches include cyclic vomiting syndrome, abdominal migraine, and benign paroxysmal vertigo. Recurrent stereotypic episodes of vomiting and intense nausea, with pallor and lethargy, occur in young infants and children with cyclic vomiting syndrome. Once gastrointestinal pathology is appropriately ruled out, medications used to treat migraines may relieve the gastrointestinal symptoms. A strong family history of migraines is commonly found the children with cyclic vomiting syndrome and, as the children grow older, they may develop typical attacks of migraine headaches. The other choices are distracters. (Winner & Hershey, *Curr Pain Headache Rep* 2007; ICHD-II, *Cephalalgia* 2004)

**172. The answer is E.** A chronic daily headache (CDH) is a headache of any type, either primary or secondary, that occurs for at least 15 days per month for longer than three months. Primary chronic daily headaches are divided into short-duration (<4 hours) and long-duration (>4 hours) types. The most common long-duration types are CTTH and transformed migraine. This disabling headache type is prevalent in about 4% of the adult population, more commonly in women. It is associated with less education and lower income. Stressful life events, like bankruptcy of hedge funds, may be correlated with development of CDH. Classification of CDH emphasizes the increasing frequency of these headaches that segue from episodic to chronic. Headache attributed to medication overuse, an important cause of primary CDH, can occur with excess and prolonged use of acute pain medication. Medication overuse predicts a worse prog-

nosis for headache treatment, but the use of a daily preventative medication, with judicious use of acute pain medication, can decrease primary CDHs, which may then evolve back to episodic headaches. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 2; ICHD-II, *Cephalalgia* 2004)

**173. The answer is A.** Frequent morning headaches, as distinct from migraine or TTH, are associated with a variety of sleep disorders including obstructive sleep apnea (OSA), narcolepsy, restless legs syndrome, insomnia, and snoring. Frequent morning headaches due to OSA may improve with continuous positive pressure airway pressure (CPAP). As more is learned about multiple types of sleep disorders (including OSA) and headaches, the correlation is clear, although the precise mechanisms to explain the association are not. The relationship between migraine headaches and OSA, and the reason for their possible response to CPAP is not clear. While migraines are more common in women, OSA is more common in men. Patients with migraine headaches have an increased incidence of sleep disorders such as insomnia and REM sleep behavior disorders. (Poceta, *Curr Pain Head Rep* 2003)

**174. The answer is A.** The complex relationship between sleep and migraines is incompletely understood. Mechanisms involving the regulation of melatonin, prolactin, and cortisol, as well as brainstem nuclei with connections to the trigeminovascular system and sleep centers, may explain the connection. Change in sleep habits, including too much or too little sleep, can trigger migraine headaches. However, induction of sleep can abort a migraine headache for many sufferers. Pediatric and adult migraine sufferers often have sleep disturbances, such as insomnia and sleep behavior disorders. Migraine attacks are most frequent on awakening, with one study indicating that almost half of all migraines occurred between 4 AM and 9 AM. (Poceta, *Curr Pain Head Rep* 2003)

**175. The answer is A.** The MOH caused by triptan overuse is a migraine-like daily headache or a significant increase in migraine attack frequency. The MOH associated with triptan overuse occurs faster and with less medication than does MOH associated with other acute medications for headache. The number of doses per day is much smaller for patients who develop headaches from overuse of triptans than for patients with MOH who overuse other analgesics. The intensity and duration of withdrawal symptoms are significantly milder and shorter when excessive triptans are discontinued, as compared to other acute medications. Restricting triptans to no more than 10 single doses per month will decrease the development of triptan-induced MOH. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 11, 2005)

**176. The answer is A.** Over a third of patients with ischemic stroke or TIA may have a headache, although it is often mild and overshadowed by the accompanying focal neurologic complaints. A headache is more commonly associated with a posterior circulation infarct. Although the size of the infarct does not always correlate with the severity of the headache, headaches are much less common with lacunar syndromes. Studies have found no difference in headache frequency between cardioembolic and atherothrombotic strokes. Patients with a migraine history are more likely to have a headache at onset of cerebral ischemia, than are non-migraineurs. (Olesen, Goadsby, Ramadan, et al., *Headaches*, Chapter 108, 2005)

**177. The answer is A 3, B 5, C 2, D 4, E 1.** Hemicrania continua is a severe continuous hemicranial pain characteristically responsive to indomethacin. A low-CSF volume headache is characteristically positional, worse when upright, relieved when recumbent. The SUNCT syndrome has attacks lasting about 5–240 seconds. Hypnic headaches characteristically awaken an elderly patient from sleep with generalized or bilateral pain lasting under 60 minutes. MOHs can occur with any medication used excessively ( $\geq 10$ –15 days a month for  $\geq 3$  months) for acute relief of headache pain. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache* 2005)

**178. The answer is A.** Hemicrania continua is a unilateral headache without side-shift. The pain is daily and continuous, without pain-free periods, and is of moderate intensity with exacerbations of severe pain. The pain is associated with ipsilateral lacrimation, conjunctival injection, nasal congestion, ptosis, or miosis. The headache pain can be associated with migrainous features. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 9, 2005)

**179. The answer is E.** The holocephalic or unilateral headache of idiopathic intracranial hypertension (IIH) can be associated with multiple other symptoms. There can be multiple episodes of loss or dimming of vision lasting seconds, which are called transient visual obscurations. The overweight woman, the characteristic patient who suffers from this type of headache, may note horizontal diplopia from an acquired sixth-nerve palsy as well as pain on eye movement. The elevated intracranial pressure causes aural perception of the arterial pulse, with patients often admitting to pulsatile tinnitus only on direct questioning. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 9, 2005)

**180. The answer is D.** Neck pain is a common complaint that is not specific or sensitive enough to indicate a cervicogenic headache. The prevalence of cervicogenic headache—head pain related to cervical spine pathology—is unknown, as mul-

multiple definitions have been suggested to determine its existence. Some definitions emphasize the need for correlation with an anatomic lesion in the cervical spine, whereas others are less specific in elucidating the cause of neck and head pain. The ICHD-II definition correlates the clinical, laboratory, and/or imaging evidence of a cervical spine or neck lesion with the pain, which is referred from the neck to the head and face. The headache pain should be abolished following a diagnostic blockade of a cervical structure or its nerve supply, with resolution of the pain after successful treatment of the causative disorder or lesion. Multiple radiological trials of patients diagnosed with cervicogenic headaches, not using ICHD-II criteria, did not find an increase in cervical lesions, as compared to control patients. (Da Silva & Bordini, *Curr Pain Headache Rep* 2006; ICHD-II, *Cephalalgia* 2004)

**181. The answer is B.** Neck pain commonly accompanies the head pain of migraine or TTH, without any radiological correlate in the neck or cervical spine. The neck pain associated with migraine and TTH is generally bilateral. The diagnosis of cervicogenic headache is controversial, but the neck pain associated with cervicogenic headache has been described as unilateral, without side-shift. Radiofrequency radiolysis has had variable results, including lack of benefit in a randomized, placebo-controlled studies. (Da Silva & Bordini, *Curr Pain Headache Rep* 2006)

**182. The answer is A.** The ICHD-II diagnostic criteria for migraine without aura dictates at least five attacks of headache attack lasting 4–72 hours. At least two of the criteria: unilateral pain, pulsating pain, moderate or severe pain, or aggravation with routine physical activity are required, along with either nausea/vomiting or photophobia and phonophobia. (ICHD-II, *Cephalalgia* 2004)

**183. The answer is C.** In a study of 696 patients with community-acquired bacterial meningitis, the classic triad of fever, neck stiffness, and change in mental status was seen in only 44% of patients. However, when headache (noted in 87% of the patients) was added to the triad almost all patients were diagnosed with meningitis. Neck stiffness was reported in 83%. Almost 70% had some change in mental status, and coma (Glasgow Coma Scale <8) was noted in 14%. About half of the patients had symptoms for less than 24 hours prior to treatment. Bacterial meningitis may be suspected in patients with a typical presentation, but the majority of patients do not exhibit all the three classic features at time of diagnosis. (Van de Beek, de Gans, Spanjaard, et al., *N Engl J Med* 2004)

**184. The answer is C.** Trigeminal neuralgia and SUNCT/SUNA syndrome both produce severe unilateral pain, but only SUNCT/SUNA is associated with auto-



onomic symptoms. Neither is responsive to indomethacin. The duration of trigeminal neuralgia attacks (about 1–30 seconds) and the attacks of SUNCT/SUNA (10–120 seconds) overlap. Both headache syndromes produce severe to excruciating pain around the eye, but trigeminal neuralgia may involve all three divisions of the trigeminal nerve, with pain usually in the lower face. (Pareja, Caminero, & Saastad, *CNS Drugs* 2002)

**185. The answer is B.** Contact-point headaches are defined by ICHD-II criteria as headaches due to intranasal contact between two opposing mucosal surfaces inside the nasal cavity. These headaches may be due to septal contact with the medial wall of the ethmoid or the nasal turbinates. Patients with mucosal contact-point headache should experience short-term pain relief with topical anesthetic or decongestant in the contact area, and long-term pain relief with surgical separation of the contact. The role of intranasal contact points in the development of migraine headaches is subject to debate. Although intranasal congestion has been shown to occur with migraine attacks, it may be an epiphenomenon, not a causal factor in the headache. (Behin, Lipton, & Bigal, *Curr Pain Headache Rep* 2006; ICHD-II, *Cephalalgia* 2004)

**186. The answer is A.** The ICHD-II definition for hemicrania continua is a daily and continuous unilateral moderate to severe pain without side-shift, accompanied by autonomic symptoms, with complete response to indomethacin. However, some bilateral chronic daily headaches similar to hemicrania continua respond to indomethacin. Migrainous features (nausea, vomiting, photophobia, phonophobia) may occur during the exacerbation period of hemicrania continua. Chronic paroxysmal hemicrania does not have the characteristic continuous baseline headache associated with hemicrania continua, and autonomic symptoms are more prominent in chronic paroxysmal hemicrania. Sharp, shooting unilateral pains lasting less than a minute are common with hemicrania continua, as well as with migraine or paroxysmal hemicrania. These head pains, described as “jabs and jolts”, also occur commonly in the general population and are not specific for hemicrania continua, although they may respond to indomethacin. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 9; ICHD-II, *Cephalalgia* 2004)

**187. The answer is E.** All the listed abnormalities can be found in patients with IIH. Structural causes of these cranial nerve abnormalities should be ruled out by neuroimaging prior to making the diagnosis of IIH. Rarely the neurologic examination can also be totally normal in a patient with IIH, with elevated spinal fluid pressure prior to the development of papilledema. Then the diagnosis is gener-



ally discovered incidentally with elevated opening pressure on a lumbar puncture performed for an unrelated indication. (Skau, Brennum, Gjerris, et al., *Cephalalgia* 2006)

**188. The answer is E.** All of the listed headache types are characterized by both sympathetic and parasympathetic symptoms. The TACs are a group of primary headache disorders, mediated by the hypothalamus, with unilateral head pain in association with ipsilateral cranial autonomic cranial autonomic features. The TACs include paroxysmal hemicrania, CH, and SUNCT/SUNA syndrome. Hemicrania continua is not classified as a TAC, although it shares autonomic symptoms with all the TACs and indomethacin responsiveness with paroxysmal hemicrania. (Goadsby, Cohen, & Matharu, *Curr Neurol Neurosci Rep* 2007)

**189. The answer is C.** Thunder clap headache (TCH) describes a severe and explosive headache that is either maximal in intensity at its onset or reaches peak intensity in less than a minute. It can be a primary headache, such as “crash migraine,” without identified underlying anatomic abnormality. A benign, explosive, headache may be precipitated suddenly by cough, exercise, or orgasm. Secondary causes of TCH are usually vascular, such as SAH, cerebral venous thrombosis or intraventricular hemorrhage. Nonvascular causes include intracranial hypotension, infection, and acute hydrocephalus. Almost all acute, unexplained TCHs should be evaluated with at least an uncontrasted computed tomography (CT) scan of the brain to rule out SAH, the most common and life-threatening cause of secondary TCH. (Matharu, Schwedt, & Dodick, *Curr Neurol Neurosci Rep* 2007)

**190. The answer is A.** Most cough headaches are not associated with any anatomic or vascular abnormality and can be considered primary headaches. Rarely cough headache may be associated with cerebellar tonsillar descent below the foramen magnum causing obstruction. Chiari type I malformation is defined as tonsillar descent descend  $\geq 5$  mm below the foramen magnum. A Chiari type I malformation is a common incidental finding on MRI of the brain. The other listed abnormalities are not specifically associated with cough headache. (Pascual, *Curr Headache Rep* 2005)

**191. The answer is A.** The auriculotemporal nerve is the terminal branch of the posterior division of the mandibular nerve ( $V_3$ ). Neuralgia of the auriculotemporal nerve produces moderate- to severe-intensity pain in the distribution of the nerve, which supplies sensation to the temporomandibular joint and external auditory meatus. The lack of autonomic symptoms distinguishes the neuralgia from hemicrania continua and paroxysmal hemicrania. The normal MRI of the cervical

spine rules out cervicogenic headache. The relative lack of fleeting pain, triggered by stimulation, rules out trigeminal neuralgia. She had no autonomic symptoms characteristic of hemicrania continua or paroxysmal hemicrania. (Speciali & Goncalves, *Curr Pain Headache Rep* 2005)

**192. The answer is A.** The majority of patients with SUNCT do not have the refractory period after an attack of pain that is characteristic of trigeminal neuralgia. Although the pain of SUNCT is most usually periorbital, and the pain of trigeminal neuralgia is usually in the lower face, there can be overlap in the site of attacks of both pain syndromes. The duration of stabbing pain with SUNCT can be seconds, with a mean attack frequency of ranging from a few to hundreds a day, similar to trigeminal neuralgia. Both conditions occur in both genders, although SUNCT is more common in men. SUNCT, a TAC, is associated with autonomic symptoms, which are not seen with trigeminal neuralgia. (Cohen, *Cephalalgia* 2007)

**193. The answer is C.** Headache attributed to hypoxia is associated with the acute onset of  $\text{PaO}_2 < 70$  mm Hg (normal 85 – 100 mm Hg) or, in chronically hypoxic patients, with levels persistently lower than this value. Hypoxia and hypercapnia may both induce headache, with effects that are difficult to separate. Hypercapnia with high arterial  $\text{CO}_2$  ( $\text{PaCO}_2 > 50$  mm Hg) with vasodilation and increased intracranial pressure maybe associated with headache without hypoxia. (ICHD-II, *Cephalalgia* 2004)

**194. The answer is D.** Headaches that most commonly occur during or after scuba diving are due to hypercapnia from hypoventilation in the setting of exercise. Focal neurological symptoms, alteration in consciousness, and musculoskeletal pain indicate decompression sickness. Treatment with 100% oxygen by nasal prongs or face mask acutely and then in a hyperbaric chamber is indicated with decompression sickness. Other headaches associated with diving include sinus barotrauma, arterial gas embolism, carbon monoxide toxicity, hyperbaric-triggered migraine, cervical and temporomandibular joint strain, supraorbital neuralgia, carotid artery dissection, and exertional and cold stimulus headaches. (Cheshire, *Curr Pain Headache Rep* 2004; ICHD-II, *Cephalalgia* 2004)

**195. The answer is D.** Headache with neurological deficits and CSF lymphocytosis, generally called HaNDL, is most frequent in men between 15 and 40 years of age. About a third of patients with this syndrome have a prior viral-like illness; although its etiology is unknown and viral PCR have not been identified in the CSF. The patients have a dozen or more episodes of neurologic deficits (usually

sensory deficits and aphasia with infrequent visual loss) lasting for hours, occurring episodically for up to 3 months. The accompanying headache is generally bilateral and throbbing. Lymphocytes and protein are elevated in the spinal fluid, which does not show any evidence of infection. Between attacks and after the symptomatic period, the patient is without neurological deficits or symptoms. (Gomez-Aranda, Canadillas, Marti-Masso, et al., *Brain* 1997; Pascual & Valle, *Curr Pain Headache Rep* 2003)

**196. The answer is A.** SUNCT is a rare, male-predominant, non-indomethacin responsive TAC. It is defined by the presence of conjunctival injection and tearing and may be a subset of SUNA, which is defined by the presence of less specific cranial autonomic symptoms. This TAC is particularly refractory to preventative and acute treatment and it not responsive to indomethacin. Activation of the posterior hypothalamus has been noted on functional imaging of SUNCT patients. (Cohen, *Cephalalgia* 2007)

**197. The answer is B.** Women of childbearing age are frequently afflicted with common primary headache disorders such as migraine and TTH. The prevalence of headaches during pregnancy or the immediate postpartum period is reported to be as high as 35%. During pregnancy and the postpartum period, women may have new-onset headaches that are generally primary. A woman's first migraine may occur during pregnancy. However, some of these new-onset headaches may be secondary to cerebrovascular disorders or mass lesions. In a prospective evaluation of 1,101 pregnant women with a headache history, Melhado et al. (2007) found that headaches during gestation were due to migraine in over 80% of women with a pregestational headache history. Generally, these migraine headaches improve or resolve after the end of the first trimester. However, in the rare women with a new-onset headache during pregnancy, over half had a secondary headache. Less than half of pregnant women with a new-onset headache, without any prior headache history, ended up having a primary headache disorder. Emergent neuroimaging should be obtained when appropriate, since studies reveal underlying headache pathology, both in the brain and in sinuses, in up to a quarter of pregnant women with new-onset headache. (Melhado, Maciel, & Guerreiro, *Can J Neurol Sci* 2007)

**198. The answer is C.** Most pregnant women with an acute headache and a prior headache history have a primary headache such as migraine or TTH. Because the care of a pregnant woman must address the health of both the mother and the fetus, evaluation of the pregnant woman with a headache should focus on the most likely headache diagnosis, while ruling out a secondary cause of headache.

An abnormal neurologic examination, including an abnormal mental status, and increased headache duration may predict abnormal neuroimaging. The amount of fetal radiation exposure from a 10-section CT scan is well below the amount associated with fetal abnormalities, and fear of fetal radiation exposure should not preclude emergent CT imaging when it is felt to be appropriate. (Ramchandren, Cross, & Liebskind, *Am J Neuroradiol* 2007)

**199. The answer is D.** Trigeminal autonomic cephalalgias, which include cluster headache, paroxysmal hemicrania, and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing/cranial autonomic features (SUNCT/SUNA), have different attack duration and frequency. Cluster headaches have the longest attack duration (about 15–180 minutes and relatively low attack frequency). Paroxysmal hemicrania has intermediate duration (approximately 2–30 minutes) and intermediate attack frequency. Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) have the shortest attack duration (approximately 5–240 seconds) and the highest attack frequency. (Cohen, Matharu, & Goadsby, *Headache* 2007; Goadsby, Cittadini, Burns, et al., *Curr Opin Neurol* 2008)

**200. The answer is D.** A SAH is the most neurologically devastating cause of a headache of apoplectic onset. Other conditions that can cause the sudden onset of a severe headache include “crash migraine,” intracranial hemorrhage, pituitary apoplexy, exertional headache, and benign TCH. Neck pain may be present with either migraine or SAH. Although SAH has been classically described as “the worse headache of my life,” the pain may be severe to moderate, with the main characteristic being the sudden onset. Migraine and SAH both are more common in middle-aged women. A subarachnoid headache may occur in a primary headache sufferer, which can complicate recognition of a different type of headache by both the patient and the physician. (Olesen, Goadsby, Ramadan, et al., *Headaches*, Chapter 109 2005)

**201. The answer is E.** Cyclic vomiting, abdominal migraine, benign paroxysmal vertigo, alternating hemiplegia of childhood, and paroxysmal torticollis are all periodic disorders correlated with migraine headaches. Head pain may not be part of the symptom complex, although there may be a family history of migraine or the child may eventually develop migraine headaches. Cyclic vomiting is repeated episodes of severe vomiting and dehydration without headache. Abdominal migraine is associated with recurrent episodes of midline abdominal pain, with other gastrointestinal symptoms, but without headache. Vertigo in young children may evolve into a migraine disorder in later childhood. Young

children with paroxysmal torticollis with vomiting and ataxia may eventually develop migraine headaches. (Silberstein, Lipton, & Dodick, *Wolff's Headache*, Chapter 27, 2007)

**202. The answer is E.** Headache associated with sexual activity (HSA) can be distressing to the patient and perplexing to the physician. The cause of a HSA may be readily apparent in patients taking nitric oxide (NO) donors for erectile dysfunction. Rarely, a cerebrovascular cause of a HSA, such as a hemorrhagic or ischemic stroke, is diagnosed based on characteristics of the headache and other accompanying neurologic symptoms. A postural HSA may be related to leakage of CSF associated with sexual activity. Although a HSA can be frightening, especially when it occurs repetitively, its cause is generally benign. The ICHD-II defines two types of HSA: a preorgasmic headache with dull head and neck pain increasing with sexual excitement (HSA type 1) and a sudden, severe, explosive orgasmic headache (HSA type 2). (Frese, Eikermann, Frese, et al., *Neurology* 2003)

**203. The answer is E.** Any of the above cerebrovascular diagnoses should be considered in this woman who developed a headache followed by a secondarily generalized seizure. A SDH, presenting with headache, focal seizure, and postictal paresis, may occur as a complication of epidural anesthesia. Risk of an ischemic stroke or an intracerebral hemorrhage increases in the postpartum period. An embolic infarct due to amniotic fluid or choriocarcinoma may present with a focal seizure and a fixed neurologic deficit and should be considered postpartum. Cerebral venous thrombosis may present in the hypercoagulable postpartum period as a headache followed by a seizure with venous infarction causing a focal neurological deficit. Eclampsia should also be considered in this woman with headache, seizure, and a focal neurologic deficit. (Zakowski, *Sem Perinat* 2002; Feske, *Semin Neurol* 2007)

**204. The answer is D.** Sturge-Weber syndrome is a neurocutaneous syndrome in which patients have a facial port-wine stain and ocular abnormalities (glaucoma and choroidal hemangioma). Sturge-Weber syndrome is characterized intracranially by leptomeningeal vessel calcification and arteriovenous angiomas. Osler-Weber-Rendu disease (hereditary hemorrhagic telangiectasia) is an autosomal dominant disease with skin, nasal, and visceral telangiectasia, as well as intracerebral vascular malformations. Neurofibromatosis is associated with occlusive arterial disease. Cerebrovascular disease in Marfan syndrome usually leads to large artery dissection, as does Ehlers-Danlos syndrome type IV. (Kasner & Gorelick, *Prevention and Treatment of Ischemic Stroke*, Chapter 8, 2003)

**205. The answer is E.** Migraines are common in women of childbearing age, and headaches may be problematic during pregnancy. Most women note decreased frequency and severity of headaches as pregnancy progresses; however, some women find that their migraine headaches are worse or unchanged. A woman may have her first migraine during pregnancy. Women with migraine have an increased risk of complications of pregnancy including ischemic stroke, preeclampsia, and eclampsia. Headaches generally worsen after delivery for both hormonal and environmental reasons. (Loder, *Semin Neurol* 2007)

**206. The answer is A.** This woman has cerebral venous thrombosis (CVT). Lowered intravascular volume with dehydration, sepsis, or malnutrition may predispose to thrombosis in cerebral venous sinuses. Genetically determined thrombophilias predisposing to CVT include activated protein C resistance, protein S and protein C deficiencies, antithrombin III deficiency, the prothrombin gene mutation, and hyperhomocysteinemia. Antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant,  $\beta_2$  glycoprotein-1 antibodies) are less likely to be associated with venous clotting than the more common Factor V Leiden deficiency, assayed by activated protein C resistance. Pregnancy, puerperium, oral contraceptives, and hormone replacement therapy may be associated with CVT. A cardiac evaluation will not yield specific results. (Olesen, Goadsby, Ramadan, et al., *Headaches*, Chapter 112, 2005)

**207. The answer D.** Familial hemiplegic migraine is a genotypically heterogeneous, autosomal dominant, migraine subtype with three major subtypes presently determined. The most common gene associated with FHM is the CACNA1A, the FHM1 gene, which encodes the pore-forming  $\alpha 1A$  subunit of P/Q-type voltage-dependent neuronal calcium channels. Fully reversible motor weakness plus fully reversible visual, sensory, or speech deficits are necessary for the diagnosis of FHM1. This migraine subtype affects men and women equally. The degree of motor deficit ranges from mild clumsiness to hemiplegia. Despite reversal of symptoms that occur with the headaches, focal neurological deficits can be present in patients with FHM1. Permanent cerebellar symptoms, found in up to 20% of patients with FHM1, include nystagmus and gait ataxia. (Olesen, Goadsby, Ramadan, et al., *Headaches*, Chapter 61, 2005)

**208. The answer is D.** The length of time of a CH attack is generally 15–180 minutes. The unilateral pain with autonomic symptoms is excruciating to the agitated sufferer. An attack of paroxysmal hemicrania lasts about 2–30 minutes. The pain of SUNCT lasts from about 5–240 seconds. The pain of trigeminal neuralgia lasts from a fraction of a second to 2 minutes. (ICHD-II, *Cephalalgia* 2004)

**209. The answer is B.** This man presents with posterior circulation symptoms suggestive of an acute cerebellar infarct. Although his symptoms could be due to an acute vestibular disorder, his age and medical history make ischemic vertebrobasilar disease the first concern. An MRI with diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) sequences to look for an acute ischemic lesion and a magnetic resonance angiograph (MRA) of the posterior circulation, looking for arterial occlusion, would establish the diagnosis of an ischemic posterior circulation stroke in the face of a negative CT scan. An ultrasound study of the neck would not give adequate visualization of the vertebrobasilar system from arch to intracranial vessels. This patient has a risk of edema formation around the area of cerebellar infarction, with concern about obstruction of spinal fluid outflow and obstructive hydrocephalus. Close monitoring by the nursing staff, more frequently than every 6 hours, should pick up change in mental status from brainstem compression. This man does not have symptoms suggestive of SAH, and a lumbar puncture in the face of possible fourth ventricular obstruction in the posterior fossa increases herniation risk. Plus, therapeutic anticoagulation is a contraindication for a lumbar puncture. (Tohgi, Takahashi, Chiba, et al., *Stroke* 1993)

**210. The answer is E.** The diagnosis of MOH is based on clinical characteristics and may require focused repetitive questioning of the patient before characteristics are elicited and the diagnosis is revealed. Chronic daily headache due to medication overuse may be triggered by physical or emotional events in individuals with a low pain threshold. Although withdrawal of the offending overused medication is necessary in order for preventative medications to be effective, symptoms with abrupt withdrawal of acute medication may be unpleasant. The reward is spontaneous improvement of the headache days to weeks after the overused medication is discontinued. Daily medication taken to prevent a chronic daily headache due to medication overuse is generally ineffective with continued overuse of acute medication. The use of a preventative medication in combination with the withdrawal of the offending overused medication is usually necessary to abolish MOH. (Goadsby, Silberstein, & Dodick, *Chronic Daily Headache*, Chapter 11, 2005)

**211. The answer is C.** Acute migrainous vertigo, a central or a peripheral vestibular disorder, may present with vertigo accompanied by spontaneous and/or positional nystagmus. A study of the clinical spectrum of acute migrainous vertigo found pathologic nystagmus in 70% of patients during an acute attack, with a few patients showing additional ocular motor deficits. Almost all patients had gait imbalance. Hearing loss was not a symptom associated with migrainous vertigo. (Von Brevern, Zeise, Neuhauser, et al., *Brain* 2005)



**212. The answer is A.** Dipyridamole is an antiplatelet agent that increases the intracellular concentration of cyclic adenosine monophosphate (cAMP). Dipyridamole has a vasodilatory effect, which is the major contributor to the transient headaches sometimes seen when initiating this agent at high doses. About a third of patients starting the medication experience a headache in the first few days to a week of treatment. Titrating the medication from once at night, with supplemental aspirin, to twice a day over a week may decrease the incidence of the headache, which generally dissipates after several days. (Lipton, Göbel, Einhäupl, et al., *Neurology* 2004)

**213. The answer is E.** Decreased vision, papilledema, sixth-nerve palsy, and optic atrophy have been reported in the enigmatic HaNDL syndrome. However, visual symptoms are less common than sensory, speech, and motor complaints. Retinal migraine is usually characterized by attacks of fully reversible monocular visual loss associated with migraine headache. Transient vision loss may be an initial symptom of idiopathic intracranial hypertension (IIH) with permanent vision loss resulting if the elevated intracranial pressure is not relieved. Optic nerve sheath decompression can be used to try to avoid visual loss with IIH. Vision loss or distortion is the most common aura experienced by migraineurs. (Morrison, Phuah, Reddy, et al., *Ophthalmology* 2003; Grosberg, Solomon, Friedman, et al., *Cephalalgia*, 2006)

**214. The answer is B.** This syndrome is variously referred to as HaNDL, migrainous syndrome with cerebrospinal pleocytosis, or pseudomigraine with temporary neurological symptoms and lymphocytic pleocytosis. The most common symptoms noted in patients with this syndrome of headache with neurological deficits and abnormal CSF are sensory loss and aphasia. Visual symptoms are much less common. Episodes of headache and neurological deficits recur up to 20 times over 3 months. The patient is headache-free with a normal neurological examination between episodes. (ICHD-II, *Cephalalgia* 2004)

**215. The answer is D.** A patient with IIH may have abnormalities of cranial nerves II (papilledema with a visual field deficit) and/or VI (double vision). The cerebrospinal fluid pressure in IIH is  $>200$  mm H<sub>2</sub>O in the nonobese and  $>250$  mm H<sub>2</sub>O in the obese patient with IIH. The typical patient with IIH is an obese woman of childbearing age, but the disorder may not be associated with obesity in prepubertal children or men. Intracranial disease causing secondary (as opposed to idiopathic) increased intracranial pressure (including cerebral venous thrombosis) must be ruled out by neuroimaging. To make the diagnosis of IIH, no anatomic, metabolic, toxic, or hormonal cause of intracranial hypertension should be present. (Skau, Brennum, Gjerris, et al., *Cephalalgia* 2006)



**216. The answer is B.** Up to 60% of patients with IIH note pulsatile tinnitus, either unilateral or bilateral, although patients may only report it on direct questioning. Pulsatile tinnitus, synchronized with the heart rate, usually resolves with normalization of spinal fluid pressure. Turbulence from blood flowing from the hypertensive intracranial space into the low pressure of the jugular vein is a proposed mechanism for pulsatile tinnitus. Other causes of pulsatile tinnitus include a dural arterio-venous fistula, an intracranial bruit, or other cerebrovascular disorders with audible increased flow. (Skau, Brennum, Gjerris, et al., *Cephalalgia* 2006)

**217. The answer is D.** The periodic syndromes that appear to be precursors to migraine headaches in infants and children include cyclic vomiting syndrome, abdominal migraine, and benign paroxysmal vertigo. They may respond to medications used to treat migraine. These children and infants often have a family history of migraine and may go on to have typical migraine headaches. There may be overlap between the gastrointestinal symptoms of cyclic vomiting syndrome and abdominal migraine, differing in the severity of the abdominal pain and the vomiting. Benign paroxysmal vertigo of childhood is characterized by recurrent brief episodes of vertigo. Children should be appropriately evaluated to rule out underlying neurologic or gastrointestinal causes prior to assigning a migraine precursor diagnosis. Selective mutism with unwillingness to speak under specific circumstances may be a symptom of a childhood anxiety disorder, but it is not a precursor to migraines in adulthood. (Winner & Hershey, *Curr Pain Headache Rep* 2007)

**218. The answer is C.** This man needs to be evaluated for the most commonly identified cause of viral encephalitis, herpes simplex virus type 1 (HSV1) encephalitis, as he has the recent onset of headache and alteration in mental status. The definitive diagnosis of this treatable viral encephalitis is made from CSF analysis. Polymerase chain reaction (PCR) techniques amplify the genome of HSV1 and PCR in the CSF should be obtained when there is a suspicion of HSV1 encephalitis. False-negative CSF HSV1 PCR tests may occur within the first 72 hours of mild symptoms. Patients with HSV1 encephalitis may develop MRI abnormalities in the temporal lobes, especially with fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) sequences. An MRI should be obtained as part of the evaluation of this man, but the diagnosis is made based on spinal fluid analysis. This man's clinical presentation and EEG findings should raise concern about HSV1 encephalitis, even without temporal lobe changes on his CT scan. Although other causes of infectious or paraneoplastic encephalitis should be considered, the diagnosis of encephalitis specifically due to HSV1 is critical because

treatment with the antiviral drug acyclovir dramatically decreases the morbidity and mortality of the infection. If HSV1 encephalitis is suspected, the patient should be empirically treated with acyclovir until the CSF results are available; however, the treatment with acyclovir risks acute renal failure. While prompt treatment improves outcome and survival, some neurological deficits may still occur with appropriate treatment. (Tyler, *Rev Neurol Dis* 2004)

**219. The answer is E.** Basilar-type migraine appears to be a subtype of migraine with aura, as opposed to a distinct migraine type. The symptoms of basilar-type migraine are associated with brainstem functions but overlap many of the symptoms described by patients with migraine with aura. Unlike hemiplegic migraine, there are no specific genetic markers for basilar-type migraine. The aura associated with basilar-type migraine lasts in the range of 60 minutes with symptoms of vertigo, dysarthria, tinnitus, bilateral visual symptoms including diplopia, bilateral paresthesias, decreased level of consciousness, hypacusia, and ataxia. The basilar-type migraine aura symptoms overlap the symptoms reported with migraine with typical aura, and it is not clear that the two are distinct entities. (Kirchmann, Thomsen, & Olesen, *Neurology* 2006)

**220. The answer is B.** Familial hemiplegic migraine is a rare, autosomal dominantly inherited subtype of migraine with aura and transient hemiplegia that is associated with specific genetic mutations. Hemiplegic migraine can occur also without a clear inheritance pattern or genetic linkage. FHM mutations are known in three genes, the CACNA1A (FHM1) gene, the ATP1A2 (FHM2), and the SCN1A (FHM3) gene. Up to 75% of FHM families have a mutation in the P/Q-type calcium channel Ca(v)2.1 subunit CACNA1A gene on chromosome 19p13. FHM2 is associated with a missense mutations in the ATP1A2, Na(+),K(+)-ATPase pump, gene, on chromosome 1q23. FHM3 is associated with the SCN1A gene, on chromosome 2q24, which encodes the neuronal voltage-gated sodium channel NaV1.1.7. However, not all genetic mutations in FHM have been identified. A study searching for FHM mutations in Danish FHM families identified a total of 147 FHM patients from 44 different families. Linkage analysis showed that only 14% (six out of 42) of FHM families in the general Danish population had FHM mutations in the CACNA1A or ATP1A2 gene. CACNA1A gene mutations were identified in three of the FHM families, and three FHM families were identified with novel mutations in the ATP1A2 gene. None of the Danish FHM families had a mutation in the SCN1A gene. (Thomsen, Kirchmann, Bjornsson, et al., *Brain* 2007)

**221. The answer is E.** Trigeminal autonomic cephalgias include CH, paroxysmal hemicrania, and SUNA with its subcategory SUNCT. Even typical TACs can

be caused by an underlying lesion, and neuroimaging is recommended in all patients with a TAC or TAC-like syndrome. (Favier, van Vliet, Roon, et al., *Arch Neurol* 2007)

**222. The answer is C.** The clinical significance and mechanism of a sentinel headache are unclear. Headache is an almost universal experience, with a large proportion of the population suffering from frequent severe headaches. A severe sudden headache occurring in the days to weeks prior to SAH, known as a sentinel headache, has been reported with frequency varying from 15% to 60%. The report of a headache occurring before a SAH headache could be coincidental or could reflect recall bias. However, a headache prior to the subsequently detected SAH could be due to changes in aneurysmal size or to minor bleeding from the aneurysm. Rebleeding is an important cause of mortality and morbidity after aneurysmal SAH. Rates vary in the range of 2–20% depending on the definition of rebleeding, the timing of aneurysmal treatment, and the patient population. Ultra early treatment with aneurysm clipping or coiling could be offered to those patients with SAH who appear to be at especially high risk of rebleeding, with the goal of improving outcome after SAH. A study investigated whether patients with a sentinel headache prior to SAH had a higher rate of rebleeding than patients who did not report such a headache prior to SAH. Those patients with SAH who had sentinel headaches occurring in the 4-week period prior to a SAH had a 10-fold increase in early rebleeding and may benefit from ultra early aneurysm obliteration. (Beck, Raabe, Szelenyi, et al., *Stroke* 2006)

**223. The answer is E.** Medication-overuse headache (MOH) occurs when treatment with the acute headache medication is both frequent and regular, generally  $\geq 10$  days a month for  $\geq 3$  months a year. Patients with MOH rarely respond to preventative headache medications while still overusing acute medications. Withdrawal from opioid overuse is particularly difficult and is associated with a high rate of recidivism. Triptan overuse is less common and is relatively easy to treat, aided by the insurance company restrictions on obtaining large quantities of the medication. (ICHD-II, *Cephalalgia* 2004)

**224. The answer is D.** This woman has chronic postcraniotomy headaches, for which preventative medication is appropriate. Acute and chronic head and face pain occur after craniotomies for multiple intracranial lesions, including posterior fossa surgery for acoustic neuroma. The ICHD-II recognizes chronic postcraniotomy headache as a headache, maximal in the surgical area, which develops within 7 days of the craniotomy and persists for at least 3 months. An acute postcraniotomy headache has the same characteristics but lasts for less than 3

months. A study of headaches after acoustic neuroma resection found that possible predictors of chronic postoperative headache include female gender, lack of previous headache, and small tumor size. Persistent postoperative headache pain is more common in women and is associated with depression and anxiety, but psychiatric consultation alone will not obliterate this woman's headaches. Further neurosurgery is unlikely to help, and she does not appear to have positional headaches due to intracranial hypotension from a spinal fluid leak that would be diagnosed by cisternography. Liberal use of narcotics will risk MOH. Non-narcotic analgesics for acute pain relief and tricyclic antidepressants or gabapentin for preventative therapy are appropriate. (Rimaaja, Haanpaa, Blomstedt, et al., *Cephalalgia* 2007)

**225. The answer is A.** Headache is common in patients with SLE, with a reported prevalence as high as 70%. In a study of SLE and rheumatoid arthritis (RA), patients the headache frequency was reported to be 41% and 17% respectively. Headache types in SLE patients were migraine 24%, TTH 11%, and mixed headache 5%. Headache is very common in lupus patients and is associated with Raynaud's phenomenon and  $\beta_2$  glycoprotein-1 antibodies. The other listed diseases are not specifically associated with headache, although they are prevalent in adult women who may be prone to headaches. (Weder-Cisneros, Teliez-Zenteno, Cardiel, et al., *Cephalalgia* 2004)

**226. The answer is E.** Neurologic disorders are an integral part of the antiphospholipid antibody syndrome. Antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant,  $\beta_2$  glycoprotein-1 antibodies) are mostly strongly associated with cerebrovascular disease, specifically arterial and venous thrombosis, but other associated neurologic manifestations include cognitive dysfunction, dementia, seizures, movement disorders, transverse myelopathy, and headaches. Headache is a common complaint of patients with antiphospholipid antibodies, but the strength of the correlation between these antibodies and migraine is controversial. Active migraine has been associated with higher disease activity, antiphospholipid antibodies, and worsening of Raynaud's phenomenon. (Roldan & Brey, *Curr Rheum Rep* 2007; Appenzeller & Costallat, *Cephalalgia* 2004)

**227. The answer is D.** Both in the general population and in patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), MRI evidence of cerebral ischemia and infarction is correlated with cognitive dysfunction. In CADASIL, a cerebral white matter disease caused by mutations in the NOTCH3 gene, patients experience recurrent ischemic strokes, migraine-like headaches, psychiatric disease, and cognitive de-

cline. A study from the Netherlands tested 62 symptomatic and asymptomatic members of 15 CADASIL families and found that severity of cognitive dysfunction in NOTCH3 mutation carriers was independently associated with MRI infarct lesion load ( $p < 0.05$ ). Previous studies have shown an association between white matter hyperintensities on brain MRI and cognitive dysfunction in CADASIL. (Liem, van der Grond, Haan, et al., *Stroke* 2007)

**228. The answer is A.** Sufferers of “the exploding head syndrome” describe unpleasant or terrifying attacks of a painless explosion within their head, often accompanied by sensations of sounds or lights. These attacks tend to occur at the onset of sleep. The etiology of attacks is unknown, although they are considered to be benign. Relief may be noted with clomipramine (Anafranil), a tricyclic antidepressant. Reassurance that the headache is benign may suffice, and the headaches may spontaneously remit. (Green, *Curr Pain Headache Rep* 2001)

**229. The answer is E.** All of the listed headache syndromes are associated with sleep. Hypnic headaches, CHs, and turtle headaches characteristically occur with awakening from sleep. Hypnic headaches and turtle headaches may occur in the morning associated with awakening. CHs, which can also occur at other times during the day, characteristically occur a few hours after the initiation of sleep. Exploding head syndrome tends to occur as the sufferer falls asleep. Turtle headache is a transient headache associated with sleeping with the head under the covers, resulting in hypoxia and hypercarbia. (Poceta, *Curr Pain Headache Rep* 2003)

**230. The answer is B.** This woman has fulminant idiopathic intracranial hypertension (IIH) with acute and rapidly progressive visual loss. In a study of 16 obese women, fulminant IIH was defined as the acute onset of symptoms and signs of intracranial hypertension (less than 4 weeks between onset of visual symptoms and severe visual loss), with rapid worsening of visual loss over a few days, and without evidence of brain lesion or cerebral venous thrombosis. Even with rapid and aggressive surgical treatment with optic nerve sheath fenestration or either lumboperitoneal or ventriculoperitoneal shunting, visual acuity and visual fields were generally still impaired. Fundi and visual acuity are generally unremarkable in posterior reversible encephalopathy syndrome (PRES), and MRI findings are characteristic. Patients with PRES may have visual complaints including hemianopic defects. This woman’s moderate chronic headaches of weeks’ duration are not characteristic of pituitary apoplexy or SAH. The woman’s presentation is not consistent with Susac syndrome, which is characterized by retinal arterial occlusion, encephalopathy, and sensorineural deafness. (Thambisetty, Lavin, Newman, et al., *Neurology* 2007)

**231. The answer is B.** This man has nonaneurysmal perimesencephalic (pretruncal) SAH, which has an etiology and natural history distinct from SAH due to aneurysm rupture. This type of hemorrhage, which is presumed to be venous in origin, is restricted to the cisterns surrounding the brainstem and suprasellar cistern. No aneurysm is found on vascular imaging. These nonaneurysmal hemorrhages may represent approximately 5% of all SAHs. Although the CT angiogram in this man is negative, a catheter angiogram is still indicated to rule out an aneurysm that should be treated by surgical or endovascular techniques. Hemorrhage would not be expected with an infarct of a pituitary mass. Although dissection of the intradural basilar artery could produce some SAHs, bleeding of this extent or in this location would not be expected. (Flaherty, Haverbusch, Kissela, et al., *J Stroke Cerebrovasc Dis* 2005)

**232. The answer is B.** Nervus intermedius or geniculate neuralgia causes a severe stabbing pain in the external auditory canal, due a neuralgia of the sensory branch of the facial nerve or the geniculate ganglia. Temporomandibular joint pathologies could be included in the differential diagnosis of these disorders. Treatment with usual medications for neuropathic pain may provide relief. Surgical excision or ablation of the nervus intermedius and the geniculate ganglion has been used for relief of intractable pain. She does not have the skin lesions of Ramsey-Hunt syndrome. Trigeminal neuralgia would not involve pain inside the ear. (Figueiredo, Vazquez-Delgado, Okeson, et al., *Cranio* 2007)

**233. The answer is B.** Pseudomigraine with lymphocytic pleocytosis, also known as HaNDL, is a syndrome with temporary neurologic deficits, moderate to severe headache, and occasional fever. This constellation of migraine-like headache, focal neurological deficits, and abnormal spinal fluid (elevated protein and lymphocytosis) is more common in men. The combination of neurological deficits, which almost always includes sensory complaints, lasts 5 hours on average. Aphasia and motor deficits are also common, with migraine-like visual changes being the least common deficit. The multiple episodic attacks of headache and neurological impairment generally resolve within 3 months. (ICHD-II, *Cephalalgia* 2004; Pascual & Valle, *Curr Pain Headache Rep* 2003)

**234. The answer is A.** This woman has burning mouth syndrome (BMS), a chronic orofacial pain disorder characterized by a continuous, spontaneous, intense burning sensation of the mouth or tongue. The estimated prevalence of BMS reported in recent studies ranged between 0.7% and 4.6% of the general population. The cause of this disorder, which is more common in postmenopausal women, is unknown. Burning mouth syndrome may be idiopathic or due to nutri-

tional deficiencies, estrogen deficiency, oral infections, denture-related lesions, or hypersensitivity reactions. Dry mouth is associated with medications, including tricyclic antidepressants, and diseases such as Sjögren's syndrome, anxiety, and diabetes. Pain confined to the tongue is called glossodynia. (Maltzman-Tseikhin, Moricca, & Niv, *Pain Pract* 2007)

**235. The answer is E.** Symptoms of multiple sclerosis (MS) include multiple acute cranial nerve palsies due to brainstem disease. Brainstem involvement occurs as the presenting feature of MS in up to 15% of cases. (Commins & Chen, *Am J Otol* 1997)

**236. The answer is A.** Reversible cerebral vasoconstriction syndromes are a set of disorders, of multiple etiologies, which are characterized by vasoconstriction on angiography. Spinal fluid is generally normal. The MRI may show ischemia or edema, frequently in the parietal-occipital area, or the MRI may be normal. Young women note the sudden onset of a severe headache, which may be accompanied by focal neurologic deficits, but with a clear sensorium. The headache associated with primary angiitis of the central nervous system (PACNS) is usually subacute and progressive in an encephalopathic man. Although cerebral angiography may occasionally be normal in PACNS, spinal fluid generally shows a lymphocytic pleocytosis, and the MRI shows infarcts. (Berstein, *Curr Treat Options Cardiovasc Med*)

**237. The answer is A 2, B 1, C 4, D 3.** Call and Fleming, along with their co-authors, described a clinical-angiographic syndrome with reversible vasoconstriction of unknown etiology about 20 years ago. Four patients were described by Call et al. who had transient, fully reversible vasoconstriction and dilatation prominently involving arteries around the circle of Willis. The patients had severe headaches and fluctuating or recurring motor or sensory deficits. Caroli's triad is urticaria, as a preicteric symptom of viral hepatitis, arthritis, and headache. Raeder's syndrome, unilateral periocular pain combined with ipsilateral miosis and ptosis, was first described by a Norwegian ophthalmologist in 1918. The cause of the syndrome in the original report was a skull-base tumor, but the syndrome may have many etiologies. Tolosa-Hunt syndrome is caused by a nonspecific inflammation of the cavernous sinus or the superior orbital fissure that results in a painful ophthalmoparesis. (Call, Fleming, Sealson, et al., *Stroke* 1988; Cribier, *Clin Rev Allergy Immunol* 2006; Salvesen, *Cephalalgia* 1999; La Mantia, Curone, Rapoport, et al., *Cephalalgia* 2006)

**238. The answer is E.** Headaches are common in the 6-week period after delivery. The most common cause of a postpartum headache is the resurgence of



an underlying primary headache disorder, such as migraine. Sheehan's syndrome produces hypothyroidism, adrenal failure, or hypogonadism as a result of ischemic pituitary necrosis due to severe postpartum hemorrhage. Although the diagnosis of the endocrinological dysfunction may be delayed for years after delivery, Sheehan's syndrome may present with a postpartum headache. Preeclampsia can occur up to 6 weeks after delivery. Postpartum CVT may present with a persistent headache, often accompanied by seizures and focal neurological deficits due to venous infarcts and hemorrhage. (Dökmetaş HS, Kilicli F, Korkmaz, et al., *Gynecol Endocrinol* 2006; Loder, *Semin Neurol* 2007)

**239. The answer is D.** Osler-Weber-Rendu disease (hereditary hemorrhagic telangiectasia) is an autosomal dominant disease with skin, nasal, and visceral telangiectasia. Arteriovenous malformations are found in the brain, liver and lung. The presence of pulmonary AVMs is associated with shunting and cerebral abscesses. This man has a intracerebral hemorrhage producing his acute headache and focal neurologic examination. Neurofibromatosis is associated with occlusive arterial disease. Cerebrovascular disease in Marfan syndrome usually leads to large-artery dissection, as does Ehlers-Danlos syndrome. Sturge-Weber syndrome is characterized pathologically by leptomeningeal vessel calcification and arteriovenous angiomas. (Kasner & Gorelick, *Prevention and Treatment of Ischemic Stroke*, Chapter 8, 2003)

**240. The answer is D.** Chronic paroxysmal hemicrania (CPH) and SUNCT syndrome are both TACs that are associated with severe unilateral pain in association with autonomic symptoms. CPH, but not the SUNCT headache, is responsive to indomethacin. CPH is more common in women, whereas SUNCT/SUNA syndromes are more common in men. CPH attacks are of longer duration (about 2–45 minutes) and occur less frequently than the attacks of SUNCT, which last about 10–120 seconds. Both headache syndromes produce severe to excruciating pain around the eye. Pareja, Caminero, & Sjaastad, *CNS Drugs* 2002)

**241. The answer is E.** The ICHD-II diagnostic criteria for migraine aura include fully reversible visual and sensory symptoms, which can be either positive or negative. Aura symptoms may also include fully reversible dysphasic speech disturbance. The aura symptoms should develop gradually over  $\geq 5$  minutes and last between 5 and 60 minutes. (ICHD-II, *Cephalalgia* 2004)

**242. The answer is E.** The ICHD-II diagnostic criteria for cyclic vomiting, a childhood periodic syndromes that is commonly a precursor of migraine, includes vomiting during stereotypic attacks that occur at least four times an hour



for at least 1 hour. Nausea and vomiting last from 1 hour to 5 days. The child is symptom-free between attacks. The diagnosis is made after the child has been evaluated for gastrointestinal or cerebral disease. (ICHD-II, *Cephalalgia* 2004)

**243. The answer is A.** The ICHD-II diagnostic criteria for TTH includes at least two of: bilateral location, pressing/tightening (nonpulsating pain), mild or moderate intensity, or absence of aggravation by routine physical activity. TTH duration is from 30 minutes to 7 hours. Although anorexia may occur, there should be no nausea or vomiting and no more than one of either photophobia or phonophobia. (ICHD-II, *Cephalalgia* 2004)

**244. The answer is D.** According to the ICHD-II diagnostic criteria for CH, the headache should be accompanied by at least one of: conjunctival injection and/or lacrimation, eyelid edema, nasal congestion and/or rhinorrhea, forehead and facial sweating, ptosis and/or miosis, and a sense of restlessness or agitation. (ICHD-II, *Cephalalgia* 2004)

**245. The answer is D.** Basilar-type migraine, which is more commonly diagnosed in children, may be a subtype of migraine with aura, as opposed to a distinct migraine type. Basilar-type aura symptoms may occur in patients with migraine with aura. A study of patients with basilar-type aura found that the median duration was 60 minutes. Symptoms included vertigo, dysarthria, tinnitus, diplopia, bilateral visual symptoms, bilateral paresthesias, decreased level of consciousness, hypacusia, and ataxia. The study found no clinical, epidemiologic, or genetic evidence that basilar migraine was an independent disease entity different from migraine with aura. (Kirchmann, Thomsen, & Olesen, *Neurology* 2006; ICHD-II, *Cephalalgia* 2004)

**246. The answer is B.** The reported prevalence of headache associated with SLE is up to 70%. A study of headaches in patients with lupus or RA found that 41% of the patients with lupus had headaches, as compared to only 17% of patients with RA. Almost a quarter of the patients with lupus had migraine headaches, whereas 11% of lupus patients had TTH. Less common causes of headaches in lupus patients include mixed headache types, cerebral venous thrombosis, and medication complications. An association exists between mild and transient headaches and chloroquine. Migraine headaches in patients with SLE are associated with Raynaud's phenomenon,  $\beta_2$ -glycoprotein-1 antibodies, and depression. (Weder-Cisneros, Teliez-Zenteno, Cardiel, et al., *Cephalalgia* 2004)

**247. The answer is E.** Hypnic headache appears to be a chronobiologic disorder that is found in patients over age 50, who experience a headache awakening them

from sleep. The onset of hypnic headache attacks is associated with rapid eye movement (REM) sleep, as determined by polysomnography. The moderate to severe headache pain lasts 10–180 minutes and occurs at least 15 times per month. Lithium may be most effective preventative medication, although indomethacin, flunarizine, and caffeine are also used. (Evers & Goadsby, *Neurology* 2003)

**248. The answer is B.** The Pott puffy tumor is a subperiosteal abscess of the frontal bone that appears as a localized swelling of the forehead associated with frontal osteomyelitis. The subperiosteal abscess may extend intracranially to produce a subdural empyema collection. The abscess is treated with surgical resection and a prolonged course of intravenous antibiotics. The Pott puffy tumor is a serious complication of undiagnosed or partially treated frontal sinusitis. (Komborgas & Solanki, *J Neurosurg* 2006)

**249. The answer is D.** Headaches caused by a third ventricular colloid cyst are characteristically worse when erect, due to transient obstruction of spinal fluid outflow through the foramen of Monro, but the hydrocephalus-related headaches are relieved when the patient is supine. The frontal headaches may be intermittent, severe, and transient, and can be associated with nausea and vomiting. Colloid cysts of the third ventricle account for 0.5% of intracranial tumors. They are more common in men than in women, and are usually diagnosed between the third and fifth decades of life. Hydrocephalus and a round intraventricular lesion are noted on CT or MRI scan. A colloid cyst, located anteriorly in the third ventricle, may result in sudden death from acute hydrocephalus, if not treated with surgical resection. The other anatomic lesions do not produce positional headache due to hydrocephalus. (Spears, *Curr Pain Headache Rep* 2004)

**250. The answer is D.** New daily persistent headache (NDPH) is the acute onset of a headache within 3 days that is persistent for 15 days or more each month for at least 3 months. It is a female-predominant heterogeneous subtype of CDH. NDPH may be a presentation of other primary headaches such as new onset migraine, TTH, or benign TCH. The diagnosis dictates the exclusion of the many secondary types of NPHD, which is especially critical early in the course of the disease, when a secondary etiology is more likely. Secondary causes of a daily persistent headache include postmeningitic headache, MOH, intracranial neoplasms, GCA, chronic meningitis, chronic SDH, posttraumatic headaches, sinusitis, post-SAH headache, SIH, cervical artery dissections, IIH without papilledema, and CVT. These headaches, both idiopathic and secondary, can be difficult to treat. (Evans, *Curr Pain Headache Rep* 2003)

**251. The answer is B.** Dizziness or vertigo is the most common single symptom of a cerebellar infarct, which generally presents with a constellation of posterior circulation symptoms. Over half of patients with a cerebellar infarct have nausea and vomiting, and a third of them have a headache at presentation. Signs on presentation include ataxia, dysarthria, nystagmus, and hemiparesis. Most patients with a cerebellar infarct are alert at presentation, but mental status may deteriorate as cerebellar edema compresses the fourth ventricle producing hydrocephalus and brainstem compression. (Tohgi, Takahashi, Chiba, et al., *Stroke* 1993)

**252. The answer is D.** Cluster headache and trigeminal neuralgia are clinically and diagnostically distinct, with different gender predilection (male for CHs; female for trigeminal neuralgia), usual age of onset (CHs begin before age 25; patients with trigeminal neuralgia are generally between age 50 and 70), and CH, but not trigeminal neuralgia, has autonomic symptoms. The pain in both disorders is excruciating, but in CH the pain is typically periorbital; the pain of trigeminal neuralgia is usually in the maxillary ( $V_2$ ) and mandibular ( $V_3$ ) divisions of the trigeminal nerve. The pain of CH is of longer duration at 15–180 minutes, rather than the seconds of trigeminal neuralgia pain. (Rozen, *Headache* 2001)

**253. The answer is D.** Carotid disease (atherosclerosis, fibromuscular dysplasia, carotid cavernous fistula), glomus tumor, dural arterio-venous fistula, idiopathic intracranial hypertension, and palatal myoclonus are all causes of pulsating sounds generated by vascular or other structures of the cranium, head, and neck regions. IIH produces pulsatile tinnitus by the transmission of arterial pulsations to dural venous sinuses. (Sismanis, *Neurologist* 1998)

**254. The answer is C.** Spontaneous intracranial hypotension causes the new onset of a daily persistent positional headache with increased pain while upright and marked improvement in pain while supine. The headache is caused by the downward movement of the brain in the erect position, with traction on pain-sensitive structures, including cerebral veins and sinuses. Although SIH is generally considered to be a benign condition, it can result in a change in level of consciousness and focal neurologic symptoms, especially when associated with an SDH. Although patients are often quite disabled over the short-term by the severe postural head pain, the long-term prognosis is generally favorable, with resolution of the headache in days to weeks. The presence of a SDH increases the chance of neurologic deficits and recurrence of severe headaches. Etiologies of the SDH in SIH include traction on bridging veins, development of new dural vessels in delayed SDH, or evolution of nonhemorrhagic to hemorrhagic subdural collections. (Lai, Fuh, Lirng, et al., *Cephalalgia* 2006)

**255. The answer is D.** Ehlers–Danlos syndrome type IV, the vascular type, results from mutations in the gene for type III procollagen (*COL3A1*). Patients with Ehlers-Danlos syndrome type IV have abnormally elastic tissue and are at risk for cerebral aneurysms and arterial dissections. They may present with a sudden-onset severe headache due aneurysmal SAH. They do not have either vasculitis or inflammatory disease, nor do they have any propensity for arterial or venous thrombosis. (Pepin, Schwarze, Superti-Furga, et al., *N Engl J Med* 2000)

**256. The answer is B.** This woman has Ramsay-Hunt syndrome with peripheral facial nerve palsy accompanied by an erythematous vesicular rash on the ear (zoster oticus). Patients may also have lesions on the anterior two-thirds of the tongue, with loss of taste, and palatal lesions. J. Ramsay-Hunt, a former chairman of Neurology at Cornell Medical College, described the clinical presentation of facial paralysis and rash, which is now recognized to be caused by resurgence of a latent varicella zoster virus infection of the geniculate ganglion of the CN VII. Early treatment with antiviral medication and prednisone improves the outcome of recovery from facial palsy. (Sweeney & Gilden, *J Neurol Neurosurg Psychiatry* 2001)

**257. The answer is C.** Retinal migraine presents with attacks of reversible monocular visual loss lasting less than an hour, associated with an ipsilateral migraine headache. In a review of 46 patients (six new cases and 40 from the literature) with retinal migraine, this type of migraine was most common in women in the second to third decade of life. Patients with retinal migraine may have a history of migraine with aura. Nearly half of the reported cases with recurrent transient monocular visual loss subsequently experienced permanent monocular visual loss, perhaps due to an ocular infarct. (Grosberg, Solomon, Friedman, et al., *Cephalalgia* 2006)

**258. The answer is B.** Tension-type headache is the most common form of headache; however, patients with episodic TTH (ETTH) rarely seek medical consultation. Patients with ETTH may use, and overuse, over-the-counter acute pain medications and develop MOH. Chronic tension-type headache, especially when combined with MOH, is one of the most difficult types of headache to treat. The pathogenesis of TTH is a combination of peripheral (myofascial nociception) and central mechanisms (sensitization and inadequate endogenous pain control). Treatment of CTTH combines pharmacologic (nonhabituating medications) and nonpharmacologic therapies (relaxation, biofeedback, cognitive behavioral therapy, stress management, exercise). (Fumal & Schoenen, *Lancet Neurol* 2008)

**259. The answer is A 2, B 5, C 3, D 4, E 1.** The patient's history may offer clues to indicate the cause of encephalitis. Travel to Asia may be associated with den-

gue, Japanese encephalitis, and Murray Valley encephalitis. The *Aedes aegypti* mosquito transmits a flavivirus that causes the severe headache, fever, arthralgias, myalgias, and rash of dengue fever. Headache is associated with systemic and cerebral malarial infection from the *Anopheles* mosquito transmission of *Plasmodium falciparum* or *Plasmodium vivax*. Cerebral malaria is a dreaded and potentially fatal consequence of travel to Africa, but malaria can be avoided by prophylaxis. Leptospirosis can be acquired from rat urine while swimming in infected fresh water. The lymphocytic choriomeningitis (LCM) virus is transmitted in rodent feces, and humans with barns may be exposed. Hikers in forests in the Eastern United States, as well as other areas, including the New Forest in the United Kingdom, may be exposed to *Borrelia burgdorferi* infection causing Lyme disease. (Solomon, Hart, & Beeching, *Pract Neurol* 2007)

**260. The answer is C.** Numb chin syndrome, mental (inferior alveolar) nerve neuropathy, may be a presenting symptom of cancer with metastatic disease (bone metastases or leptomeningeal seeding) at the mental foramen. Cancers that have been reported with a numb chin or lateral lower lip include breast cancer, small-cell lung cancer, prostatic cancer, and lymphoproliferative malignancies. Noncancerous causes include MS, HIV infection, rheumatological diseases, and GCA. A patient with a mental nerve neuropathy should be evaluated for an underlying neoplasm or systemic disorder. (Laurencet, Anchisi, Tullen, et al., *Crit Rev Oncol Hematol* 2000)

**261. The answer is D.** Patients with mitochondrial encephalomyopathy with lactic acidosis and strokelike episodes (MELAS) have normal early development, short stature, seizures, hemiparesis, and visual deficits. Other mitochondrial disorders with cerebral disease include Kearns-Sayre syndrome (progressive external ophthalmoplegia, pigmentary retinopathy and cerebellar ataxia) and myoclonus epilepsy with ragged-red fibers (MERRF). These mitochondrial disorders are sporadic or may be transmitted by maternal inheritance. CADASIL is caused by mutations in NOTCH3 epidermal growth factor-like repeat that maps to chromosome 19. In a large Belgian family with occipitotemporal lobe epilepsy associated with migraine with visual aura, haplotype analysis defined a candidate region located at chromosome 9q21-q22 based upon recombinations in affected individuals. (Rosen N, *Headache* 2008; Deprez, Peeters, Van Paesschen, et al., *Neurology* 2007)

**262. The answer is D.** This woman has a rare, but increasingly recognized, limbic encephalitis that can present with headache, cognitive dysfunction and psychiatric symptoms. This paraneoplastic encephalitis is associated with a teratoma, usually found in an ovary. Characteristic N-methyl-D-aspartate recep-

tor antibodies are found in the serum and cerebrospinal fluid of these patients who are predominantly women. Supportive care, immunosuppressive treatment, and, most importantly, tumor resection can be curative. However, some women with this paraneoplastic encephalitis do die or are left with residual neurological deficits despite appropriate care. All the other listed causes of headache and encephalopathy should be ruled out but only this paraneoplastic limbic encephalitis could be cured by surgery. Herpes simplex encephalitis is diagnosed by CSF PCR testing. Whipple's disease is a rare multisystem condition caused by the bacillus *Tropheryma whipplei*. The central nervous system is involved in 20 to 40% of patients. Hashimoto's encephalopathy or corticosteroid-responsive encephalopathy associated with autoimmune thyroiditis is characterized by elevated titres of antithyroid antibodies in the serum and/or cerebrospinal fluid. The lack of focal neurological deficits and the normal MRI scan make PACNS less likely; although the diagnosis should be ruled out, with a brain biopsy if indicated. (Sabin, Jednacz, & Staats, *N Engl J Med* 2008)

**263.** The answer is A. Ramsay-Hunt syndrome is peripheral (lower motor neuron) facial nerve weakness with an erythematous vesicular rash on the ear (zoster oticus) or in the mouth. Ramsay-Hunt syndrome is caused by a varicella zoster virus infection, whereas Bell's palsy is associated with herpes simplex virus. Both disorders are treated with prednisone and antiviral medications; although recent guidelines note that antiviral medications have not been proven to be of benefit in the treatment of Bell's palsy. Compared with Bell's palsy (peripheral facial weakness without rash), patients with Ramsay-Hunt syndrome often have more severe weakness at onset and incomplete recovery. In a prospective study, 14% of patients with Ramsay-Hunt syndrome developed vesicles after the onset of facial weakness, thus early Ramsay-Hunt syndrome may be indistinguishable from Bell's palsy. Some patients with presumed Bell's palsy may actually have Ramsay-Hunt syndrome *zoster sine herpette* (without rash). (Sweeney & Gilden, *J Neurol Neurosurg Psychiatry* 2001)

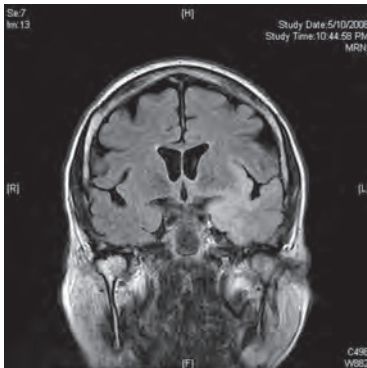
**264. The answer is B.** Patients with TTH may note associated symptoms generally seen in patients with migraine headaches. Occasionally, the diagnosis of TTH may be difficult to distinguish from migraine without aura. The specific diagnostic ICHD-II criteria for TTH include photophobia, photophobia, or mild nausea. However, the patient with TTH should not complain of moderate to severe nausea nor vomiting. Stricter criteria for the diagnosis of TTH, published in an appendix to ICHD-II, permit anorexia, but dictate that the patient should not complain of nausea, vomiting, photophobia, or phonophobia. (Furnal & Schoenen, *Lancet Neurol*, 2008)

**265. The answer is A.** Cluster headaches are strongly associated with tobacco smoking and are characteristically triggered by alcohol consumption. Patients learn to avoid alcohol during their cluster period. Trigeminal neuralgia is characteristically triggered by facial or oral stimulation, such as shaving or brushing the teeth. Eating is unlikely to trigger attacks of trigeminal neuralgia or CH. (Rozen, *Headache* 2001)

# 4

## HEADACHE EVALUATION AND DIAGNOSTIC TESTING QUESTIONS

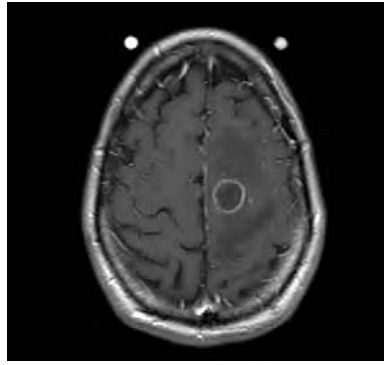
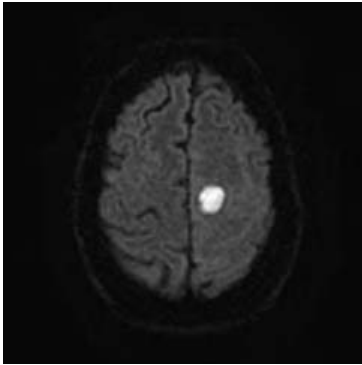
- 266.** Which of the following is an advantage of computed tomography venography (CTV) as compared to magnetic resonance venography (MRV)?
- A. Computed tomography venography (CTV) is safer for use in pregnancy than magnetic resonance venography (MRV).
  - B. CT venography does not require contrast injection and is safe in patients with renal disease.
  - C. CT venography images may be acquired more quickly, decreasing motion artifact.
  - D. Images from CTV are easier to process than are MRV images.
  - E. All of the above
- 267.** What is the most specific test to confirm herpes simplex type 1 (HSV1) encephalitis in the patient with this MRI scan?



- A. Microscopic tissue examination
- B. Polymerase chain reaction (PCR) assay for viral genome in the spinal fluid
- C. PCR assay for viral genome in the serum
- D. Electroencephalogram (EEG)
- E. Clinical acumen



268. These images indicate:



- A. A cerebral abscess.
- B. A metastatic lesion from a primary lung tumor.
- C. A primary brain tumor.
- D. Central nervous system (CNS) lymphoma.
- E. All of the above

269. This image shows:



- A. A glioblastoma multiforme
- B. An arteriovenous malformation (AVM)
- C. Dural metastatic disease
- D. Cerebral venous thrombosis
- E. An oligodendroglioma

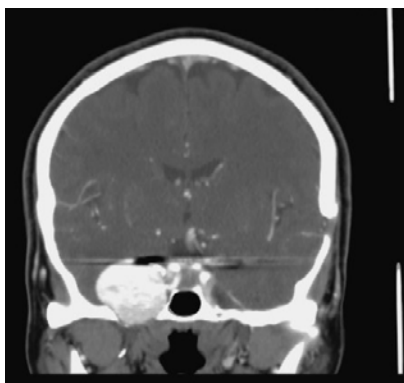
**270.** A 49-year-old woman with a long history of migraine headaches notices what she describes as a heart beat in her right ear. Her neurological and otologic examinations are normal, without retrotympanic mass. The tinnitus cannot be heard by the examiner with the stethoscope tubing in her external auditory canal. Which of the following imaging techniques is most appropriate to evaluate this woman's symptoms?

- A. Carotid ultrasonography
- B. Computed tomography (CT) scan of the temporal bone
- C. Magnetic resonance image (MRI) scan of the brain
- D. CT angiography (CTA) and venography (CTV)
- E. Catheter angiography

**271.** The diagnosis of a Chiari type 1 malformation is best made using a:

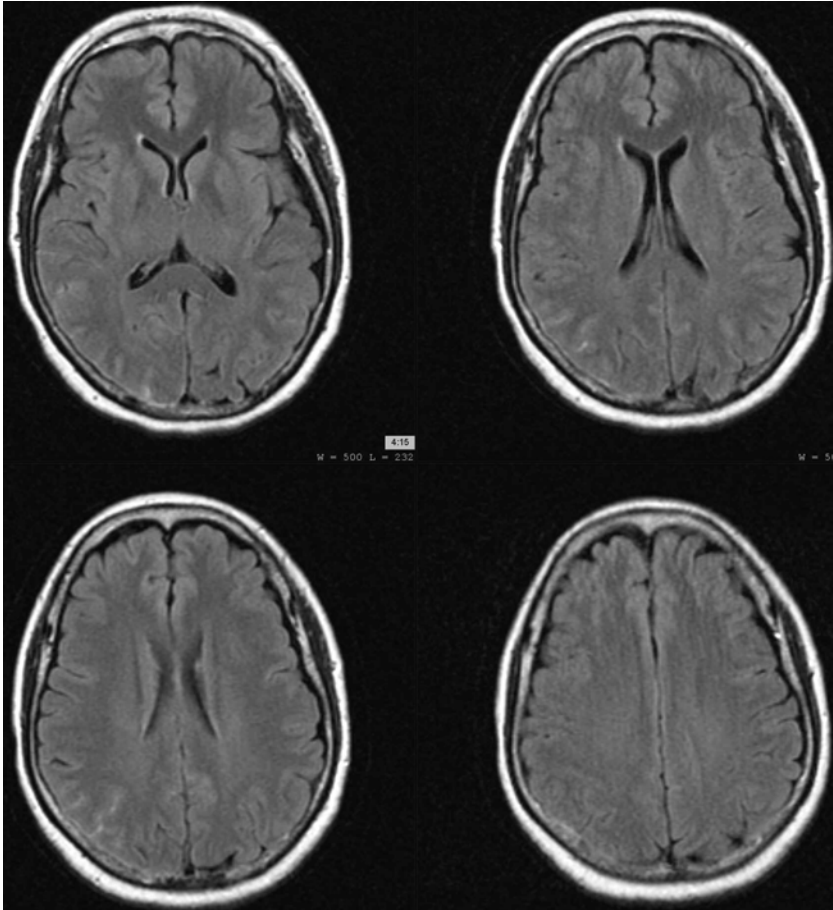
- A. Computed tomography (CT) scan of the cervical spine.
- B. Sagittal magnetic resonance image (MRI) scan of the brain.
- C. Radionuclide cisternography.
- D. Transcranial Doppler.
- E. MRI of the lumbar spine.

**272.** This woman has pain behind her right eye and double vision. She had a CT scan of the brain with contrast. What is the cause of her eye pain and diplopia?



- A. Acute angle closure glaucoma
- B. Sphenoid wing meningioma
- C. Internal carotid artery aneurysm
- D. Tolosa-Hunt syndrome
- E. Sarcoidosis

**273.** A 45-year-old woman had a 3-week history of progressively worsening headaches. She presented to the emergency room after a secondarily generalized seizure. The next day, she was alert but abulic with mild left leg weakness. Her CT scan of the brain is shown below. Spinal fluid analysis showed 410 white cells/mm<sup>3</sup> (predominantly lymphocytes), 12,000 red blood cells/mm<sup>3</sup>, a protein of 163 mg/dL, and normal glucose. She had no evidence of infection in her spinal fluid. What is the most likely diagnosis?



- A. Herpes encephalitis
- B. Central nervous system (CNS) vasculitis
- C. Sarcoidosis
- D. Headache with neurologic deficits and cerebrospinal fluid lymphocytosis (HaNDL)
- E. Human immunodeficiency virus (HIV) disease

**274.** A 78-year-old woman complains of an intermittent bitemporal headache and neck pain. Her hair is disheveled, and she has lost weight because of aching in her face with eating. Which noninvasive test will indicate the diagnosis with greatest accuracy?

- A. Ultrasound of the superficial temporal artery
- B. Erythrocyte sedimentation rate (ESR)
- C. C-reactive protein (C-RP)
- D. Von Willebrand factor
- E. Oculoplethysmography (OPG)

**275.** A 48-year-old woman reported recent headaches, which she attributed to eye strain while using her home computer for hours without a break. She was amazed that her headaches were better during a trip to visit her mother-in-law. However, she obtained an MRI scan of her brain when her headaches returned when she came back home. What is the cause of her headaches?



- A. Presbyopia
- B. Encephalitis
- C. Carbon monoxide (CO) poisoning
- D. Migraines
- E. Creutzfeldt-Jacob disease (CJD)

**276.** A patient reports to you that she has been told not to have an MRI scan with gadolinium-based contrast agents, however, she does not remember why. Which of her organs is probably diseased?

- A. Liver
- B. Kidneys
- C. Thyroid
- D. Skin
- E. Pancreas

**277.** Which of the following characteristics of cerebrospinal fluid (CSF) most distinguishes a subacute subarachnoid hemorrhage (SAH) from a traumatic lumbar puncture?

- A. The presence of crenated red blood cells
- B. A decrease of <15% in the number of red blood cells from tube 1 to tube 4
- C. A constant number of red blood cells from tube 1 and tube 4
- D. Xanthochromia
- E. Red-colored spinal fluid

**278.** What is usually associated with this image?



- A. Cerebral metastases
- B. Rupture of bridging veins
- C. Middle meningeal artery groove fracture
- D. Intracranial aneurysm
- E. All of the above

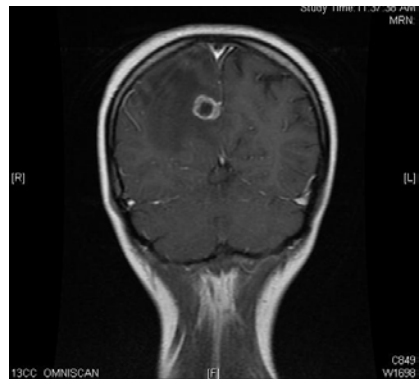
279. Pick the pathology associated with this image.



- A. Intracranial hypotension
- B. Intracranial hypertension
- C. Cerebral arterial ischemia
- D. Cerebral venous thrombosis
- E. Cerebrospinal fluid (CSF) infection

280. These are axial CT and coronal MRI images of the brain a 45-year-old woman with a recent history of mild headaches who was admitted to the hospital with a seizure at work. She was a long-time smoker and would occasionally disappear from her hospital room to go outside and smoke. What is the most likely diagnosis?

- A. Glioblastoma multiforme
- B. Primary central nervous system (CNS) lymphoma
- C. Lung cancer metastatic to brain
- D. Cerebral abscess
- E. Embolic infarcts



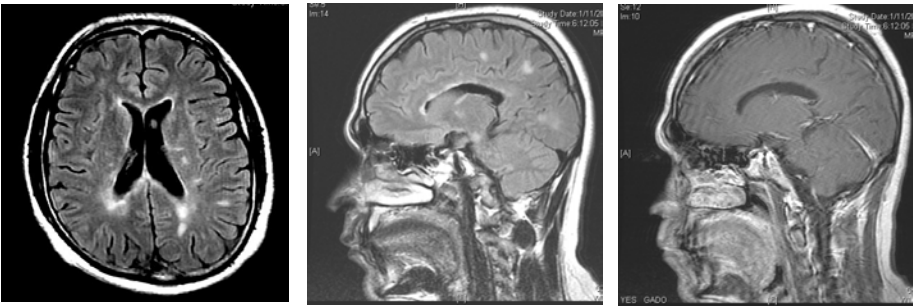
**281.** What is the usual finding on cerebral angiogram of a patient who presents with sudden onset of a severe headache with a SAH isolated to the perimesencephalic cisterns?

- A. Basilar tip aneurysm
- B. Posterior cerebral artery aneurysm
- C. Pontine cavernous malformation
- D. Cervical spine dural arteriovenous fistula
- E. Normal cerebral vasculature

**282.** Intracranial hypotension is associated with which of the following findings on MRV?

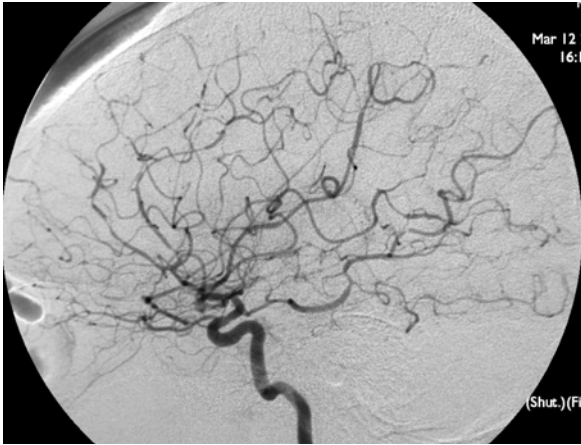
- A. Distention of the dominant transverse sinus
- B. Stenosis of the transverse sinus
- C. Occlusion of cortical veins
- D. Narrowing of the distal transverse sinuses
- E. All of the above

**283.** These MRI images of the brain belong to a 26-year-old man with chronic headaches. What is his most likely diagnosis?



- A. Chronic migraines
- B. Multiple sclerosis (MS)
- C. Susac syndrome
- D. Lyme disease
- E. Central nervous system (CNS) vasculitis

284. What is diagnosed on this angiographic image?



- A. Arteriovenous malformation (AVM)
- B. Cavernous malformation
- C. Middle cerebral artery aneurysm
- D. Primary angiitis of the central nervous system (PACNS)
- E. Normal cerebral vessels

285. Which of the following MRI findings is characteristically found in patients with intracranial hypotension after lumbar puncture?

- A. Pachymeningeal enhancement
- B. Deep white matter lesions (WMLs)
- C. An empty sella
- D. Chiari type 1 malformation
- E. All of the above



**286.** A 3-year-old boy complained to his parents that his head hurt. He was withdrawn and less active than usual, which his parents initially interpreted as a reaction to their marital problems. When they noted that he seemed to always be looking down, they took him to the pediatrician, who ordered an MRI scan. What does it show?



- A. Choroid plexus papilloma
- B. Pineal tumor
- C. Thalamic glioma
- D. Giant aneurysm of the internal carotid artery
- E. Vein of Galen malformation

**287.** What is the most common cause of the finding on this CT image?

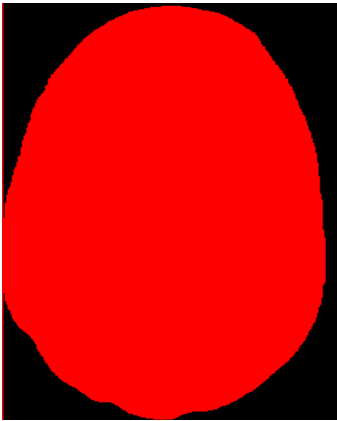


- A. Tearing of bridging cortical veins
- B. Middle meningeal artery groove fracture
- C. Metastatic melanoma
- D. Intracranial hypotension
- E. Intracranial aneurysm

**288.** Which of the following statements best describes the risks of neuroimaging for headaches during pregnancy?

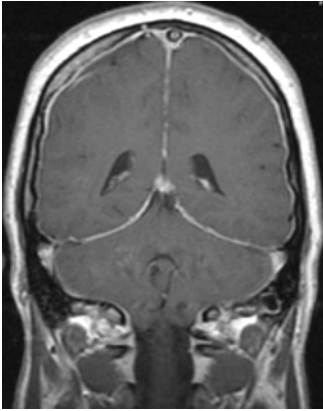
- A. MRI has been associated with elevation of core temperature that can endanger the fetus.
- B. An MRI should never be performed during pregnancy.
- C. A CT scan should never be performed during pregnancy.
- D. Contrast agents should be avoided when possible.
- E. All of the above

**289.** Which of the following is *not* seen on this image?



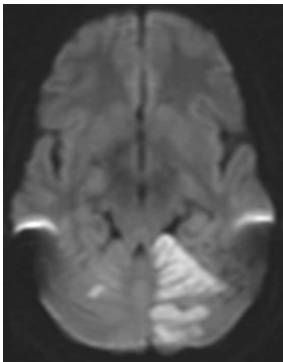
- A. Ventricular compression
- B. Meningioma
- C. Subdural hematoma
- D. Dural calcification
- E. Midline shift

290. Pick the patient associated with this image.



- A. An overweight woman with papilledema
- B. A woman with a positional headache
- C. An HIV-positive man with a headache
- D. A man taking ibuprofen 20 days a month
- E. A man with a headache and a seizure

291. A 33-year-old woman was seen in the emergency department with a headache, nausea, and vomiting. She was diagnosed with a migraine but she since her walking was unsteady, an MRI was obtained. The image is shown below. She was then evaluated with a catheter cerebral angiogram, resulting in the image shown below. What is her diagnosis?



- A. Vasospasm
- B. Systemic lupus erythematosus (SLE)
- C. Vertebral artery dissection
- D. Primary angiitis of the CNS
- E. Internal carotid artery occlusion

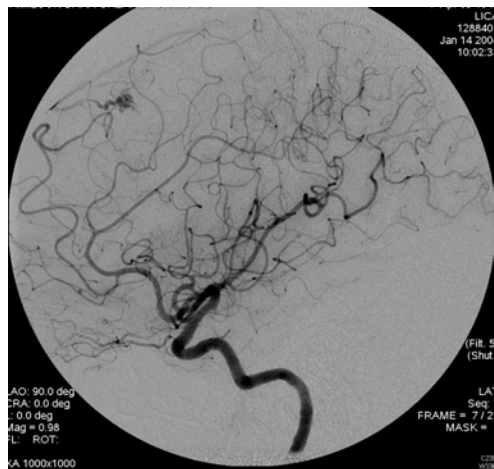
**292.** MRI in patients with headaches due to intracranial hypotension may show:

- A. Spinal meningeal diverticula.
- B. Subdural fluid collections.
- C. Pachymeningeal enhancement.
- D. Sagging of the brain.
- E. All of the above

**293.** White matter lesions in the brain are associated with which disorder?

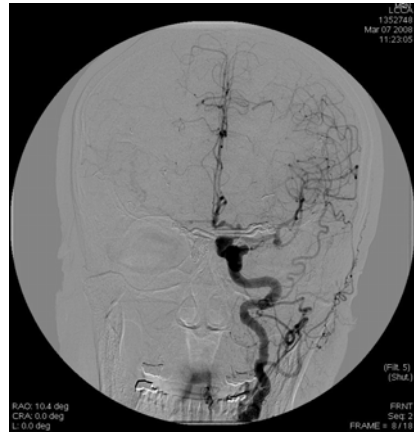
- A. Mitochondrial myopathy, encephalopathy, lactic acidosis and stroke (MELAS)
- B. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)
- C. Migraine headaches
- D. Binswanger's disease
- E. All of the above

**294.** What does this cerebral angiogram show?



- A. An arteriovenous malformation
- B. A cavernous malformation
- C. An aneurysm
- D. Vasculitis
- E. Middle cerebral artery occlusion

295. What does this angiographic image show?

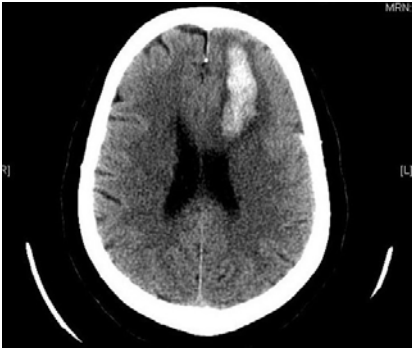


- A. Internal carotid artery stenosis
- B. Internal carotid artery dissection
- C. Internal carotid artery aneurysm
- D. Middle cerebral artery dissection
- E. Arteriovenous malformation

296. Which of the following are imaging findings of spontaneous intracranial hypotension (SIH)?

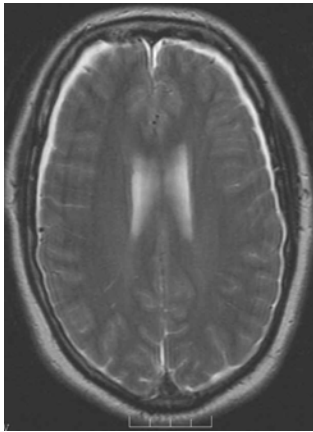
- A. Cerebellar tonsillar descent
- B. Reduction of the prepontine space
- C. Early radioisotope uptake in the bladder
- D. Subdural fluid collections
- E. All of the above

297. Which of the following can cause the lesion seen on this CT scan?



- A. Cerebral amyloid angiopathy
- B. Hypertension
- C. Melanoma
- D. Arteriovenous malformation (AVM)
- E. All of the above

298. The woman with this MRI scan has headaches. What is her diagnosis?



- A. Migraines
- B. Spontaneous intracranial hypotension
- C. Meningitis
- D. Cerebral venous thrombosis
- E. Metastatic cancer

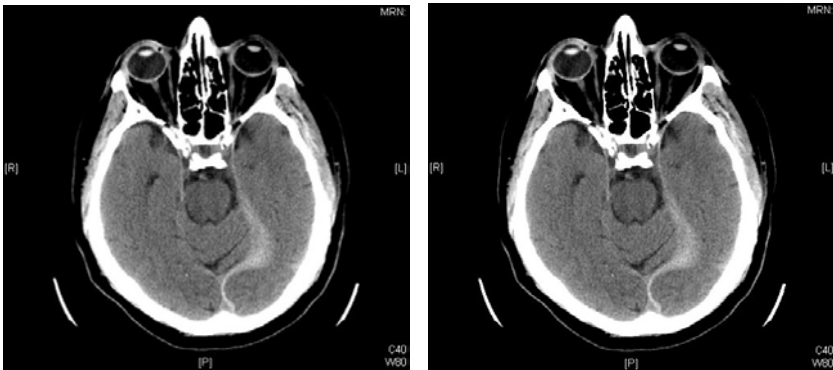
**299.** Patients with CADASIL show changes on MR scanning. Which of the following is characteristically seen on their MR scans?

- A. Cerebellar infarcts
- B. T2 hyperintensities in the anterior temporal pole
- C. Anterior and middle cerebral artery border zone area infarcts
- D. Optic nerve lesions
- E. Lesions in the corpus callosum

**300.** Which of the following is characteristic of the spinal fluid profile in patients with pseudomigraine with lymphocytic pleocytosis (headache with neurological deficit and CSF lymphocytosis)?

- A. The glucose level is decreased.
- B. Protein levels are rarely increased.
- C. Opening pressure is increased in more than 50% of cases.
- D. Oligoclonal bands are elevated in about a third of patients.
- E. All of the above

**301.** A 70-year-old man fell, hitting his head on a table. He was surprised by the fall and mildly confused. The next morning, he noted a posterior headache with mild nausea. His family doctor, who obtained a CT scan that day, received a call from the radiologist. What did she report?



- A. An intracerebral hemorrhage
- B. A cerebellar infarct
- C. A subdural hematoma (SDH)
- D. An epidural hematoma (EDH)
- E. Subarachnoid hemorrhage (SAH)

**302.** Which of cause of CNS infection is generally associated with the lowest CSF glucose level?

- A. Viral meningoencephalitis
- B. Tuberculous meningitis
- C. Rickettsial meningitis
- D. Partially treated bacterial meningitis
- E. Fungal meningitis

**303.** What does this image show?



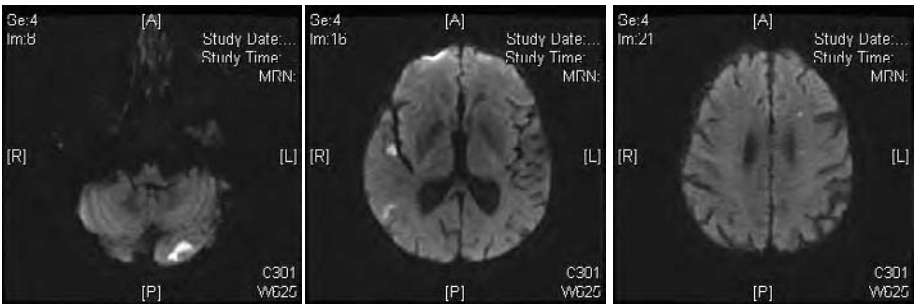
- A. Normal cerebral veins on a CT scan
- B. Normal cerebral arteries on a CT scan
- C. Normal cerebral veins on an MR scan
- D. Normal cerebral arteries on an MR scan
- E. Normal cerebral veins on a catheter angiogram



**304.** A 32-year-old woman came to the emergency department with the sudden onset of a moderately severe headache. Her neurological examination was unremarkable except for mild neck stiffness. A CT scan of the brain showed blood in the interpeduncular cistern but was otherwise unremarkable. A CT angiogram of the brain and neck did not show any vascular lesion. She was admitted for a four-vessel catheter angiogram, which was negative. An MRI of the cervical spine with and without contrast was negative. What do you suggest next?

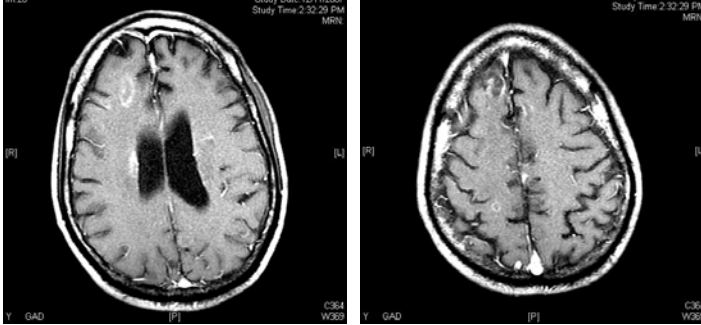
- Send her home for outpatient follow-up without further imaging.
- Send her home and repeat a cerebral angiogram in 6 weeks.
- Observe her in the intensive care unit until the period of vasospasm has passed.
- Observe her in the intensive care unit for 2 weeks.
- Admit her to the routine floor and repeat the cerebral angiogram in 2 weeks.

**305.** A 38-year-old woman noted headaches, fatigue, and malaise that developed over 2 weeks. Her primary care doctor attributed her symptoms to depression but noted a mild temperature elevation. Blood work showed mild anemia, normal thyroid function tests, and an erythrocyte sedimentation rate (ESR) of 92. When she developed left arm weakness, an MRI was obtained with the images shown below. Which of the following tests will confirm her diagnosis?



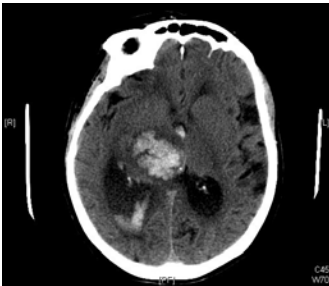
- Psychiatric consultation
- Electroencephalogram (EEG)
- Spinal fluid analysis
- Magnetic resonance venography (MRV)
- Transesophageal echocardiogram

**306.** A 28-year-old man with a history of drug and alcohol abuse was seen in a clinic complaining of new-onset headache and fatigue. He was slightly lethargic, with obvious track marks on his arms. His neurological examination was otherwise unremarkable. An MRI was obtained. Contrast-enhanced images are shown below. What is the *least* likely diagnosis?



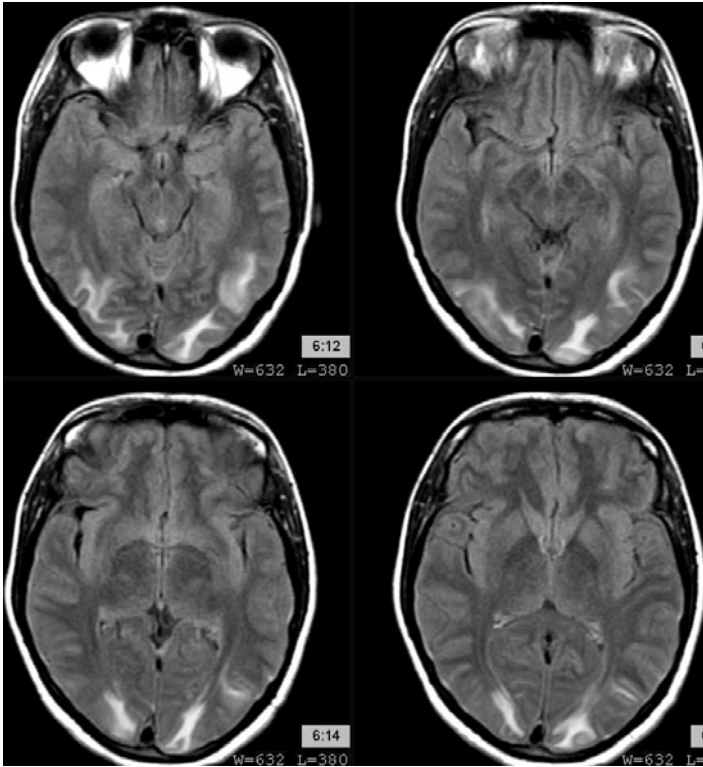
- A. Embolic infarcts
- B. Cerebral abscesses
- C. Toxoplasmosis
- D. Cytomegalovirus
- E. Cryptococcal infection

**307.** A 55-year-old overweight truck driver developed a severe headache. Over the next half hour, he became unresponsive. He was brought to the emergency department with the CT scan shown below. According to his family, he did not go to see doctors and was not taking any medications. He drank alcohol and smoked cigarettes. What is the most likely cause of his headache?



- A. Lung cancer with metastatic disease to the brain
- B. Cerebral amyloid angiopathy
- C. Arteriovenous malformation (AVM)
- D. Chronic untreated hypertension
- E. Cerebral aneurysm

308. This is the MRI FLAIR sequence of:

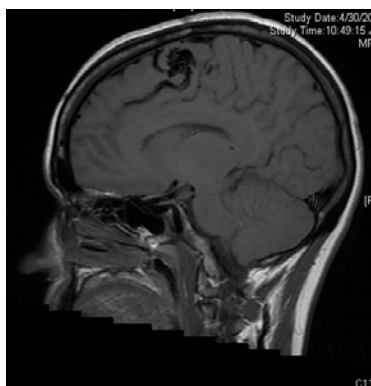


- A. A 32-year-old woman a headache and elevated blood pressure at 2 weeks postpartum.
- B. A 58-year-old woman with hypercalcemia due to multiple myeloma who suffered a headache and a seizure.
- C. A 69-year-old hypertensive man with confusion and multiple episodes of transient visual loss.
- D. A 42-year-old woman on renal dialysis with a headache and a focal seizure.
- E. All of the above

309. The diagnosis of HSV1 encephalitis is made based on which of the following tests?

- A. MRI scan of the brain
- B. CT scan of the brain
- C. Brain biopsy
- D. Spinal fluid analysis
- E. Electroencephalogram (EEG)

**310.** This MRI scan of the brain is from a 33-year-old woman with migraine headaches. What does it show?



- A. Normal brain
- B. A cerebral aneurysm
- C. An arteriovenous malformation (AVM)
- D. A cavernous malformation
- E. A cerebral venous thrombosis

**311.** This MRI image of a teenage boy with headaches shows:

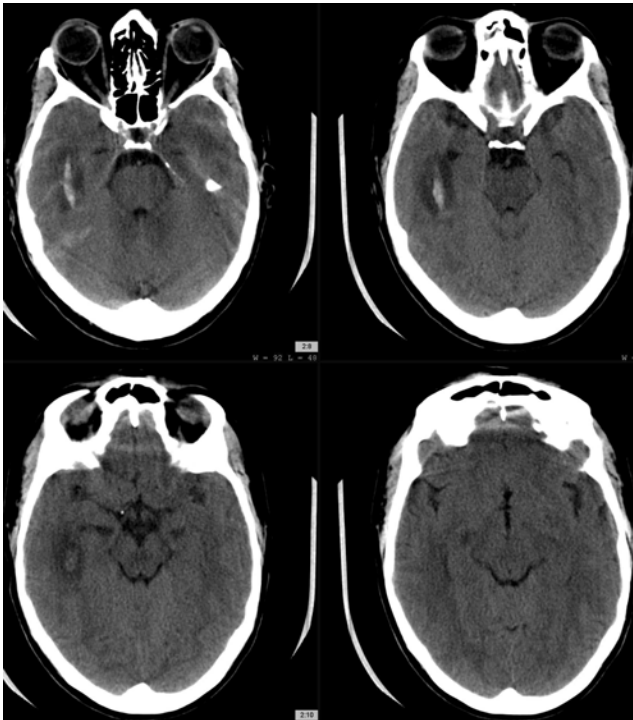


- A. A cerebellar arachnoid cyst
- B. A Chiari type 1 malformation with a cervical syrinx
- C. A spinal cord cavernous malformation
- D. A spinal cord infarct
- E. A normal cervical spine

**312.** Which headache type is associated with spinal meningeal diverticula?

- A. Migraine headaches
- B. Cluster headaches
- C. Spontaneous intracranial hypotension
- D. Idiopathic intracranial hypertension (IIH)
- E. All of the above

**313.** A 34-year-old woman with a history of migraine headaches ran the New York Marathon when the temperature was 86°F. After she finished the race, she had a headache of gradually increasing severity, and she was confused about how to get to the bar where she had planned to meet her friends after the race. When they finally found her wandering around Central Park, she was disoriented and could not tell her friends where she left her car. They took her to an emergency department where this CT scan was obtained. What is her most likely diagnosis?



- A. Exercise-induced migraine
- B. Right internal carotid artery dissection
- C. Intracerebral hemorrhage
- D. Subarachnoid hemorrhage (SAH)
- E. Cerebral venous sinus thrombosis

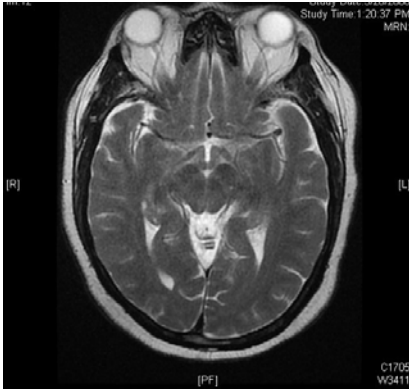
**314.** Which of the following statements best describes headache evaluation and treatment in the emergency department (ED)?

- A. Most patients evaluated for headaches in the ED have secondary headache types.
- B. Only one in a hundred migraine patients will visit the ED in a year.
- C. Narcotics are rarely given for migraine headaches in the ED.
- D. A triptan with rapid-onset action should be given to a migraine patient in the ED.
- E. Neurological consultation is rarely indicated for headaches in the ED.

**315.** A 35-year-old woman with systemic lupus erythematosus (SLE), taking prednisone 20 mg daily, complained of headaches for 2 weeks and a low-grade fever. When seen by her rheumatologist, she was mildly lethargic with a stiff neck, but her neurological examination was otherwise unremarkable. She was admitted to the hospital 2 days later, when an uncontrasted CT scan was normal. Spinal fluid analysis showed a white cell count of 420 cells/min, predominantly mononuclear cells, with a protein of 250 mg/dL. Glucose was moderately decreased, and there were no red cells in the spinal fluid. Which diagnostic test on the spinal fluid is most likely to give you the correct diagnosis?

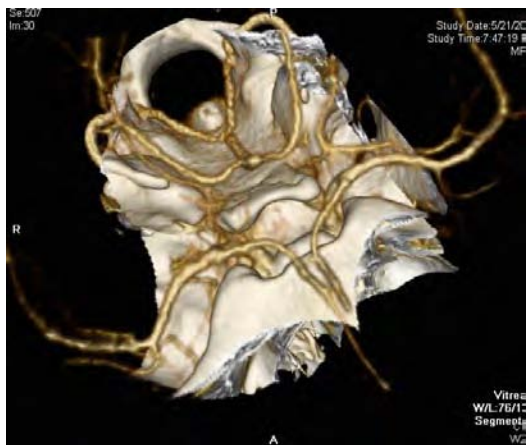
- A. Gram stain
- B. Polymerase chain reaction (PCR) for HSV1
- C. Latex agglutination testing for cryptococcal antigen
- D. Venereal Disease Research Laboratory (VDRL) test
- E. N-methyl-D-aspartate (NMDA) receptor subunit NR<sub>2</sub> (anti-NR<sub>2</sub>) antibodies

**316.** This MRI scan of the brain is from a 40-year-old man with migraine headaches. What does it show?



- A. Normal brain
- B. A left middle cerebral artery aneurysm
- C. A right middle cerebral artery aneurysm
- D. A left frontal arteriovenous malformation
- E. A right frontal cavernous malformation

**317.** These CT angiography images are associated with:



- A. Basilar artery occlusion
- B. Atretic vertebral artery
- C. Posterior communicating artery aneurysm
- D. Anterior communicating artery aneurysm
- E. Pretruncal (perimesencephalic) SAH

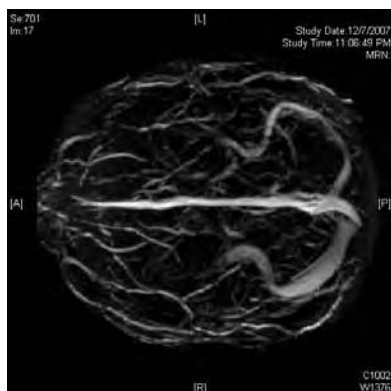
**318.** Which of the following may be associated with headaches caused by a subdural hematoma?

- A. Lumbar drain insertion after a spinal cord infarct
- B. Breast cancer
- C. Treatment with high doses of vitamin E
- D. Spinal anesthesia for knee replacement
- E. All of the above

**319.** An increased CSF white cell count that is predominantly lymphocytes may be associated with:

- A. Viral meningoencephalitis
- B. Tuberculous meningitis
- C. Partially treated bacterial meningitis
- D. Fungal meningitis
- E. All of the above

**320.** A 23-year-old man had episodic unilateral throbbing headaches, occasionally accompanied by blurred vision, of relatively recent onset. His mother had frequent headaches, and the man was not terribly concerned about his headaches. He did, however, visit his family doctor, who did a fundoscopic examination and diagnosed papilledema. He was told to lose weight to decrease his blood pressure. An MRI was interpreted as being normal, and the MRV is shown below. What is this man's most likely diagnosis?



- A. Vein of Galen malformation
- B. Cerebral venous thrombosis
- C. Astrocytoma
- D. Migraines
- E. Dural venous fistula



**321.** A teenage boy is seen by a neurologist for episodic unilateral throbbing headaches preceded by a visual aura. The headaches occur on either side and are accompanied by nausea, vomiting, photophobia, and phonophobia. An MRI of the brain is obtained, and the mother calls to request the results. She is told that she should take her son to a neurosurgeon for an evaluation because of an incidental finding that warrants neurosurgical evaluation. Which of the following is the most likely lesion noted on the MRI scan?

- A. Arteriovenous malformation (AVM)
- B. Developmental venous anomaly
- C. Cavernous malformation
- D. Arachnoid cyst
- E. Pineal cyst

**322.** A 30-year-old man was in a minor fender-bender automobile accident. A few days later, he noted neck pain and a mild unilateral headache. After two sessions with his chiropractor, his headache felt worse and he noted some speech difficulty and facial numbness. He underwent MRA imaging shown below. What does it show?



- A. Normal vasculature
- B. Left internal carotid artery dissection
- C. Right internal carotid artery dissection
- D. Left vertebral artery dissection
- E. Right vertebral artery dissection

**323.** An MRI scan of the brain, ordered because of headaches, may reveal unexpected findings. Match the unexpected vascular finding in the brain with its most appropriate characteristic. Use each answer only once.

- |  |   |
|--|---|
| A. Developmental venous anomaly                | 1. Annual symptomatic hemorrhage risk as high as 30%.                 |
| B. Intraparenchymal arteriovenous malformation | 2. No symptomatic hemorrhage risk                                     |
| C. Cavernous malformation                      | 3. May develop, with low hemorrhage risk, in adulthood                |
| D. Dural arteriovenous fistula                 | 4. May cause pulsatile tinnitus                                       |
| E. Capillary telangiectasia                    | 5. Low bleeding risk but may be associated with lung and skin lesions |

**324.** Which best describes white matter lesions (WMLs) on MRI of asymptomatic individuals?

- White matter lesions are rarely seen in asymptomatic individuals.
- White matter lesions in asymptomatic individuals are rarely periventricular.
- White matter lesions in asymptomatic individuals almost always indicate a future diagnosis of multiple sclerosis.
- White matter lesions are seen on FLAIR MRI sequences.
- Periventricular WMLs indicate increased ischemic or demyelinating disease risk, as compared to deep WMLs.

**325.** What does this MRI scan show?



- A normal brain
- A Chiari type 1 malformation
- A Chiari type 3 malformation
- Pachymeningeal enhancement
- A cervical syrinx

- 326.** Meningitis due to varicella zoster virus (VZV) is best diagnosed with:
- A. Polymerase chain reaction (PCR) testing of the spinal fluid.
  - B. Polymerase chain reaction testing of the skin lesions.
  - C. Immunofluorescent staining of the skin lesion.
  - D. Culture of skin biopsy.
  - E. Tzanck smear.
- 327.** A 12-year-old boy played soccer for his middle school team. During a practice after school, he headed a soccer ball that a player kicked directly at him. Later that evening, he became progressively more lethargic until he was unresponsive. A CT scan of his brain did not show any lesions. What testing may reveal the cause of his coma after mild head trauma?
- A. Electroencephalogram (EEG)
  - B. Positron emission tomography (PET)
  - C. Catheter cerebral angiography
  - D. CACNA1A gene testing
  - E. NOTCH3 gene testing
- 328.** Which of the following primary headache types can be diagnosed with the greatest confidence without neuroimaging?
- A. Cluster headaches
  - B. Paroxysmal hemicrania
  - C. Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT)
  - D. Hemicrania continua
  - E. Migraine headaches
- 329.** Which neuroimaging study is most likely to be abnormal in patients suspected of having IIH?
- A. CT scan of the brain
  - B. CT venography
  - C. MRI scan of the brain
  - D. Contrast-enhanced MRV
  - E. Non-contrast enhanced MRV

**330.** What is noted in the right cerebellum on this MRI scan?



- A. An arteriovenous malformation (AVM)
  - B. A developmental venous anomaly (DVA)
  - C. A cavernous malformation (hemangioma)
  - D. A cerebellar infarct
  - E. A capillary telangiectasia
- 331.** Which of the following is associated with CADASIL?
- A. Seizures
  - B. Myocardial infarction (MI)
  - C. Ischemic stroke
  - D. Coma
  - E. All of the above
- 332.** A Chiari type 2 malformation is associated with an abnormality diagnosed by which of the following imaging modalities?
- A. Carotid ultrasonography
  - B. Transcranial Doppler (TCD)
  - C. MRI of the lumbar spine
  - D. CT of the chest/abdomen/pelvis
  - E. All of the above

**333.** The site of a spinal CSF leak in SIH can be determined by:

- A. An MRI of the brain.
- B. A CT scan of the brain.
- C. MR myelography.
- D. An MRI scan of the cervical spine.
- E. A CT scan of the lumbar spine.

**334.** The pathologic diagnosis of Tolosa-Hunt syndrome requires evidence of:

- A. Granuloma formation.
- B. Lewy bodies.
- C. Tissue necrosis.
- D. Positive glial fibrillary acidic protein (GFAP) staining.
- E. All of the above.

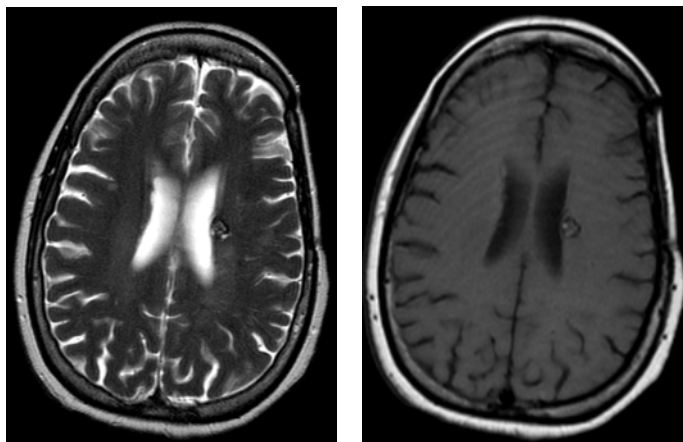
**335.** A 45-year-old woman had an asymptomatic middle cerebral artery aneurysm clipped successfully after she had an MRI scan, obtained for chronic headaches, which showed the incidental aneurysm. Her younger sister had a ruptured vertebrobasilar aneurysm, which presented with an SAH. Their mother collapsed and died suddenly at age 47 before she could get to a hospital. What evaluation could you recommend for this woman?

- A. Renal ultrasound
- B. Chest CT scan
- C. Holter monitor
- D. Transthoracic echocardiogram
- E. Dermatological consultation

**336.** An 18-month-old toddler fell outside his home, hitting his head against the concrete driveway. A CT scan showed a nondisplaced right parietal skull fracture. He was sent home from the hospital, but over the next several days he indicated that his head hurt. He refused to walk and would not play with his brother. He was brought back to the emergency department after he had a seizure at home. He was lethargic, with an elevated temperature. When he cried he moved his left side less than his right. What do you think his CT scan of the head showed?

- A. Epidural hematoma
- B. Intraparenchymal hemorrhage
- C. Subdural empyema (SDE)
- D. Shift of the calcified pineal gland
- E. Normal brain

**337.** What do these two MRI scans show?



- A. An arteriovenous malformation (AVM)
- B. A cavernous malformation
- C. A subependymal cyst
- D. A ischemic stroke
- E. No lesion in the brain

**338.** Which MRI sequencing shows a hyperintense signal in an acute ischemic stroke?

- A. Perfusion-weighted imaging (PWI)
- B. Diffusion-weighted imaging (DWI)
- C. Apparent diffusion coefficient (ADC)
- D. Fluid attenuation inversion recovery (FLAIR)
- E. Gradient recalled echo (GRE)

**339.** Biopsy of which tissue is used to diagnose CADASIL?

- A. Skin
- B. Liver
- C. Superficial temporal artery
- D. Sural nerve
- E. All of the above

**340.** A 27-year-old with migraines, dyslexia, and epistaxis is seen in headache clinic. She said that she was told not to take aspirin because there was something wrong with her platelets. Her mother also had headaches and episodic bleeding. She has a miotic left pupil on neurological examination. You, the attending covering the clinic, are perplexed, but the astute neurology resident suggests that this woman has an eponymic syndrome. What study will discover another abnormality that is characteristic of her syndrome?

- A. Serum calcium level
- B. Lower extremity ultrasonography
- C. Carotid ultrasonography
- D. A CT scan of the chest
- E. An abdominal CT scan

**341.** Magnetic resonance cerebral venography can be performed in patients with:

- A. Severe claustrophobia
- B. Pacemakers
- C. Severe renal disease
- D. All of the above
- E. None of the above

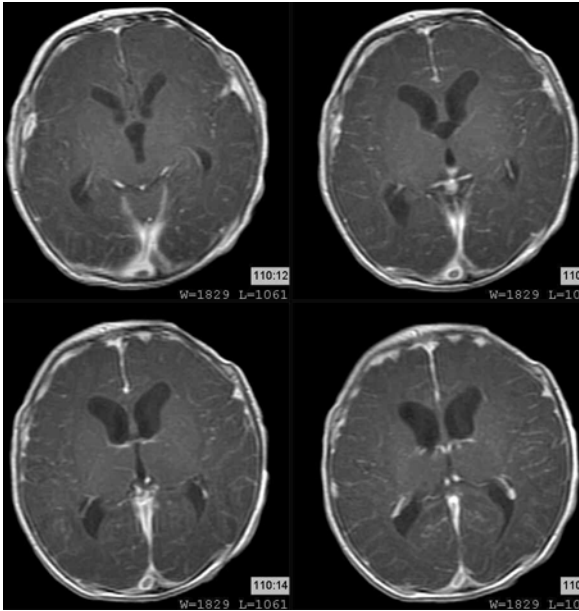
**342.** A 30-year-old otherwise healthy woman had a headache, fever, nausea, and vomiting for 4 days. When seen in the emergency department, she was uncomfortable with a stiff neck and a mildly elevated temperature but her general and neurologic examinations were otherwise normal. A CT scan of the head was normal. Her spinal fluid showed a lymphocytic pleocytosis, mildly elevated protein, and normal glucose. What is the most likely cause of her symptoms?

- A. Herpes simplex type 1 encephalitis
- B. Herpes simplex type 2 meningitis
- C. Leptomeningeal carcinomatosis
- D. Enterovirus meningitis
- E. Tuberculous meningitis

**343.** Which of the following is suspicious for a spinal CSF leak?

- A. Early appearance of contrast in the kidney on CT myelography.
- B. Early uptake of isotope in the bladder and kidneys on radionuclide cisternography.
- C. Subdural fluid collection.
- D. Sagging of the brain.
- E. All of the above

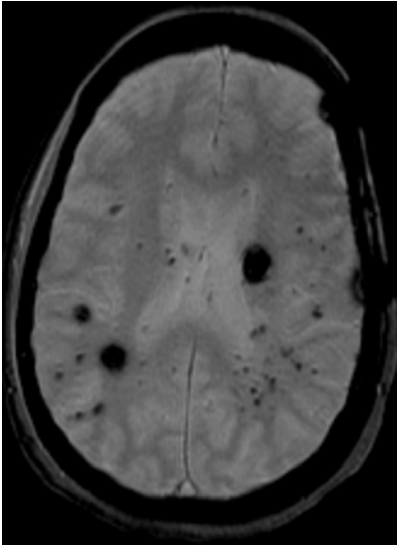
344. What does this contrast-enhanced MRI scan of a child's brain show?



- A. Congenital hydrocephalus
  - B. Bacterial meningitis
  - C. Agenesis of the corpus callosum
  - D. Intracranial hypotension
  - E. Normal brain
345. Patients with suspected CADASIL can be evaluated with:
- A. Cerebral angiography
  - B. Liver biopsy
  - C. Brain biopsy
  - D. Genetic testing
  - E. All of the above



**346.** A 20-year-old healthy man with migraine headaches had an MRI scan. What is the most likely cause of this MRI image?



- A. Cerebral amyloid angiopathy
- B. Arteriovenous malformation (AVM)
- C. Familial cavernous malformations
- D. Metastatic melanoma
- E. Normal brain with artifact

**347.** Which of the following is associated with a predominance of mononuclear cells in the spinal fluid?

- A. Viral meningitis
- B. Partially treated bacterial meningitis
- C. Tuberculous meningitis
- D. Cryptococcal meningitis
- E. All of the above

**348.** Which of the following studies may provide related information in patients with idiopathic intracranial hypertension?

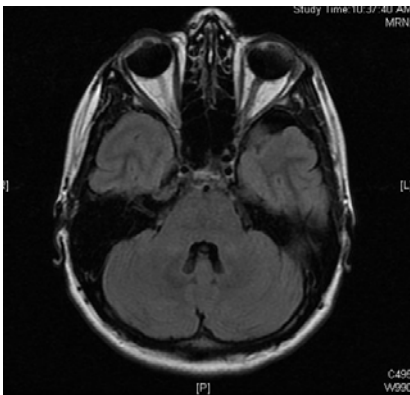
- A. MRI of the cervical spine
- B. MRA of the brain vessels
- C. MRA of neck vessels
- D. MRV of the brain
- E. Radionuclide cisternography

**349.** This is the CT scan and the MRI FLAIR images of a 32-year-old woman who developed a headache with bizarre behavior. What is her most likely diagnosis?



- A. Left temporal infarct
- B. Glioblastoma multiforme
- C. Bipolar disorder
- D. Herpes simplex virus type 1 (HSV1) encephalitis
- E. Schizophrenia

**350.** This is the axial FLAIR MRI image of a 26-year-old man with migraine headaches. How should the lesion seen in the left middle cranial fossa be treated?

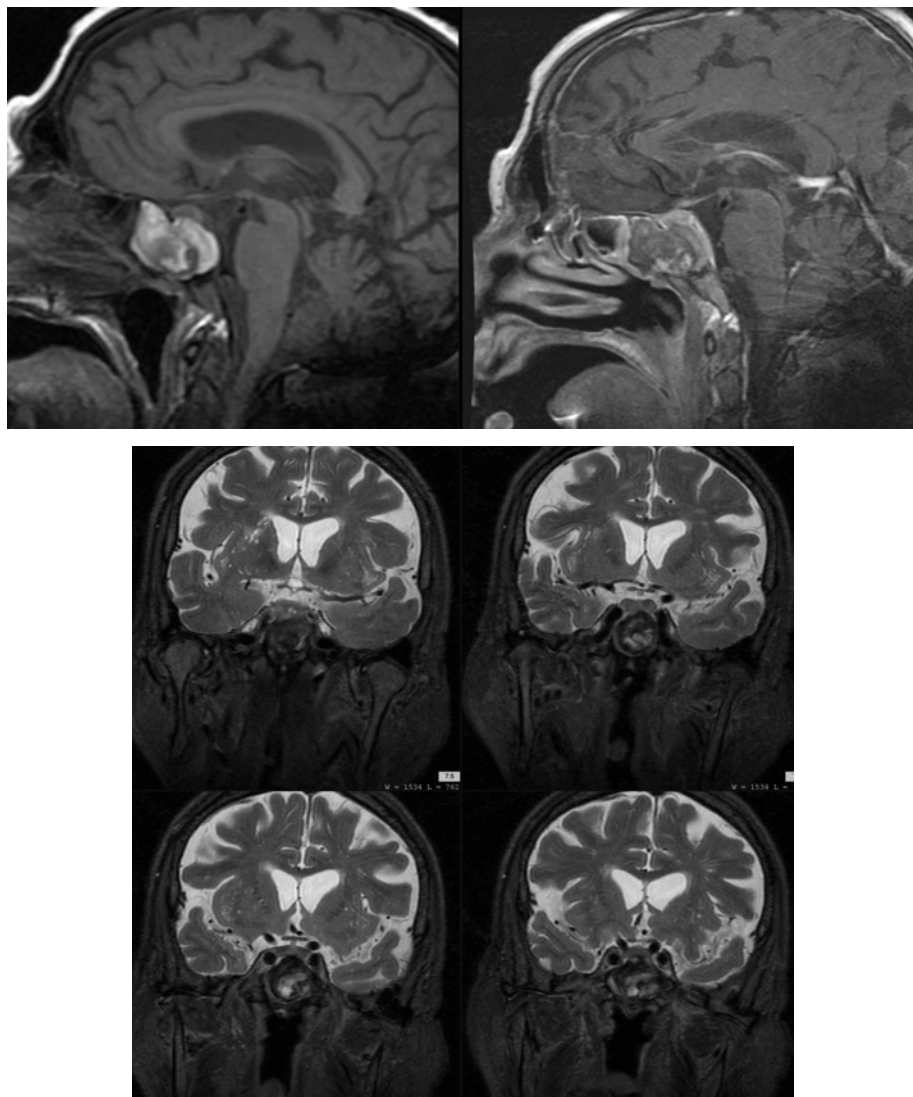


- A. Endovascular embolization
- B. Ventricular shunting
- C. Radiation therapy
- D. Endoscopic fenestration
- E. Reassurance

**351.** A 51 year old woman complained that she developed mild to moderately severe headaches involving her entire head without any particular triggers or exacerbating factors. She denied being a “headache person” but her headaches had been present almost daily for about a year. She denied any other complaints. Her examination was unremarkable without papilledema. She had distinct facial features with a large nose and prominent cheek bones. She was seen with her husband, who seemed quite solicitous, but he did complain that she snored. She was not wearing her any rings on her fingers, although her husband was wearing a wedding ring. What should you do for this woman?

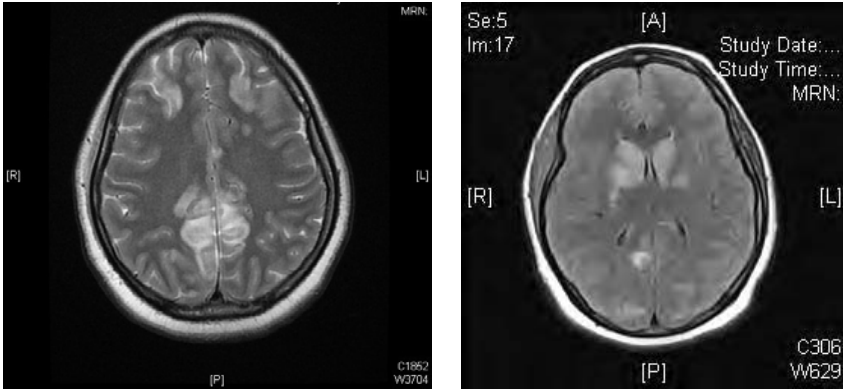
- A. Diagnose chronic daily headache and give her a prescription for gabapentin
- B. Diagnose perimenopausal headaches and give her a prescription for estrogen replacement
- C. Suggest laser ablation of her uvula
- D. Order a CT scan of the chest and blood work
- E. Order an MRI of the brain and blood work

**352.** A 40-year-old man complains of a constant “sinus headache” with facial pain, unresponsive to multiple medications suggested by his family doctor. An MRI was ordered that showed these coronal and sagittal images. What does it show?



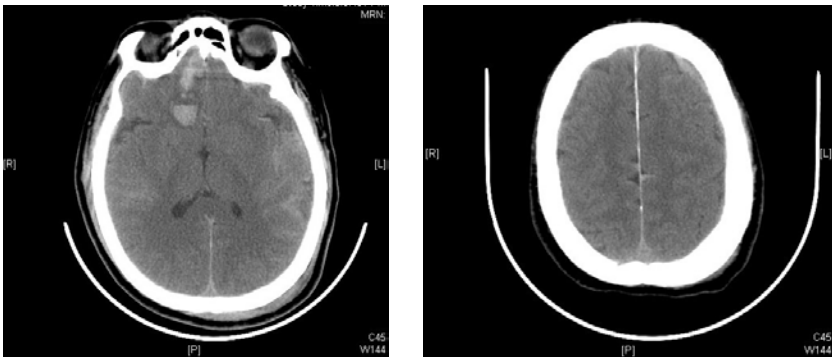
- A. Cavernous sinus thrombosis
- B. Aneurysm of the intracavernous internal carotid artery
- C. Pituitary macroadenoma
- D. Lymphoma in the frontal sinus
- E. Mucocele in the sphenoid sinus

**353.** These are axial FLAIR (on right) and T2 (on the left) MRI images of a pregnant woman. What does she have?



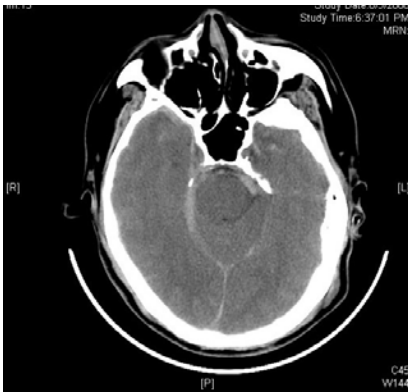
- A. Basilar artery occlusion
- B. Cerebral venous thrombosis (CVT)
- C. Posterior reversible encephalopathy syndrome (PRES)
- D. Herpes simplex encephalitis
- E. Status epilepticus

**354.** A 50-year old-man complained of a headache. What happened to him prior to obtaining these CT scan images?

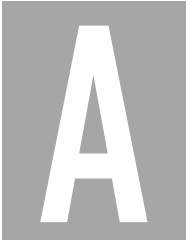


- A. He had a cervical myelogram with accidental extension of the dye column cephalad.
- B. He had severe untreated hypertension and was taking high-dose vitamin E and aspirin.
- C. He was pushed down a flight of stairs by a mugger.
- D. He had a dental abscess but refused to see a dentist.
- E. He was being treated for lung cancer.

355. What does this CT scan of a man with a headache show?



- A. Bacterial meningitis
- B. Subdural hematoma (SDH)
- C. Epidural hematoma (EDH)
- D. Subarachnoid hemorrhage (SAH)
- E. Normal brain



# HEADACHE EVALUATION AND DIAGNOSTIC TESTING

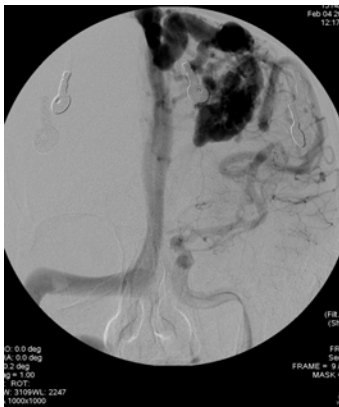
## ANSWERS

**266. The answer is C.** Computed tomography venography (CTV) is widely available, with a more rapid image acquisition time than magnetic resonance venography (MRV). Although CTV does not have some of the patient-related contraindications of MR studies, it does require injection of iodinated contrast dye, which may be nephrotoxic in patients with renal disease and should be avoided in pregnant women. CTV has the radiation exposure of CT scanning, making it generally contraindicated in pregnancy, as compared to MR scanning. MRV images can be obtained with (gadolinium-enhanced) or without (two-dimensional time-of-flight) contrast enhancement, as compared to CTV, which always requires contrast injection. Image processing with CT angiography (CTA) and venography is complicated and time consuming, but clinically useful information can often be obtained from preprocessing source images. (Agid, Shelef, Scott, et al., *Neurologist* 2008)

**267. The answer is B.** Diagnosis of herpes simplex virus type 1 (HSV1) encephalitis early in its clinical course is critical because treatment with the antiviral drug acyclovir dramatically decreases morbidity and mortality. The use of polymerase chain reaction (PCR) techniques to amplify the genome of HSV1 from cerebrospinal fluid (CSF) is the diagnostic procedure of choice, having supplanted pathologic examination of biopsied brain tissue. False-negative CSF HSV1 PCR assays may occur within the first 72 hours after onset of symptoms. Almost all patients with proven HSV1 encephalitis have unilateral or bilateral temporal lobe abnormalities on neuroimaging, but this finding may not be specific to HSV1 encephalitis and can be found in other causes of viral, as well as non-viral, encephalitis. The coronal fluid-attenuated inversion recovery (FLAIR) MRI image of the patient with HSV1 encephalitis, shows an abnormal signal in the left mesial temporal area. There is no specific electroencephalographic (EEG) pattern in HSV1 encephalitis, but a focal or lateralized abnormality, especially temporal periodic discharges, in the presence of a viral encephalitis is concerning for HSV1 encephalitis. (Tyler, *Rev Neurol Dis* 2004)

**268. The answer is E.** These magnetic resonance images (MRIs) show a cortical lesion with a capsule and surrounding edema. The lesion could be a primary (e.g., glial, lymphoma) or metastatic (e.g., lung, breast, melanoma) brain tumor. A demyelinating lesion, resolving hematoma, or a subacute infarct could have a similar MRI appearance, but this degree of surrounding edema would not be expected. The MRI was done prior to a stereotactic biopsy, which revealed a cerebral abscess. The patient presented with a headache and fever. Recovery was complete after drainage and antibiotics. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**269. The answer is B.** This MRI axial image shows a large arteriovenous malformation (AVM) with a prominent cortical draining vein. An AVM is a tightly packed mass of enlarged vascular channels with arteriovenous shunting, without an intervening capillary bed. The MRI shows a wormy lesion that can be found anywhere in the brain or spinal cord but is more likely to be supratentorial than infratentorial. Hemorrhage of an AVM may produce headache with a focal neurological deficit. The angiographic images here show the AVM with feeding arteries and the large draining vein. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)



**270. The answer is D.** This woman has subjective (heard only by the patient) pulsatile tinnitus, which generally has a benign etiology. It may be noted by patients with idiopathic intracranial hypertension (IIH). However, pulsatile tinnitus, due to vibrations of turbulent flow reaching the cochlea, may indicate a potentially concerning vascular lesion. Multiple imaging modalities are often needed to distinguish between benign vascular etiologies such as an audible intracranial bruit and a more concerning condition such as a vascular malformation. Four-vessel catheter angiography is the most sensitive modality to diagnose a dural AVM producing subjective auditory symptoms. MRI, MRA, and MRV



are used to look for carotid artery disease, cerebral venous disease, and IHH. A patient with pulsatile tinnitus and a retrotympenic mass may be screened with a CT scan of the temporal bone, looking for a cholesteatoma or glomus tumor. A study of 16 patients with multiple vascular causes of pulsatile tinnitus concluded that the single CTA/CTV study of the middle and inner ear and of the vascular structures replaces the other multiple imaging modalities used to evaluate the patient with pulsatile tinnitus. These CT studies are excellent screening tools for arterial and venous etiologies of pulsatile tinnitus. Although dural arteriovenous fistula may be detected on CTA/CTV, the technique is not as sensitive as conventional angiography, which may still be indicated if the pulsatile tinnitus is objective (heard by both the patient and the examiner). (Krishnan, Mattox, Fountain, et al., *AJNR* 2006)

**271. The answer is B.** The diagnosis of a Chiari type 1 malformation is made in an adult when a sagittal MRI of the brain shows pointed or triangular-shaped cerebellar tonsils that descend 5 mm or more below the foramen magnum. The CSF space around the cervicomedullary junction is obliterated by the low hanging cerebellar tonsils. An upper cervical syrinx may be seen. A CT scan of the cervical spine may show a crowded foramen magnum on high cervical axial images. Patients with demonstrable blockade at the foramen magnum may experience more favorable response to surgical decompression than patients without spinal fluid blockage. Transcranial Doppler is not useful in the diagnosis of a Chiari type 1 malformation. An MRI of the lumbar spine would not show pathology in a Chiari type 1 malformation. The radiologic diagnosis of a Chiari type 1 is generally an incidental finding, although headache precipitated by Valsalva maneuver and syncope may rarely correlate with the finding. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**272. The answer is C.** This woman has a large right internal carotid artery aneurysm in the right cavernous sinus. The CTA source images show a large vascular lesion emanating from the right cavernous sinus extending into the middle cranial fossa. This is not a sarcoid granuloma, a dural-based meningioma, or an inflammatory pseudotumor of Tolosa-Hunt syndrome. This large carotid artery aneurysm is symptomatic and is not an incidental finding in a woman with glaucoma. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**273. The answer is B.** This woman has central nervous system (CNS) vasculitis with bilateral frontal infarcts (explaining her abulia) and subarachnoid hemorrhage (SAH). The CT scan shows bilateral hypodensities in the frontal white matter and blood in the sulci posteriorly on the right. Her presentation with

headaches, seizures, and infarcts is consistent with CNS vasculitis or vasculopathy; however, other diagnoses including cerebral venous thrombosis (CVT) and reversible cerebral vasospasm should be considered. Herpes simplex virus encephalitis would not produce frontal hypodensities on CT scan and does not produce this degree of CSF lymphocytosis or protein elevation. Headache with neurological deficits and CSF lymphocytosis (HaNDL) does not present with a seizure and does not cause infarcts. Sarcoidosis and human immunodeficiency virus (HIV) disease would not characteristically present with multifocal infarcts and SAH. (West, *Curr Rheum Rep* 2003)

**274. The answer is C.** This elderly woman has a headache, neck pain, scalp tenderness, and jaw claudication, suspicious for giant cell arteritis (GCA). She does not comb her hair because of pain in her scalp, and her weight loss may also be related to systemic aspects of the arteritis. All the listed tests may be abnormal in the evaluation of GCA, but some of these non-invasive tests are more useful than others in indicating need for a biopsy. Both erythrocyte sedimentation rate (ESR) and c-reactive protein (CRP) are generally elevated in GCA. The ESR is >50 mm/hour in 89% and over 100 in 41% of patients with GCA. However, the ESR may be normal in 1–2% of patients with GCA. C-RP, an acute phase plasma protein, may be more specific for detecting inflammation and is not elevated by anemia. The C-RP may be elevated when the ESR is normal in GCA. Ultrasound of the superficial temporal artery may show a characteristic halo around the arteritic vessel, but detection is operator dependent. The elevation of von Willebrand factor, an acute phase reactant, is a nonspecific test. Dampening of the amplitude of the wave form on oculoplethysmography (OPG) may be seen with involvement of the ophthalmic artery, but OPG is now rarely used in the diagnosis of GCA. The definitive diagnosis of GCA is made when microscopic examination of the superficial temporal artery shows multinucleated giant cells, lymphocytic infiltration, destruction of the internal elastic lamina, and fibrinoid necrosis. (Olesen, Goadsby, Ramadan, et al., *Headaches*, Chapter 110, 2005)

**275. The answer is C.** This woman has carbon monoxide (CO) poisoning, with the MRI axial FLAIR image showing bilateral hyperintensities in the globus pallidi. Her headaches were due to a leaking furnace and resolved when her furnace was replaced. Bilateral basal ganglia hypodensity can be seen on CT scan in CO poisoning. Creutzfeldt-Jacob disease (CJD) and Japanese encephalitis may show bilateral T2 hyperintensities in the basal ganglia on MRI, but these diagnoses do not seem likely without cognitive problems. This is not a normal MRI scan to correlate with presbyopia or migraine headaches. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**276. The answer is B.** Nephrogenic fibrosing dermopathy/nephrogenic systemic fibrosis (NFD/NSF) has been found in patients with acute or chronic renal failure who have been exposed to gadolinium-containing contrast agents. NFD/NSF is a fibrosing cutaneous disorder is characterized clinically by an acute onset of hardening and thickening of the skin of the extremities and trunk, often resulting in flexion contractures, and histologically by an increase in spindle-shaped cells, collagen, and sometimes mucin deposition in the dermis. Gadolinium has been detected in skin tissue samples of affected patients. Other organs involved may include lungs, myocardium, or striated muscles. (Introcaso, Hivnor, Cowper, et al., *Int J Dermatol* 2007; Grobner & Prischl, *Kidney Int* 2007)

**277. The answer is D.** Whereas xanthochromia or yellow coloration of spinal fluid may not be found for up to 12 hours after the leakage of a cerebral aneurysm, its presence in rapidly analyzed spinal fluid is suggestive of a subacute SAH. The reliability of the detection of xanthochromia may be increased using spectrophotometry, but the technique is not readily available and may be associated with false positives. Xanthochromia may also be seen in spinal fluid with markedly elevated protein. Crenated red blood cells and either a constant number or slight decrease in the number of cells seen in sequential tubes can be seen in subacute SAH or less frequently with a traumatic lumbar puncture. Red spinal fluid can indicate traumatic venous hemorrhage or aneurysmal arterial hemorrhage. With a traumatic lumbar puncture, the red cell count is usually markedly decreased in sequential tubes of spinal fluid. (Silberstein, Lipton, & Dodick, *Wolff's Headache*, Chapter 5, 2007)

**278. The answer is C.** This CT image shows the hyperdense, biconvex epidural collection of blood that is almost always due to a traumatic arterial hemorrhage. Arterial epidural hematoma (EDH) is nearly always secondary to a middle meningeal groove fracture with middle meningeal artery rupture. This image shows the “swirl sign,” with hypodensity within the hematoma due to active bleeding with unretracted, semi-liquid clot. Nontraumatic EDH and venous EDH due to trauma are very rare. Patients may appear neurologically normal after head trauma before deterioration in mental status—the “lucid interval” associated with EDH. Prompt surgical evacuation of an EDH prior to cerebral herniation generally results in good outcome. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**279. The answer is A.** This sagittal MRI image shows the brain pulled down, with the cerebellar tonsils hanging below the foramen magnum and crowding of the cerebrospinal spaces at the base of the brain, characteristic of intracranial hypotension. The MRI of the brain in a patient with a positional headache due

to dural puncture or spontaneous intracranial hypotension (SIH) may show diffuse enhancement of the pachymeninges (dural and pial layers of the meninges), sagging of the brain with cerebellar tonsils hanging below the foramen magnum, subdural collections and obliteration of the basal cisterns. (Ahmed, Jayawarma, & Jude, *Postgrad Med J* 2006; Schievink, *JAMA* 2006)

**280. The answer is C.** All of the listed causes of multifocal brain lesions could present with headaches and a seizure in a smoker, but the most plausible diagnosis is metastatic lung cancer. The CT scan shows bilateral hypodensities consistent with edema surrounding bilateral lesions. The coronal MRI scan shows a lesion attached to the dura (falx), consistent with a dural/parenchymal metastatic lesion. Glioblastoma multiforme, cerebral abscesses, and embolic infarcts may be multifocal, and primary CNS lymphoma may be bihemispheric. Adenocarcinoma from an occult lung primary was diagnosed on biopsy. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**281. The answer is E.** About 15% of nontraumatic SAH patients have an occult, non-aneurysmal cause of hemorrhage, especially when the bleeding is confined to the cisterns surrounding the brainstem and suprasellar cistern. These hemorrhages occur in a variety of patients, but they tend to be young males without traditional vascular risk factors. The cause of these perimesencephalic or pretruncal hemorrhages is unknown but may be venous in origin. (Flaherty, Haverbusch, Kissela, et al., *J Stroke Cerebrovasc Dis* 2005)

**282. The answer is A.** Patients with CSF depletion syndromes, such as SIH and post dural puncture headache (PDPH), exhibit intracranial venous enlargement as a response of the dural sinuses to the loss of intracranial volume and pressure. The “venous distension sign” in intracranial hypotension describes the distended convex appearance of the inferior margin of the midportion of the dominant transverse sinus. Narrowing of the distal transverse venous sinuses is strongly associated with IIH. Stenosis or occlusion of venous sinuses or cortical veins is associated with CVT. (Agid, Shelef, Scott, et al., *Neurologist* 2008)

**283. The answer is B.** All of the listed answers are associated with WMLs on MRI; however, these images show the characteristic lesions of multiple sclerosis (MS). The axial FLAIR image shows bilateral, asymmetric linear and ovoid hyperintense lesions. There are linear hyperintensities called “Dawson’s fingers” noted neuropathologically by James Dawson in 1916 along the path of deep medullar veins. The sagittal images show calloseptal lesions, which are different from the WMLs seen in migraineurs. Callosal lesions (central > calloseptal interface)

are characteristic of Susac syndrome but are not seen characteristically in Lyme disease and CNS vasculitis. There is a hypointense callosal lesion on the T1 with contrast image and multiple calloseptal lesion hyperintensities on the FLAIR image. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**284. The answer is D.** This catheter angiographic image shows arterial sausageing, occlusion, and luminal irregularity which is seen in 60–80% of patients with primary angiitis of the central nervous system (PACNS). Since PACNS predominantly involves small cerebral vessels, up to 40% of patients may have negative angiography. PACNS may present with generalized headaches followed by seizures and focal neurologic deficits. The MRI, which may be unrewarding, often shows abnormalities including ischemic lesions, leptomeningeal enhancement, hemorrhage, a mass lesion, or diffuse white matter disease. While the spinal fluid in PACNS may show an elevated white blood cell count and protein, pathological examination of brain tissue may be needed for diagnosis. (West, *Curr Rheum Rep* 2003)

**285. The answer is A.** The MRI of a patient with the postural headache of intracranial hypotension after lumbar puncture may show enhancement of the dural and pial layers of the meninges (pachymeninges). Deep white matter lesions (WMLs) may be seen in patients with migraine with aura. An empty sella is non-specific but may be seen in patients with IIH. The congenital Chiari type 1 malformation, with cerebellar tonsils hanging >5 cm below the foramen magnum, is variably associated with chronic headaches. (Silberstein, Lipton, & Dodick, *Wolff's Headache*, Chapter 5, 2007)

**286. The answer is B.** A toddler with headache, lethargy, and Parinaud syndrome (dorsal midbrain syndrome) is a common presentation for a pineal tumor with hydrocephalus. Parinaud syndrome is paralysis of upgaze, pupil accommodation paresis, retraction of eyelids, and convergence–retraction nystagmus. The child may show a “setting sun” sign with conjugate down gaze in primary position. This coronal MRI scan shows a heterogeneous solid tumor in the pineal region, which was diagnosed as pilocystic astrocytoma, a rare pineal tumor, on pathology. In children, pineoblastomas and germ cell tumors are more common pineal gland tumors. The MRI shows dilation of the lateral ventricles consistent with obstructive hydrocephalus from cerebral aqueduct compression. (Drummond & Rosenfeld, *Childs Nerv Syst* 1999)

**287. The answer is A.** This crescent-shaped, homogeneous, hyperdense extra-axial hemorrhage, which spreads diffusely over the cerebral hemisphere, is a subdural hematoma (SDH). Most SDHs are due to trauma with stretching and tearing of

bridging cortical veins as they cross the subdural space to drain into dural sinuses. Trauma resulting in a SDH may be severe, but even minor injury may result in a life-threatening SDH in the elderly. A spontaneous SDH may occur as a result of anticoagulant or antiplatelet therapy or in association with hemorrhage into dural metastases. Rarely a SDH may be seen with spontaneous or iatrogenic intracranial hypotension. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging 2004*)

**288. The answer is D.** An MRI should be performed in preference to a CT scan during pregnancy; however, a standard CT scan of the head exposes the uterus to less than 1 mrad. A radiation dose of 15 rads is associated with fetal abnormalities. While the electric field of an MRI can slightly increase core temperature ( $<1^{\circ}\text{C}$ ), the scan does not have any deleterious effect on the fetus. Contrast agents should be avoided unless necessary for the health of the mother. (Silberstein, Lipton, & Dodick, *Wolff's Headache*, Chapter 5, 2007)

**289. The answer is B.** This CT scan shows a diffuse crescent-shaped, subdural collection of blood. There are two areas of calcification along the falx, but these are not dural-based meningiomas. A meningioma, even with calcification, would not be as hyperdense on an unenhanced CT scan. Mass effect is present from the SDH, producing a right-to-left midline shift and compression of the right lateral ventricle. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging 2004*)

**290. The answer is B.** This coronal MRI image shows gadolinium enhancement of the pachymeninges (dural and pial layers of the meninges) surrounding the brain characteristic of intracranial hypotension. MRI of the brain in a patient with a positional headache due to dural puncture or SIH may show diffuse enhancement of the pachymeninges, sagging of the brain with cerebellar tonsils below the foramen magnum, and obliteration of the basal cisterns. Leptomeningeal enhancement (pial and arachnoid layers of the meninges) is characteristically seen with infectious, inflammatory, or neoplastic disorders. (Ahmed, Jayawarma, & Jude, *Postgrad Med J* 2006; Schievink, *JAMA* 2006)

**291. The answer is C.** The diffusion weighted imaging (DWI) sequence shows an acute left cerebellar hemispheric infarct in a patient with headache, nausea, vomiting, and ataxia. The angiographic image of the aortic arch shows tapering-to-occlusion of the left vertebral artery distal to its origin off the left subclavian artery, consistent with a vertebral artery dissection. The other extracranial arteries in the neck appear normal, without evidence of arteriopathy. Dissection of extracranial arteries may be associated with arteriopathies, such as fibromuscular dysplasia, Ehlers-Danlos syndrome, Loeys-Dietz syndrome or Marfan syndrome.

Trauma is often a suspected etiology, but a dissection may occur spontaneously in an individual without known vascular pathology. (Savitz & Caplan, *N Engl J Med* 2005)

**292. The answer is E.** Spinal meningeal diverticula on cervical and thoracic spinal MRI and characteristic changes on cranial MRI (subdural fluid collections, pachymeningeal contrast enhancement, sagging of the brain) are seen in patients with the clinical syndrome of orthostatic headaches due to intracranial hypotension due to spontaneous or iatrogenic/traumatic spinal CSF leakage. (Schievink, Maya, Louy, et al., *AJNR* 2008)

**293. The answer is E.** Mitochondrial myopathy, encephalopathy, lactic acidosis and stroke (MELAS) and cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) are progressive disorders associated with worsening WMLs. Migraine headaches have been associated with supratentorial WMLs seen on MRI. White matter lesions are characteristically seen in patients with MS, with lesions especially prominent in the corpus callosum on sagittal FLAIR imaging. Binswanger's disease is characterized by progressive WMLs caused by small-vessel ischemia in older individuals with multiple vascular risk factors. (Silberstein, Lipton, & Dodick, *Wolff's Headache*, Chapter 5, 2007)

**294. The answer is A.** This cerebral arteriogram shows a small left AVM in a patient who presented with a left frontal intracerebral hemorrhage. There is a nidus of tightly packed enlarged arteries seen in the distal anterior cerebral artery territory. There is no aneurysm, arterial occlusion, or multifocal luminal changes seen in this image to support another cerebrovascular diagnosis. A cavernous malformation would not be seen on an arteriogram; it is best imaged by MRI scanning. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**295. The answer is C.** These angiographic images show a left common carotid arterial injection with an aneurysm in the intracavernous portion of the internal carotid artery (ICA). There is aneurysmal dilatation at the origin of the left ICA at the bifurcation of the common carotid artery, but there is no ICA stenosis or dissection. There is no middle cerebral artery dissection or AVM. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**296. The answer is E.** Characteristic imaging findings may be seen on MRIs of the brain and spine, nuclear cisternography, and myelography of patients with SIH. Findings on gadolinium-enhanced MRI of the brain include pachymeningeal enhancement, descent of cerebellar tonsils, descent of the optic chiasm,



decreased size of peripontine cisterns, subdural fluid collections, and decreased ventricular size. On nuclear cisternography, early uptake of radioisotopes is seen in the kidneys and bladder, and radioisotope ascent to the cerebral convexities is delayed. (Schwedt & Dodick, *Curr Pain Headache Rep* 2007)

**297. The answer is E.** This left lobar intracerebral hemorrhage could be caused by all of the listed conditions. This particular patient had a left frontal AVM diagnosed after the hemorrhage by catheter angiography. Cerebral amyloid angiopathy can cause lobar hemorrhages in elderly individuals. Hemorrhage due to chronic hypertension occurs less commonly in cortical lobar locations than in subcortical structures, such as the thalamus and basal ganglia. Primary and metastatic malignancies may bleed and present as an intracerebral hemorrhage. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**298. The answer is B.** This T2-weighted MRI image with contrast shows pachymeningeal enhancement and small, right greater than left, SDHs. These findings are characteristic of intracranial hypotension, either spontaneous or post dural puncture. This woman's headaches should be positional, severe when standing, and relieved when recumbent. The SDHs are not characteristic of meningitis or CVT, and CVT would not show the pachymeningeal enhancement. The meningeal signal abnormalities from dural metastatic disease would be less homogeneous. This is an abnormal MRI scan, not consistent with migraine headaches. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**299. The answer is B.** White matter lesions in CADASIL include bilateral, multifocal, T2/FLAIR hyperintensities in the deep white matter and periventricular WMLs involving the anterior temporal pole, external capsule, basal ganglia, and/or pons. The most specific neuroradiologic marker that differentiates CADASIL from ischemic leukoaraiosis is T2 hyperintensities in the anterior temporal pole. Arterial border zone lesions are consistent with ischemia, and lesions in the corpus callosum and optic nerves are much more common in MS than in CADASIL. Cerebellar infarcts are more characteristically seen in patients with migraine with aura. (Gladstone & Dodick, *Neurologist* 2005)

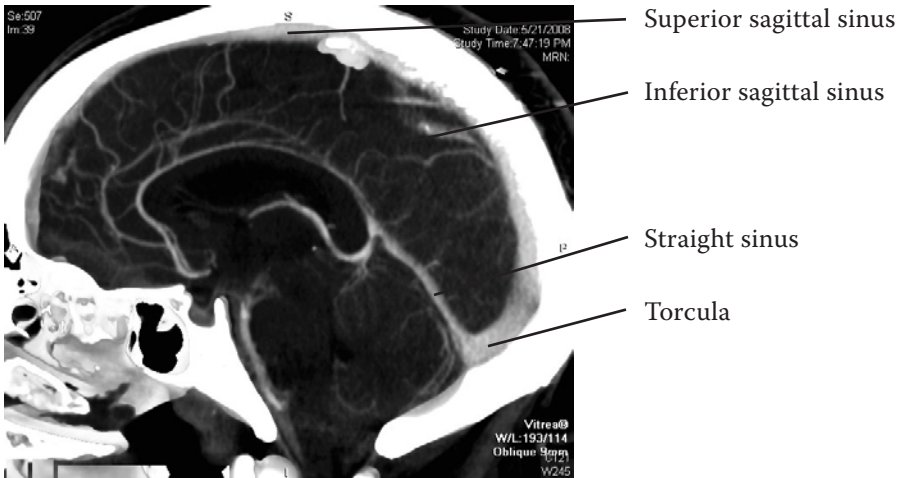
**300. The answer is C.** The spinal fluid in patients with pseudomigraine with lymphocytic pleocytosis, also known as HaNDL, shows characteristic pleocytosis with lymphocytic predominance; however, other abnormalities are noted as well. The opening pressure is increased in more than 50% of patients. Protein levels are increased in more than 90% of patients, but glucose levels are normal. Oligoclonal bands are generally absent. (Pascual & Valle, *Curr Pain Headache Rep* 2003)



**301. The answer is C.** Based on this man’s history, a SDH is more likely than a traumatic SAH or EDH. He could have sustained a traumatic vertebral artery dissection, but he does not complain of dizziness and gait imbalance to indicate a cerebellar infarct. The CT images show a SDH below the tentorium on the left. He did well without surgery, and the infratentorial SDH gradually resolved. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**302. The answer is B.** A normal CSF glucose-to-plasma ratio is usually around 65%, with an abnormal level considered to be <50%. In viral meningoencephalitis, there is usually a normal CSF glucose-to-plasma ratio. Tuberculous meningitis, rickettsial meningitis, bacterial meningitis, and fungal meningitis are all associated with decreased CSF glucose. However, tuberculous meningitis may be associated with very low CSF glucose, with a ratio <30% of plasma glucose. (Solomon, Hart, & Beeching, *Pract Neurol* 2007)

**303. The answer is A.** This is a normal CT venogram using multidetector-row CT angiography (MDCTA). MDCTA may be used to image cerebral arteries and veins when MRI is not available or contraindicated, but the study does require an iodinated contrast dye load that may be contraindicated with renal disease. CTV is fast and cost-effective in diagnosing CVT. In a small study comparing MDCTA with venous MRA, the sensitivity and specificity of MDCTA for the diagnosis of CVT were 100%. CTV may be used to screen for CVT, although its use in the diagnosis of more subtle venous abnormalities such as thrombosis of cortical veins, thrombosis of the cavernous sinus, and thrombosis of the internal cerebral veins is still unclear. (Linn, Ertl-Wagner, Seelos, et al., *AJNR* 2007; Agid, Shelef, Scott, et al., *Neurologist* 2008)



**304. The answer is A.** This woman has a benign clinical picture and a perimesencephalic (pretruncal) nonaneurysmal pattern of SAH on initial CT scans. This CT pattern is usually not associated with aneurysmal rupture; however, a ruptured posterior circulation aneurysm may present with a perimesencephalic SAH pattern in up to 10% of cases. A CT angiogram may be used to confirm the absence of an aneurysm in the circle of Willis with a typical perimesencephalic hemorrhage. Digital subtraction angiography can be performed in patients who have the characteristic perimesencephalic SAH pattern on admission CT scans. A repeat cerebral angiogram is not needed when the CT scan of the brain shows a probable venous source of SAH and the initial technologically satisfactory cerebral angiogram is negative. An MRI of the cervical spine may be performed to rule out the rare association with a cervical dural arteriovenous fistula. (Alén, Lagares, Lobato, et al., *J Neurosurg* 2003)

**305. The answer is E.** The clinical history is suggestive of subacute bacterial endocarditis with mild anemia and an elevated erythrocyte sedimentation rate (ESR). The diffusion-weighted images show multiple acute ischemic strokes in bilateral anterior and posterior arterial territories, consistent with a cardiac source of embolization. An echocardiogram showed vegetations on her mitral valve, and blood cultures grew out *Streptococcus viridians*. With 6 weeks of antibiotics she recovered completely. (Kanter & Hart, *Neurology* 1991)

**306. The answer is E.** This man was HIV positive, expanding the possible etiologies for his headache in association with multiple contrast-enhancing brain lesions. An infectious or neoplastic etiology should be considered in the evaluation of headache in an untreated HIV-infected individual, especially with low CD4 counts and discernible viral load. Embolic infarcts could result from bacterial endocarditis, arteritis, cocaine-induced vasospasm, or injected drug contaminants. Cerebral abscesses from multiple pathogens may be seen with HIV infection with intravenous drug abuse. Cerebral mass lesions, which may be single, but are more often multiple, are common with toxoplasmosis, cytomegalovirus infection, and CNS lymphoma. Cryptococcal infection is generally an encephal meningitis and rarely presents with multifocal mass lesions or cryptococcomas. (Thurnher & Donovan Post, *Neuroimaging Clin N Am* 2008)

**307. The answer is D.** The thalamic location of this intracerebral hemorrhage is characteristic of a patient with chronic untreated hypertension. Note the extravasation of blood into the right lateral ventricle. The CT scan does not show the lobar hemorrhage seen in elderly patients with cerebral amyloid angiopathy. This is not a SAH from a ruptured cerebral aneurysm. A thalamic AVM could

produce this hemorrhage, but in this man a hypertensive hemorrhage is more likely. The most common locations for hypertensive hemorrhage are the thalamus, basal ganglia, pons, and cerebellum. While lung cancer metastatic to the brain can hemorrhage, metastatic disease is more commonly seen at the grey-white junction than the thalamus. (Badjatia & Rosand, *Neurologist* 2005)

**308. The answer is E.** These FLAIR images show posterior WMLs of reversible vasogenic subcortical edema due to reversible posterior leukoencephalopathy syndrome (RPLS), also called posterior reversible encephalopathy syndrome (PRES). The patients with RPLS may have hypertension, pregnancy, renal disease, malignancy, or organ transplantation on immunosuppressive medications. Presenting symptoms, which generally last for days, include headache, seizures, encephalopathy, and visual symptoms. Although the MRI generally shows posterior (parieto-occipital) WMLs, there can also be brainstem, cerebellar, or frontal involvement on neuroimaging. Clinical recovery occurs in most patients within days, as the underlying hypertension or metabolic abnormality is corrected. (Lee, Wijedicks, Manno, et al., *Arch Neurol* 2008)

**309. The answer is D.** The diagnosis of HSV1 encephalitis should be based on the characteristic medical history, CSF analysis for pathogen identification by PCR amplification, serologic testing for HSV1 intrathecal antibody production, MRI, and EEG. Identification of HSV1 within the spinal fluid by PCR amplification is the most specific and sensitive method for diagnosing HSV1 encephalitis. Brain biopsy for pathological diagnosis should be reserved only for atypical or diagnostically difficult cases. Antiviral therapy, acyclovir, is used to treat herpes encephalitis, with treatment often started empirically, and length of treatment dictated by the PCR results. (Steiner, Budka, Chaudhuri, et al., *Eur J Neurol* 2005)

**310. The answer is C.** This sagittal MRI scan shows an unruptured fronto-parietal AVM discovered incidentally in a woman with migraine headaches. There is a prominent deep feeding vessel with a tightly packed mass of vessels and a draining vein. Aneurysms can be found on the arterial vessels. The T1-weighted contrasted image (see below) shows the prominent AVM. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

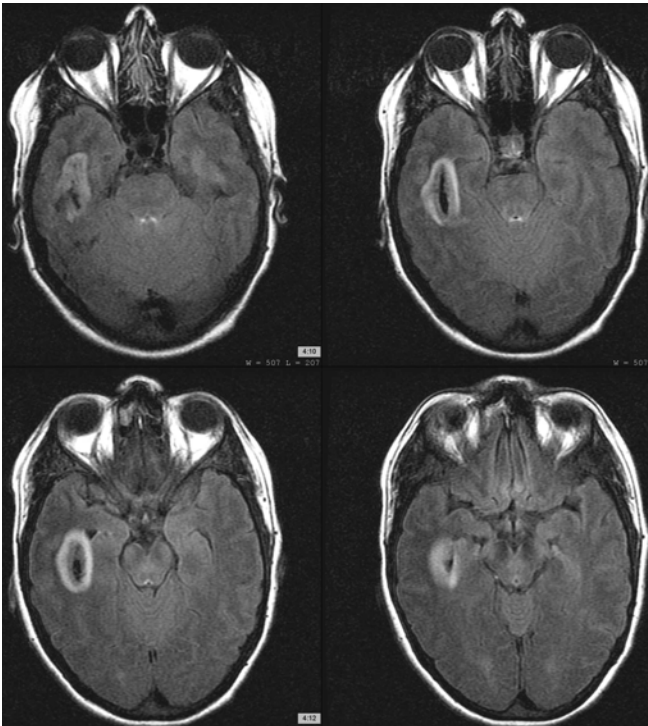


**311. The answer is B.** This sagittal image shows peg-like cerebellar tonsils protruding below the foramen magnum (Chiari type 1 malformation) and a congenital spinal fluid-filled cavity in the high to mid cervical spinal cord (cervical syrinx). The relation of this boy's headaches to his Chiari type 1 malformation and syrinx is not clear. Although a cavernous malformation may be found in the spinal cord, it does not show this homogeneous signal. A spinal cord infarct generally shows a less distinct, linear signal abnormality and is rare in the cervical spinal cord. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)



**312. The answer is C.** Meningeal diverticula (abnormal dilations of the nerve root sleeve) in the cervical and/or thoracic spine are found on spinal imaging in close to half of patients with spontaneous spinal CSF leaks and intracranial hypotension. Other imaging criteria for the diagnosis include pachymeningeal enhancement, sagging brain, and subdural fluid collections. (Schievink, Maya, Louy, et al., *AJNR* 2008)

**313. The answer is E.** This CT scan shows areas of hyperdensity and hypodensity in the right temporal lobe consistent with venous infarction and peri-infarct hemorrhage due to transverse sinus thrombosis. Dehydration, especially combined with other risk factors for venous thrombosis such as thrombophilias, infection, and hormonal changes, can precipitate thrombosis in the dural sinuses that drain blood from the brain. Headache may be a presenting symptom, followed by seizures, focal neurological deficits, or alteration in consciousness. Although the CT and MRI scans may show hemorrhage with CVT, intravenous anticoagulation is generally indicated to decrease the risk of propagation of the venous thrombus. Anticoagulation does risk further intracerebral hemorrhage. The MRI of the brain images of this patient are shown in the answer. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

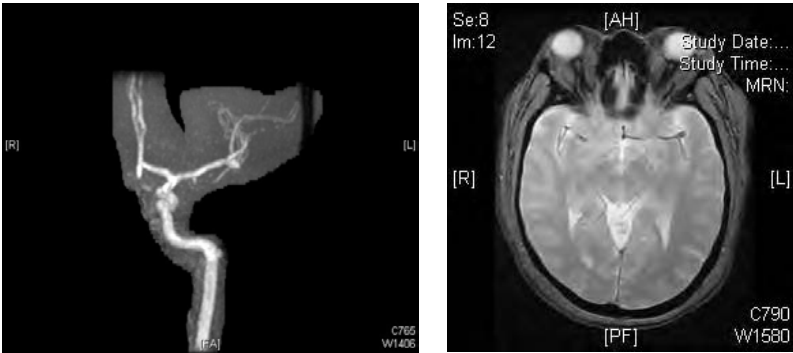


**314. The answer is D.** Headaches are a common complaint of emergency department (ED) patients, with the vast majority suffering from primary headaches, generally migraines. Migraineurs are four times more likely to visit the ED than nonmigraineurs. One study found that one in five migraineurs visited the ED in the past year. Many migraine patients visit the ED repetitively, which may indicate the lack of options for treatment, either acute or preventative, offered by outpatient practitioners. Narcotics, while commonly used to treat headaches in the ED, are rarely indicated for chronic use in the migraine patient. Subcutaneous or intranasal triptans are appropriate for the migraine patient in the ED and should be used as the mainstay of acute treatment in the ED. The misdiagnosis of migraine and the infrequent treatment with migraine-specific medication indicate the underutilization of neurological consultation for headache in the ED. (Sahai-Srivastava, Desai, & Zheng, *Headache* 2008)

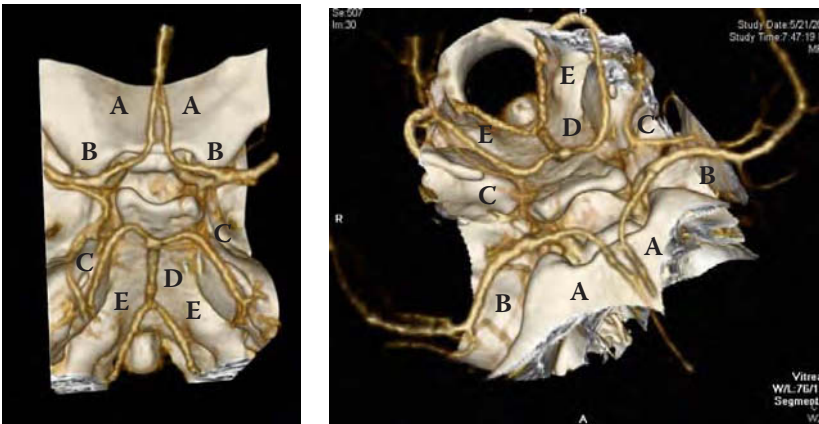
**315. The answer is C.** This immunosuppressed woman has cryptococcal meningitis presenting with headache and fever, with characteristic mononuclear cells in her spinal fluid and a decreased glucose. Bacterial meningitis is unlikely with her prolonged clinical course. Her clinical presentation is not consistent with neurosyphilis, and the absence of red cells and the decreased glucose level make a viral infection unlikely. Antibodies to N-methyl-D-aspartate (NMDA) receptor subunit NR<sub>2</sub> in the spinal fluid correlate with neuropsychiatric manifestations of systemic lupus erythematosus (SLE), but would not be diagnostic of this clinical picture. A study of patients with lupus with CNS infections found that lupus patients with cryptococcal infection generally presented with headache, fever, and vomiting. The mortality rate in these patients was about 40%. The diagnosis was made with spinal fluid examination using India ink and latex agglutination testing for cryptococcal antigen. (Hung, Ou, Lee, et al., *J Rheumatol* 2005)

**316. The answer is B.** This T2-weighted MRI scan of the brain shows an unruptured left middle cerebral artery aneurysm discovered incidentally in a man with migraine headaches. It measured approximately 5 × 7 mm. This incidental lesion could be followed by serial MRA or CTA studies or could be considered for surgical or endovascular obliteration. This unruptured aneurysm would not produce

headaches. The MRA of the left intracranial carotid artery [image below] shows the aneurysm at the bifurcation of the middle cerebral artery. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)



**317. The answer is E.** These CT angiography scans show normal vessels in the circle of Willis, which is characteristic of the vascular anatomy in patients with pretruncal (perimesencephalic) SAH. The CTA reconstructed images, as well as the source images, can delineate the vessel anatomy with precision close to the images seen with catheter angiography. The CTA study requires a larger dose of iodinated intravenous contrast dye, with a timed delivery through a large-bore intravenous needle, than does an ordinary contrasted CT scan. (Schellinger, Richter, Kohrmann, et al., *Cerebrovasc Dis* 2007)



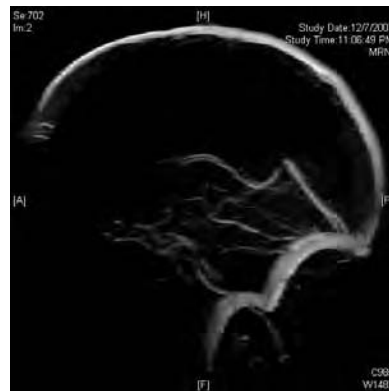
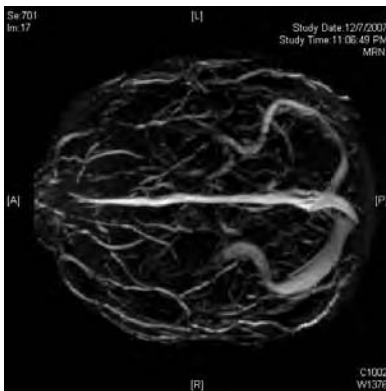
- A Anterior cerebral arteries
- B Middle cerebral arteries
- C Posterior cerebral arteries
- D Basilar artery
- E Vertebral arteries



**318. The answer is E.** Post-dural puncture headaches can be due to subdural fluid collections. Iatrogenic, or spontaneous, intracranial hypotension can cause headaches due to subdural fluid collections, hematomas, or hygromas. Cancer metastatic to the subdural space can hemorrhage. Drugs and supplements with anticoagulant and antiplatelet properties can cause spontaneous or post-traumatic subdural hematomas. (Lai, Fuh, Lirng, et al., *Cephalalgia* 2006)

**319. The answer is E.** In viral meningoencephalitis, a mild to moderate CSF pleocytosis of 5–1,000 cells/mm<sup>3</sup> with predominate lymphocytosis is usually present. Early in the infection, the CSF white cell count may be normal. Tuberculous meningitis, partially treated bacterial meningitis, and fungal meningitis are all also associated with CSF lymphocytosis. Acute bacterial meningitis is associated with a high (100–5,000 cells/mm<sup>3</sup>) white cell count with a neutrophilic predominance. (Solomon, Hart, & Beeching, *Pract Neurol* 2007)

**320. The answer is D.** This MRV study shows normal venous anatomy of the brain with the vessels as labeled. This man did not have elevated intracranial hypertension, either idiopathic or associated with CVT. This man was sent to an ophthalmologist, who diagnosed optic nerve head drusen, a generally benign condition. A vein of Galen malformation, an arteriovenous fistula involving the median prosencephalic vein, is found in infants with congestive heart failure. A dural venous fistula is associated with thrombosed dural sinuses. The normal MRI scan ruled out a parenchymal lesion such as an astrocytoma. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)





**321. The answer is A.** This teenager has migraine headaches with an incidental AVM. Depending on the location and characteristics, he should be evaluated with catheter angiography to establish his risk of intracerebral hemorrhage. Treatment with embolization, radiosurgery, or surgical excision may be appropriate, depending on the risk of the procedure relative to the risk of hemorrhage. The other lesions are seen not infrequently as incidental findings on neuroimaging, unrelated to headaches. Arachnoid and pineal cysts rarely deserve neurosurgical resection. Developmental venous anomalies do not cause symptomatic hemorrhage. Although cavernous malformations often show evidence of hemorrhage on MRI scan, their rate of symptomatic hemorrhage is low, and they are generally not resected when discovered incidentally. Incidental cavernous malformations may be associated with seizures, but they do not cause headaches. (Schwedt, Guo, & Rothner, *Headache* 2006)

**322. The answer is D.** The left vertebral artery is seen as a thread-like vessel off the left subclavian artery in these MRA images performed with gadolinium contrast. The other cervical vessels are intact. This man had a left vertebral artery dissection producing left-sided headache and focal neurological complaints. This man's clinical history is consistent with a vertebral artery dissection with uncertainty about causation due to neck movement from the automobile accident or from the chiropractic manipulation. Dissection of the arteries in the neck may present with headache, neck pain, and focal neurological complaints. A Horner's syndrome may be seen with carotid artery dissection. The arrows on the image below shows the dissected left vertebral artery. (Jensen, Chacon, & Aleu, *Neurologist* 2008)



**323. The answer is A 2, B 1, C 3, D 4, E 5.** All of these vascular lesions may be noted incidentally on MRI scans of the brain obtained because of headaches. An incidental AVM should be investigated for possible treatment because of its risk of symptomatic hemorrhage, although size and location of the AVM may preclude any intervention. Cavernous malformations, either sporadic or familial, may develop over time, whereas AVMs, developmental venous anomalies (DVAs), and capillary telangiectasias are considered to be congenital. Capillary telangiectasias may be found incidentally on autopsy and rarely present with symptomatic hemorrhage. They occur with other vascular malformations in the brain, lung, skin, and mucous membranes as part of autosomal dominant Osler-Weber-Rendu (hereditary hemorrhagic telangiectasia syndrome). Dural arteriovenous fistula may be found in a patient with objective pulsatile tinnitus. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**324. The answer is D.** White matter lesions (WMLs) are best seen as hyperintensities on T2-weighted or FLAIR MRI sequences. When noted, with varying prevalence, in asymptomatic individuals, their clinical significance is unclear. They may be nonspecific or caused by ischemia, demyelination, or gliosis. Deep WMLs indicate increased ischemic or demyelinating disease risk, as compared to periventricular WMLs. In clinically asymptomatic individuals, the reported prevalence ranges from 20% to 60% for deep WMLs and from 15% to 94% for periventricular WMLs. Hyperintense periventricular changes may be due disruption of the ependymal lining, subependymal gliosis, and myelin loss. Small lesions in the deep and subcortical white matter may corresponded to perivascular reduction in myelin content with thickened arteriolar walls. Larger and confluent white matter hyperintensities appear to indicate more extensive ischemic or demyelinating pathology. (Cutrer & Black, *Headache* 2006; Fazekas, Schmidt, Kleinert, et al., *J Neural Transm Suppl* 1998)

**325. The answer is B.** There is caudal protrusion of the cerebellar tonsils below the foramen magnum. In an adult with Chiari type 1 malformation, the tonsils lie  $\geq 5$  mm below the foramen magnum. In this patient, the protrusion was about 8 mm. (See another sagittal section below.) Generally, a Chiari type 1 malformation is an incidental asymptomatic finding on MRI. Surgical treatment is controversial. A Chiari type 2 malformation has cerebellar tonsillar herniation associated with a neural tube closure defect (i.e., a lumbar myelomeningocele). A Chiari type 3 malformation includes a high cervical or occipital meningoencephalocele. This

image does not show pachymeningeal enhancement or a syrinx. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)



**326. The answer is A.** Although varicella zoster virus (VZV) may be detected in skin lesions using PCR, viral culture, immunofluorescence, electron microscopy, or Tzanck stain, about half of patients with VZV meningitis have no skin manifestations, and the diagnosis should be made by PCR testing of the spinal fluid. Meningitis may be a complication of primary VZV infections, but it is more commonly associated with reactivation of the virus. (Logan & MacMahon, *BMJ* 2008)

**327. The answer is D.** This young boy had minor head trauma with a lucid interval followed by severe cerebral edema and coma (“delayed cerebral edema”). He was not known to have migraine headaches. Minor head trauma can lead to attacks of familial hemiplegic migraine type 1 (FHM1) in patients with a mutation in the CACNA1A gene. They can deteriorate to a potentially fatal coma. A C-to-T substitution resulting in the substitution of serine for lysine at codon 218 (S218L) in the CACNA1A calcium channel subunit gene on chromosome 19 is associated with potentially fatal coma after trivial head trauma. Neuropathologic examination in one subject with FHM1 after fatal minor head trauma showed Purkinje cell loss with relative preservation of granule cells and sparing of the dentate and inferior olivary nuclei. (Kors, Terwindt, Vermeulen, et al., *Ann Neurol* 2001)

**328. The answer is E.** The issue of neuroimaging of patients with primary headaches is controversial; however, migraine headaches can be diagnosed with confidence without neuroimaging. Other primary headache types, such as hemicranias and trigeminal autonomic cephalgias (TACs), may warrant neuroimaging if the diagnosis is uncertain by clinical criteria. Trigeminal autonomic cephalgias include cluster headache (CH), paroxysmal hemicrania and short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). Al-

though TACs, as primary headaches, are by definition not associated with an anatomic abnormality, an underlying lesion can cause even clinically typical TACs. Neuroimaging in patients with a TAC-like syndrome may reveal a lesion that may change management. (Favier, van Vliet, Roon, et al., *Arch Neurol* 2007)

**329. The answer is D.** Visualization of the cerebral venous system appears to be about equivalent using CTV and non-contrast enhanced MRV. Contrast-enhanced MRV appears to be best at noninvasive visualization of cerebral venous structures. IIH may be associated with narrowing of cerebral venous structures (e.g., distal transverse sinuses) on contrast-enhanced MRV. This correlation between abnormal distal transverse sinuses and IIH may be secondary to elevated intracranial pressure, as normalization of venous sinus anatomy has been noted with resolution of IIH. (Agid, Shelef, Scott, et al., *Neurologist* 2008)

**330. The answer is B.** Developmental venous anomalies (previously known as venous angiomas) are the most common cerebral vascular malformation, occurring in approximately 4% of the population. They are composed of dilated veins separated by normal brain tissue. They are an incidental finding in patients with headaches and do not warrant any treatment. This characteristic MRI picture of a DVA shows a group of radiating, linear flow voids (a “caput medusa”) centered on a large collecting vein. Cavernous malformations (called “cavernomas” by clinicians, “cavernous malformations” by radiologists, or “cavernous hemangiomas” by pathologists) are composed of well-circumscribed sinusoidal vascular channels containing blood and blood products. They are angiographically occult lesions that are best diagnosed on MRI, appearing as well-defined, lobulated (“pop-corn”) lesions with a heterogeneous signal. Cavernous malformations are also incidental findings in a patient with a primary headache but can cause mass effect with hemorrhage. A capillary telangiectasia is composed of dilated capillary-type blood vessels, separated by normal brain parenchyma. These lesions are generally found incidentally and rarely if ever hemorrhage. The variably sized blood vessels in an AVM are separated by normal brain parenchyma. When an AVM is discovered incidentally on an MRI scan of a patient with headaches, the appropriate intervention depends on the specific characteristics of the lesion and the patient. (Rivera, Willinsky, & Porter, *Neuroimag Clin N Am* 2003; Grahm & Lantos, *Greenfield’s Neuropathy*, Chapter 6)

**331. The answer is E.** Although the most common clinical manifestations of CADASIL are migraine headaches, ischemic episodes, cognitive deficits, and psychiatric disorders, the phenotypic spectrum is highly variable. Seizures have been described in up to 10% of patients with CADASIL. Evidence of myocardial

infarction (MI) has been found in about a quarter of patients in one study of patients with CADASIL. There have been isolated cases of CADASIL coma with episodes of migraine, prolonged aura, and fever accompanied by decreased level of consciousness or coma. (Gladstone & Dodick, *Neurologist* 2005)

**332. The answer is C.** A Chiari type 2 malformation, a hindbrain malformation, is associated with a neural tube defect, usually a lumbar myelomeningocele, diagnosed on an MRI of the lumbar spine. Brain imaging shows a small posterior fossa with cerebellar tissue, including the vermis, herniating through the foramen magnum, causing elongation of the fourth ventricle. Chiari malformations would not show a specific abnormality on transcranial Doppler (TCD), carotid ultrasonography, or a CT of the chest/abdomen/pelvis. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**333. The answer is C.** A spinal CSF leak causes intracranial hypotension in patients who have positional headache, low CSF opening pressure, and diffuse pachymeningeal enhancement on brain MRI. Radioisotope cisternography (RIC) or MR myelography (MRM) can detect the leakage site in the spine. MRM using heavily T2-weighted fast-spin echo imaging with fat suppression is noninvasive and does not use ionizing radiation or intrathecal contrast material. The image may be degraded by artifacts from motion, CSF pulsatile flow, paravertebral veins, or fat. (Yoo, Kim, Choi, et al., *AJNR* 2008)

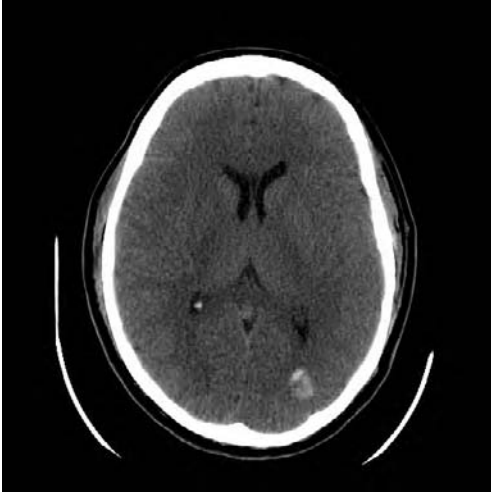
**334. The answer is A.** Tolosa-Hunt syndrome (THS) is a painful ophthalmoplegia due to idiopathic granulomatous inflammation in the region of the cavernous sinus and/or superior orbital fissure. The diagnostic criteria for THS specify that granuloma formation, demonstrated by MRI or tissue biopsy, is required for diagnosis. A review of the literature of 124 cases of clinical THS published from 1988 to 2002, found that 35% of cases had evidence of inflammation on MRI or granuloma formation on biopsy. In 33% of cases neuroimaging was normal. THS was secondary, not idiopathic, in 31% of cases in which a specific lesion was found. Positive glial fibrillary acidic protein (GFAP) staining is seen in intraparenchymal glial tissue. Lewy bodies are found in the substantia nigra of patients with Parkinson's disease. Brain tissue necrosis is nonspecific, found in a multitude of brain disorders. (La Mantia, Curone, Rapoport, et al., *Cephalalgia* 2006)

**335. The answer is A.** A familial predilection may occur in approximately 10% of patients with cerebral aneurysms. Familial cerebral aneurysms tend to be larger at time of rupture and are more likely to be multiple. Specific genetic disorders, such as polycystic kidney disease, are associated with a familial predilection for cerebral aneurysms. SAH is a common cause of death in patients with autosomal dominant polycystic kidney disease. However, the proportion of patients with polycystic kidney disease among all patients with SAH is very small. Less than 0.5% of cases of SAH are associated with polycystic kidney disease. A study of the correlation in 1,147 patients with aneurysmal SAH (mean age 53 years; 65.5% women) found that 5 (0.44%) had polycystic kidney disease. Compared with data on patients without polycystic kidney disease, SAH in patients with polycystic kidney disease occurs at an earlier age and more often in men. In patients with polycystic kidney disease, the most frequent site of aneurysms is the middle cerebral artery. (Gieteling & Rinkel, *J Neurol* 2003)

**336. The answer is C.** This toddler has a headache, fever, seizure, and unilateral weakness after a skull fracture. A repeat CT scan showed a right subdural empyema (SDE), an infected extracerebral collection in children and adults. SDE was associated with otorhinolaryngeal infections, head trauma, or surgery in a study of pediatric patients. Clinical manifestations of SDE include headache, fever, seizures, and focal neurologic signs. The most common pathogens in children include *Streptococcus pneumoniae*, group B *Streptococcus*, *Haemophilus influenzae* type B, *Salmonella*, *Escherichia coli*, and *Pseudomonas aeruginosa*. If a lumbar puncture is deemed safe, CSF analysis shows elevated white count and protein with decreased glucose levels. (Wu, Chiu, & Huang, *J Microbiol Immunol Infect* 2008)

**337. The answer is B.** These two MRI images of the brain show a cavernous malformation, a lesion with abnormally enlarged capillary cavities without intervening brain parenchyma that can be found in the brain, brainstem, or spinal cord. Cavernous malformations represent 10–20% of cerebral vascular lesions and are found in 0.1–0.5% of the population. They can be single or multiple, sporadic or dominantly inherited. They may present with intraparenchymal hemorrhage or seizures. When noted in neuroimaging on patients with headaches, cavernous malformations are usually an incidental, unrelated finding. Although the lesions are easily identified on MRI, they are occult on angiography. The image in

the answer shows a cavernous malformation on a CT scan. (Rivera, Willinsky, & Porter, *Neuroimag Clin N Am* 2003; Grahm & Lantos, *Greenfield's Neuropathology*, Chapter 6)



**338. The answer is B.** Changes in net translational movement of water across neuronal membranes (cytotoxic edema) is responsible for the increased DWI signal intensity seen in acute ischemia. The increased signal intensity on DWI may appear within minutes of the onset of stroke symptoms and may persist for up to a couple weeks. The apparent diffusion coefficients (ADC) in the ischemic area are decreased with decreased signal intensity on ADC mapping, corresponding to the increased signal on DWI. A subacute ischemic lesion may be seen on FLAIR imaging as the DWI lesion becomes less apparent. Perfusion-weighted imaging (PWI) uses a MR contrast injection to evaluate three hemodynamic parameters (relative cerebral blood flow, relative cerebral blood volume and mean transit time) that are disrupted with alterations in cerebral blood flow. DWI combined with PWI and MRA may eventually be used to select appropriate (small DWI lesion but large PWI defect) or unsuitable (very large DWI lesion, no PWI defect) patients for thrombolytic treatment. The limited availability of an MRI scanner, the prolonged time to complete the multiple magnetic resonance studies and the need to rule out metal within the body may limit the current usefulness of this technique in triaging patients with acute ischemic stroke. Changes in PWI (decreased blood flow and blood volume and increased mean transit time) have been found in migraineurs with aura. Cortical spreading depression has been associated with increased DWI signal and reduced ADC. Gradient recalled echo (GRE) pulse sequences detect the paramagnetic effects of deoxyhemoglobin and



methemoglobin in intraparenchymal hemorrhage. (Heiss, Sobesky, & Hesselmann, *Stroke* 2004; Cutrer & Black, *Headache* 2006)

**339. The answer is A.** Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is characterized by a dense granular osmiophilic material (GOM) found in the basal lamina of the vascular smooth muscle cells, seen on electron microscopic study of the skin. An electron microscopic study of skin biopsies in patients with CADASIL found a relative absence of vascular stenosis, but marked destruction of smooth muscle cells, resulting in decreased vessel wall thickness and loss of extracellular matrix area, producing vessel wall weakness. Similar changes have been observed in brain arterioles from patients with CADASIL. Blood vessel morphology of skin vessels correlated well with changes in brain arterioles. (Brulin, Godfraind, Leteurtre, et al., *Acta Neuropathol* 2002)

**340. The answer is E.** This woman has an autosomal dominantly inherited constellation of abnormalities described in 1985 by Stormorken et al. An abdominal CT scan showed absence of a spleen, characteristic of patients with Stormorken syndrome. These patients have thrombocytopathia with nasal and conjunctival bleeding, miosis, muscular fatigue, spasms, asplenia, ichthyosis, dyslexia, and headaches. Headaches in families with Stormorken syndrome have migraine or tension-type characteristics. The thrombocytopathia in this disorder is associated with abnormal serotonin storage, uptake, and release. (Sjaastad, *Headache* 1994; Stormorken, Sjaastad, Langslet, et al., *Clin Genet* 1985)

**341. The answer is C.** Severe claustrophobia, ferromagnetic foreign bodies, implanted electronic devices (e.g., pacemakers, cochlear implants, some mechanical valves), and severe renal disease are contraindications to magnetic resonance cerebral venography with intravenous gadolinium contrast. However two-dimensional time-of-flight and two- and three-dimensional phase contrast MRV do not require gadolinium, so these techniques do not risk nephrogenic systemic fibrosis in patients with renal disease. Visualization of intracranial venous structures and time-of-image acquisition are much improved with gadolinium-enhanced MRV in patients for whom the magnetic imaging with contrast is appropriate. (Agid, Shelef, Scott, et al., *Neurologist* 2008)

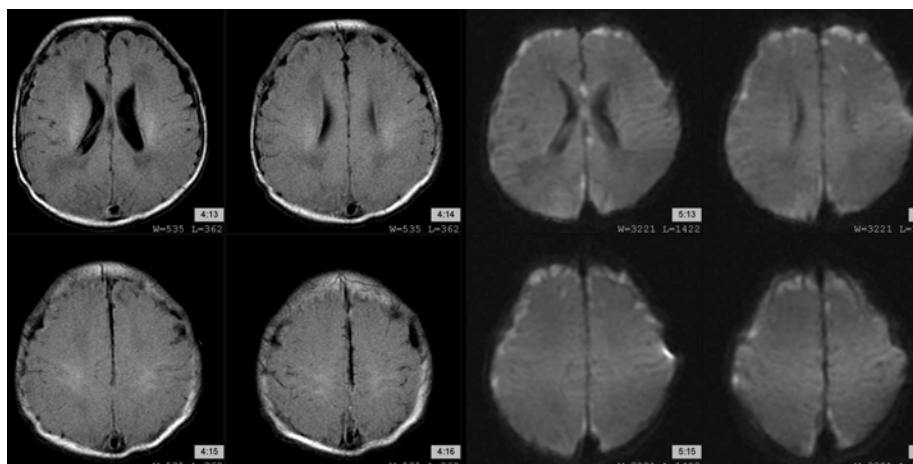
**342. The answer is D.** This woman has viral meningitis by spinal fluid profile, although spinal fluid cultures and PCR could be sent to confirm the diagnosis. In children and adults, the most common cause of viral meningitis are enteroviruses, such as Coxsackie A and B viruses and echovirus. Most cases of enterovi-



rus infection are self-limited with a good prognosis; symptomatic treatment with fluids and antipyretic is indicated. Herpes simplex virus is the second most common cause of viral meningitis in adolescents and adults in developed countries, developing as a complication of a genital herpes (type 2) infection. This healthy woman is unlikely to have a neoplastic cause for her mild meningitic symptoms without cranial nerve involvement. She is not systemically ill, with findings consistent with a basilar, infiltrating tuberculous meningitis. However, if she were HIV positive, tuberculous meningitis should have been considered. (Logan & MacMahon, *BMJ* 2008)

**343. The answer is E.** Multiple radiologic techniques can be used to diagnose a spinal CSF leak, although the presence of extrathecal CSF confirms the diagnosis. Early appearance of contrast in the kidney on CT myelography and early uptake of isotope in the bladder and kidneys on radionuclide cisternography are indirect indicators of a spinal CSF leak. Subdural fluid collection, sagging of the brain, and enhancement of the pachymeninges are characteristically found on cranial MR imaging in patients with spontaneous, and occasionally post dural puncture, intracranial hypotension. (Schievink, Maya, Louy, et al., *AJNR* 2008)

**344. The answer is B.** This axial T1-contrasted image on MRI scan of the brain of a young child shows leptomeningeal inflammation due to group B streptococcus meningitis. The images in the answer show hyperintense signal in the sulci on axial FLAIR (*left image*) and perimeningeal restriction on axial DWI imaging (*right*). (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)



**345. The answer is D.** Patients with suspected CADASIL have mutations in the Notch3 gene on chromosome 19q13. The Notch 3 gene encodes a 2,321-amino acid transmembrane receptor that functions in signaling pathways essential for the maturation of blood vessels in fetal and adult brain. Genetic screening of 23 exons has a high sensitivity and specificity for the diagnosis. Skin and muscle biopsy may show characteristic granular osmiophilic material (GOM) on electron microscopy, and the tissue may be stained with monoclonal antibodies to Notch3 protein. Brain or liver biopsy is not necessary to make the diagnosis. Angiography should be avoided in patients with CADASIL because of a potentially deleterious effect of the contrast agents. (Gladstone & Dodick, *Neurologist* 2005)

**346. The answer is C.** This MRI image with GRE sequence shows multiple hypointense lesions consistent with microhemorrhage from familial cavernous malformations. This image could be consistent with microhemorrhages from cerebral amyloid angiopathy in an elderly person. Melanoma metastatic to the brain could show evidence of hemorrhage on GRE sequence, but this many lesions in a healthy individual makes that diagnosis unlikely. These lesions are small and multifocal, not consistent with an AVM. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**347. The answer is E.** Viral meningitis, partially treated bacterial meningitis, tuberculous meningitis, and cryptococcal meningitis are all associated with a mononuclear pleocytosis in the spinal fluid. However, early in the course of viral meningitis, there may be a predominance of neutrophils in the spinal fluid. Bacterial meningitis is generally associated with a neutrophilic predominance, but mononuclear cells may be seen in the spinal fluid as bacterial meningitis is being treated with antibiotics. (Logan & MacMahon, *BMJ* 2008)

**348. The answer is D.** A study evaluating patients with presumed IIH found that about 10% had unsuspected cerebral venous sinus thrombosis (CVST). Patients with papilledema, but without space-occupying lesions, hydrocephalus, or meningitis, were evaluated with lumbar puncture, MRI, and MRV. Based on the evaluation, CVST was diagnosed in 10 (9.4%) of 106 patients with presumed IIH, and it was suspected in two additional patients. Cerebral venous sinus thrombosis was diagnosed in one of the 10 patients with MRI alone, but it was detected in all 10 patients with MRV. The authors recommended MRV in combination with MRI to identify CVST in patients with suspected IIH. (Lin, Foroozan, Danesh-Meyer, et al., *Ophthalmology* 2006)

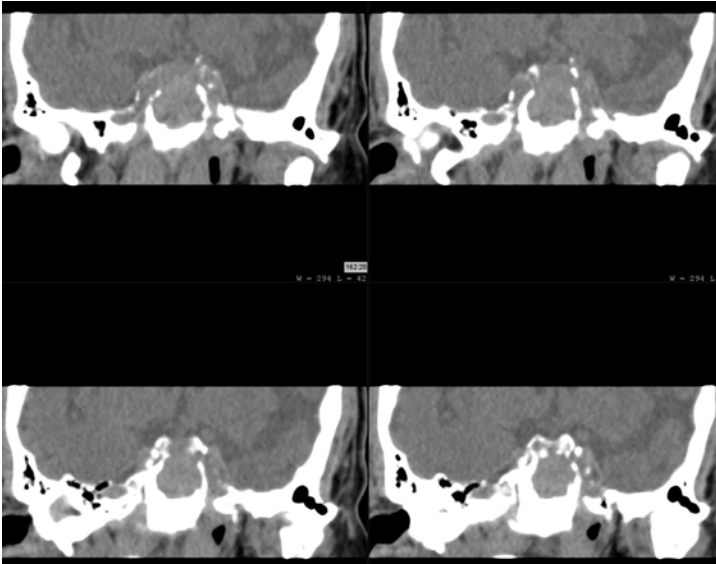
**349. The answer is D.** These images show the medial temporal lesion (most prominent on the left) characteristic of HSV1 encephalitis on both the CT scan and the MRI FLAIR images. Temporal lobe lesions are also seen with limbic encephalitis, other types of viral encephalitis, neurosyphilis, ischemia, or infiltrating neoplasms. FLAIR signal abnormalities and enhancement may be seen due to blood–brain barrier disruption with active seizures. This woman needs to have spinal fluid analysis for HSV1 PCR, as well as EEG to rule out nonconvulsive continuous temporal lobe seizures. Treatment with intravenous acyclovir should be started when the diagnosis is suspected, with decision to continue it made after the PCR results are known. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**350. The answer is E.** A small arachnoid cyst is seen at the temporal tip in the left middle cranial fossa. This is an intra-arachnoid, spinal fluid-filled cyst that does not communicate with the ventricular system. It is a common incidental finding on imaging studies obtained for headaches. These cysts can be found at any age, and are more common in men than in women. They are to be differentiated from other non-neoplastic cysts and subdural fluid collections. In this case, there is no need for any treatment for this incidental, stable lesion. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

**351. The answer is E.** This woman has acromegaly, with growth of her hands and fingers, coarsening of her facial features, and obstructive sleep apnea (OSA). She has headaches, which is common in acromegalics who note lateralized or global headaches that can mimic multiple primary headache types. Her brain MRI showed a pituitary adenoma, and blood work revealed elevated growth hormone. Her headaches resolved when she was treated with a parenteral long-acting somatostatin analogue, but constriction of her bitemporal visual fields was noted. She underwent a transsphenoidal resection of the adenoma but unfortunately developed a rare complication, panhypopituitarism, as well as the more common complication of a persistent CSF leak with an intracranial hypotension headache. (Levy, *J Neurol Neurosurg Psychiatry* 2004)

**352. The answer is E.** This MRI shows a mucocele in the sphenoid sinus, the rarest (<5%) location for sinus mucoceles, which are most often found in the frontal and ethmoid sinuses. A sinus mucocele is lined by the mucous-secreting epithelium of a paranasal sinus. It occurs when a sinus opening or compartment of a septated sinus becomes obstructed and the sinus cavity becomes mucous-filled and airless. Symptoms and signs include frontal headache, visual loss, and palsies of CN III and CN VI. Tumor infiltration of the sphenoid sinus may present in association with a mucocele or with a similar radiologic picture. The coronal

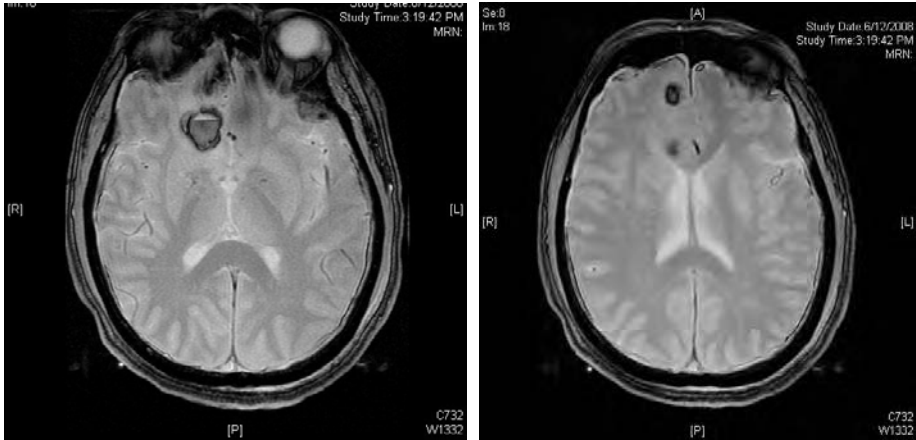
CT scan in this patient shows a homogeneous, hypodense mass that expands the sinus cavity. (Kösling, , Hintner, Brandt, et al., *Eur J Radiol* 2004)



**353. The answer is C.** The MRI images show changes characteristic of posterior reversible encephalopathy syndrome (PRES) in a woman with HELLP syndrome, a variant of preeclampsia characterized by *Hemolysis, Elevated Liver enzyme levels and a Low Platelet count*. Edema involving the white matter of the posterior portions of both cerebral hemispheres is present, especially in the parieto-occipital regions, in a relatively symmetric pattern. Most lesions in PRES are in the subcortical white matter, but lesions can be seen in the brainstem and cerebellum. The frontal and temporal cortices and the basal ganglia may also be involved. The lack of corresponding, distinct lesions on DWI would rule out acute arterial or venous infarcts. Although cortical ribboning on FLAIR can be seen with acute seizures, the lesions in this case are very prominent. Herpes simplex encephalitis lesions are characteristically in one or both mesial temporal lobes. (Bartynski, *AJNR* 2008)

**354. The answer is C.** This man has a headache due to severe head trauma. These CT scan images show a parenchymal hemorrhagic traumatic contusion in the inferior right frontal lobe with surrounding vasogenic edema and mass effect. Multifocal bilateral SAHs are present, including in the cerebral convexities. There are small, left greater than right, frontal convexity SDHs. This man's CT scan shows the effect of trauma to the back of his head. He had a left occipital skull

fracture with a scalp hematoma and contrecoup right frontal lobe contusions. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)



**355. The answer is D.** This man's CT scan shows diffuse subarachnoid blood, including along the medial aspect of the left temporal lobe and the ventral surface of the brainstem. He suffered severe head trauma, with parenchymal contusions and SDHs seen on CT and MRI scans. (Osborn, Blaser, Salzman, et al., *Diagnostic Imaging* 2004)

# 5

## HEADACHE TREATMENT QUESTIONS

- 356.** According to the Spectrum Study, treatment with a triptan:
- A. Is effective for tension-type headaches (TTHs) in patients with migraine headaches.
  - B. Is effective for TTHs in patients without migraine headaches.
  - C. Is not effective for migrainous headache in patients with migraine headaches.
  - D. Is never effective for TTHs.
  - E. Is only effective for migraine and migrainous headaches.
- 357.** Which medication is the preventative drug of choice for both episodic and chronic cluster headache (CHs)?
- A. Verapamil (Calan<sup>®</sup>)
  - B. Lithium
  - C. Indomethacin (Indocin<sup>®</sup>)
  - D. Lamotrigine (Lamictal<sup>®</sup>)
  - E. Gabapentin (Neurontin<sup>®</sup>)
- 358.** Which of the following statements best describes the care of migraine patients?
- A. The majority of migraine care is provided by neurologists.
  - B. Less than a third of migraineurs are very satisfied with their usual acute treatment.
  - C. The vast majority of people with migraine have been appropriately diagnosed.
  - D. The vast majority of migraineurs are treated with migraine-specific medication.
  - E. Most people with migraine seek medical consultation specifically for their headaches.

**359.** Match the cause of episodic unilateral facial pain with its most effective preventative pharmacologic therapy. Each answer may be used once, more than once, or not at all.

- |   |   |
|---|---|
| A. Cluster headache (CH)  | 1. Lamotrigine (Lamictal)                 |
| B. Paroxysmal hemicrania (PH)   | 2. Indomethacin (Indocin)                 |
| C. Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) | 3. Verapamil (Calan)                      |
| D. Trigeminal neuralgia   | 4. Carbamazepine (Tegretol <sup>®</sup> ) |
| E. Hemicrania continua  | 5. Phenytoin (Dilantin <sup>®</sup> )     |

**360.** Which of the following medications is approved by the U.S. Food and Drug Administration (FDA) for the treatment of fibromyalgia?

- A. Gabapentin (Neurontin)
- B. Pregabalin (Lyrica<sup>®</sup>)
- C. Intravenous (IV) immunoglobulin
- D. Oxcarbazepine (Trileptal<sup>®</sup>)
- E. Nortriptyline (Pamelor<sup>®</sup>)

**361.** Which of the following available treatments is the best short-term prevention for CHs?

- A. Steroids
- B. Injectable sumatriptan (Imitrex<sup>®</sup>)
- C. Oxygen inhalation
- D. Intranasal lidocaine
- E. Methysergide (Sansert<sup>®</sup>)

**362.** Which triptan has the longest plasma elimination half-life?

- A. Naratriptan (Amerge<sup>®</sup>)
- B. Sumatriptan (Imitrex<sup>®</sup>)
- C. Rizatriptan (Maxalt<sup>®</sup>)
- D. Frovatriptan (Frova<sup>®</sup>)
- E. Almotriptan (Axert<sup>®</sup>)

**363.** Renal stones have been associated with which medication used to prevent migraine headaches?

- A. Divalproex sodium (Depakote<sup>®</sup>)
- B. Topiramate (Topamax<sup>®</sup>)
- C. Propranolol (Inderal<sup>®</sup>)
- D. Verapamil (Calan)
- E. Magnesium

**364.** Which one of the following medications has the highest level of recommendation for the acute treatment of migraine headaches in children?

- A. Ibuprofen
- B. Acetaminophen
- C. Intranasal sumatriptan (Imitrex)
- D. Subcutaneous sumatriptan
- E. Oral rizatriptan (Maxalt)

**365.** Which of the following primary headache disorders characteristically responds to preventative treatment with indomethacin (Indocin)?

- A. Paroxysmal hemicrania (PH)
- B. Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA)
- C. SUNCTC
- D. Cluster headache (CH)
- E. Migraine without aura

**366.** A 50-year-old man noted 3 days of right leg pain that increased while walking. On examination, his right leg was cool and pale. He had been taking a caffeine–ergotamine combination preparation for several years for chronic headaches. As an astute clinician, you suspect a drug interaction. Which of his other medications is the probable culprit?

- A. Clarithromycin (Biaxin<sup>®</sup>)
- B. Atorvastatin (Lipitor<sup>®</sup>)
- C. Clopidogrel (Plavix<sup>®</sup>)
- D. Ramipril (Altace<sup>®</sup>)
- E. Propranolol (Inderal)

**367.** Which one of the following medications is a proven efficacious agent, available in the United States, for the preventative treatment of migraine headaches in children?

- A. Propranolol (Inderal)
- B. Flunarizine
- C. Cyproheptadine (Periactin<sup>®</sup>)
- D. Divalproex sodium (Depakote)
- E. None of the above



**368.** Match the triptan with a description of its delivery systems. Each answer may be used once, multiple times, or not at all.

- |                          |   |
|--------------------------|---|
| A. Zolmitriptan (Zomig)  | 1. Oral dissolving tablet, swallowed tablet only              |
| B. Sumatriptan (Imitrex) | 2. Swallowed tablet, oral dissolving tablet, intranasal spray |
| C. Rizatriptan (Maxalt)  | 3. Subcutaneous injection, swallowed tablet, intranasal spray |
| D. Almotriptan (Axert)   | 4. Swallowed tablet only                                      |
| E. Eletriptan (Relpax)   |   |

**369.** A 30-year-old woman with chronic migraines reports vivid and sometimes disturbing dreams. You want to prescribe a preventative medication for her headaches. Which preventative medication for migraines could worsen her dreams?

- A. Nortriptyline (Pamelor)
- B. Propranolol (Inderal)
- C. Paroxetine (Paxil)
- D. Fluoxetine (Prozac)
- E. All of the above

**370.** A 50-year-old woman with hypertension and elevated total cholesterol has had a long history of episodic migraine. Her blood pressure is chronically elevated, and she complies only intermittently with antihypertensive therapy. She had a small-vessel cerebral infarct 3 years ago, from which she had excellent recovery. She asked you for injectable sumatriptan (Imitrex) for her severe migraines, which occur about 15 days a month. What do you do?

- A. You suggest that she try a long-acting triptan because of the frequency of her headaches.
- B. You discuss the use of a daily preventative medication to decrease her need for acute therapy.
- C. You suggest that she try a short-acting triptan, warning her not to use more than two or three doses a week.
- D. You give her a butalbital/acetaminophen/caffeine preparation to take whenever she has head pain, up to 10 doses a week.
- E. You tell her that her headaches will go away eventually and that she can use the combination aspirin/acetaminophen/caffeine up to four to five doses daily.

**371.** The benefit of acupuncture in decreasing migraine attacks:

- A. Correlates with treatment at specific points.
- B. Has been proven to be of benefit in children.
- C. Correlates with a decrease in total headache days.
- D. Only is of benefit when the procedure is painful.
- E. May be related to the placebo effect of the treatment.

**372.** Which of the following patients is likely to have a poor outcome from behavioral management of tension-type headaches (TTHs) with stress management biofeedback and other nonpharmacological treatments, using minimal contact treatment formats?

- A. Younger patients
- B. Patients with chronic daily severe headache
- C. Patients with episodic headaches
- D. Patients without personality disorders
- E. Patients with a college education

**373.** Which of the following oral agents has been shown to be most effective in preventing attacks of short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)?

- A. Gabapentin (Neurontin)
- B. Indomethacin (Indocin)
- C. Carbamazepine (Tegretol)
- D. Lamotrigine (Lamictal)
- E. Pregabalin (Lyrica)

**374.** Which of the following medications is the first choice for a patient with trigeminal neuralgia?

- A. Gabapentin (Neurontin)
- B. Phenytoin (Dilantin)
- C. Baclofen (Lioresal)
- D. Lamotrigine (Lamictal)
- E. Carbamazepine (Tegretol)

**375.** Daily medications used to decrease the frequency and severity of chronic headaches may have other beneficial properties. Alternatively, some side effects may be more bothersome than others. Pick a preventative medication that would be most appropriate for the patients with headaches listed below. A medication may be used once, more than once, or not at all.

- |   |                                 |
|---|---------------------------------|
| A. A cheerful nurse with a familial tremor.                           | 1. Propranolol (Inderal)        |
| B. An obese litigator for medical malpractice plaintiffs.             | 2. Topiramate (Topamax)         |
| C. An anxious violinist trying to find a job with an orchestra.       | 3. Verapamil (Calan)            |
| D. A depressed thin cab driver with insomnia and a receding hairline. | 4. Divalproex sodium (Depakote) |
| E. A hypertensive marathoner with frequent diarrhea.                  | 5. Amitriptyline (Elavil)       |

**376.** Which preventative medication gives the most rapid relief of CH?

- A. Verapamil (Calan)
- B. Lithium
- C. Indomethacin (Indocin)
- D. Corticosteroids
- E. Gabapentin (Neurontin)

**377.** Match the medication used for prevention of chronic headaches with the potential fetal complication if used during pregnancy. Each answer may be used once, more than once, or not at all.

- |                           |                                    |
|---------------------------|------------------------------------|
| A. Propranolol (Inderal)  | 1. Intrauterine growth retardation |
| B. Topiramate (Topamax)   | 2. Spina bifida                    |
| C. Lisinopril (Prinivil)  | 3. Hypospadias                     |
| D. Methysergide (Sansert) | 4. Oxytocic action                 |
| E. Divalproex sodium      | 5. Cardiac abnormalities           |

**378.** Which of the following statements best describes closure of patent foramen ovale (PFO) and treatment of migraine headaches?

- A. Retrospective data from trials of patent foramen ovale (PFO) closure after presumed paradoxical embolization can be extrapolated to determine benefit of closure for migraine patients.
- B. Transcatheter closure of PFOs in migraine headache patients is not associated with serious adverse events.
- C. There is not enough current data to assess the benefit of PFO closure in patients with migraine with aura.
- D. The mechanism for PFO closure benefit can be explained based on reduction of cerebral ischemia.
- E. Aspirin used to treat patients with PFO may increase chronic headaches.

**379.** Oral contraceptives reduce the level of which drug by up to 50%?

- A. Gabapentin (Neurontin)
- B. Divalproex sodium (Depakote)
- C. Lamotrigine (Lamictal)
- D. Zonisamide (Zonegran)
- E. All of the above

**380.** Which of the following is the drug of choice for abortive treatment of a CH?

- A. Rectal ergotamine
- B. Subcutaneous sumatriptan (Imitrex)
- C. Intranasal zolmitriptan (Zomig)
- D. Sublingual rizatriptan (Maxalt)
- E. Oral sumatriptan

**381.** Which statement best describes treatment of chronic tension-type headache (CTTH)?

- A. Electromyographic (EMG) biofeedback training reduces chronic tension-type headache (CTTH) through control of pericranial muscle contraction alone.
- B. The addition of behavior therapies, such as EMG biofeedback training, to treatment with tricyclic antidepressants (TCA) offers no additional benefit over either treatment individually.
- C. The combination of behavioral and medical therapies increases the rapidity of headache response in patients with CTTH.
- D. The sustained benefit of the combination of treatments is superior to the sustained benefit of EMG biofeedback training alone.
- E. Long-term maintenance of therapy is of no benefit, especially in patients with comorbid psychiatric disease.

**382.** Which of the complementary treatments for prevention of chronic headaches has the *least* evidence for efficacy?

- A. Coenzyme Q10
- B. Magnesium
- C. Feverfew
- D. Butterbur
- E. Acupuncture

**383.** Patients with primary cough headache most often respond to prophylactic treatment with which medication?

- A. Lithium
- B. Indomethacin (Indocin)
- C. Verapamil (Calan)
- D. Lamotrigine (Lamictal)
- E. Gabapentin (Neurontin)

**384.** Which of the following short-acting triptans has been shown to prevent menstrual migraine in a large, randomized, placebo-controlled trial?

- A. Zolmitriptan (Zomig)
- B. Eletriptan (Relpax)
- C. Sumatriptan (Imitrex)
- D. Rizatriptan (Maxalt)
- E. None of the above

**385.** Which of the following has been shown to be effective in treating patients with SUNCT?

- A. Intranasal zolmitriptan (Zomig)
- B. Inhalational oxygen
- C. Intramuscular Indomethacin (Indocin)
- D. Intravenous (IV) lidocaine
- E. Oral Ketoralac (Toradol)

**386.** Which combination of medications has the greatest risk of serious cutaneous disorders?

- A. Pregabalin (Lyrica) and valproic acid (Depakene®)
- B. Divalproex sodium (Depakote) and topiramate (Topamax)
- C. Gabapentin (Neurontin) and lamotrigine (Lamictal)
- D. Divalproex sodium and lamotrigine (Lamictal)
- E. Zonisamide (Zonegran) and oxcarbazepine (Trileptal)

**387.** A young woman was brought to the emergency department by ambulance from a nightclub in Chelsea. Because of agitation and confusion, she was unable to provide a medical history or cooperate with a neurological examination. A bottle of phenelzine (Nardil) and a packet of a triptan were found in her purse. Her temperature was elevated at 38.9 degrees C. Her blood pressure was 148/96 with a heart rate of 130. She was diaphoretic and tremulous with hyperreflexia but her examination was otherwise unremarkable. Blood work showed a sodium level of 110. When her nightclub companions finally showed up in the ED by taxi they reported that she had been celebrating her 21st birthday and had tried something new. What did she try to commemorate reaching adulthood?

- A. Ecstasy
- B. Absinthe
- C. Fugu
- D. A sherm
- E. Special K

**388.** Which of the following interventions has the best evidence of decreased attack frequency and severity and decreased medication use in patients with intractable CH?

- A. Transcranial magnetic stimulation
- B. Vagal nerve stimulation
- C. Occipital nerve stimulation
- D. Ablation of the trigeminal ganglion
- E. Closure of a patent foramen ovale

**389.** Which of the following can be used to treat patients with headaches associated with sexual activity?

- A. Indomethacin (Indocin)
- B.  $\beta$ -Blockers
- C. Short half-life triptans
- D. Long half-life triptans
- E. All of the above

**390.** Pancreatitis in children has been associated with which medication used to prevent migraine headaches?

- A. Valproic acid (Depakene) or divalproex sodium (Depakote)
- B. Topiramate (Topamax)
- C. Propranolol (Inderal)
- D. Magnesium
- E. All of the above

**391.** Match the medication used for headache prevention or treatment with its caution or contraindication. Each answer can be used once, more than once, or not at all.

- |                           |   |
|---------------------------|---|
| A. Zonisamide (Zonegran)  | 1. Concomitant use of lithium             |
| B. Phenzazine (Nardil)    | 2. Allergy to sulfa medications           |
| C. Verapamil (Calan)      | 3. Concomitant use of fluoxetine (Prozac) |
| D. Amitriptyline (Elavil) | 4. Acute-angle closure glaucoma           |
| E. Topiramate (Topamax)   | 5. Sleep apnea                            |

**392.** Which medication can increase the metabolism and decrease the efficacy of oral contraceptives?

- A. Tegretol
- B. Oxcarbazepine (Trileptal)
- C. Phenytoin (Dilantin)
- D. Topiramate (Topamax)
- E. All of the above

**393.** Which of the following appears to be a property of calcitonin gene-related peptide (CGRP) antagonists in migraine treatment?

- A. Lack of vasoconstrictor effect
- B. Lack of oral formulation
- C. Predominant central effect
- D. Poor tolerability due to severe paresthesias
- E. Poor efficacy as abortive therapy

**394.** Which statement best describes the role of intravenous (IV) dexamethasone (Decadron<sup>®</sup>) in acute migraine?

- A. Pain-free outcome is increased in all acute migraine patients with intravenous (IV) dexamethasone as compared to placebo.
- B. Intravenous dexamethasone may decrease pain when the migraine has persisted for longer than 72 hours.
- C. Intravenous dexamethasone for acute migraine is associated with unacceptable side effects.
- D. Intravenous dexamethasone should not be used in combination with other IV medications.
- E. All of the above

**395.** The CGRP receptor antagonist MK-0974:

- A. Can only be given parenterally, limiting its use as an acute abortive agent.
- B. Is limited by its unfavorable side-effect profile.
- C. Has shown comparable efficacy to a triptan in a dosing trial.
- D. Appears to have limited utility in patients with vascular risk.
- E. All of the above

**396.** Which of the following medications, used to prevent migraine headaches in adults, has been most extensively studied in children and adolescents?

- A. Topiramate (Topamax)
- B. Valproic acid (Depakene)
- C. Verapamil (Calan)
- D. Amitriptyline (Elavil)
- E. Fluoxetine (Prozac)

**397.** Which of the following has been shown to be effective and well tolerated in the treatment of adolescent migraine?

- A. Intranasal zolmitriptan (Zomig)
- B. Subcutaneous sumatriptan (Imitrex)
- C. Oral frovatriptan (Frova)
- D. Butalbital/aspirin/caffeine combination
- E. All of the above



**398.** In studies of prevention of chronic migraine with topiramate (Topamax), which of the following was the most common adverse event in patients on the medication?

- A. Paresthesias
- B. Acute myopia
- C. Renal stones
- D. Cognitive dysfunction
- E. Weight loss

**399.** Which medication used for the prevention of migraine headaches has been associated with polycystic ovarian syndrome (PCOS)?

- A. Divalproex sodium (Depakote)
- B. Topiramate (Topamax)
- C. Lamotrigine (Lamictal)
- D. Magnesium
- E. Propranolol (Inderal)

**400.** Which of the following has been shown to be of benefit in treating generalized anxiety disorder (GAD)?

- A. Paroxetine (Paxil)
- B. Buspirone (BuSpar®)
- C. Venlafaxine (Effexor®)
- D. Cognitive-behavioral therapy
- E. All of the above

**401.** Which of the following angiotensin-converting enzyme (ACE) inhibitors was effective in preventing migraines in a randomized, double-blind, placebo-controlled trial?

- A. Enalapril (Vasotec)
- B. Ramipril (Altace)
- C. Perindopril (Aceon)
- D. Lisinopril (Prinivil)
- E. Benazepril (Lotensin)

**402.** Which migraine type represents a possible contraindication for treatment with triptans?

- A. Migraine with visual aura lasting 45 minutes
- B. Migraine with sensory aura
- C. Migraine headaches in postmenopausal women
- D. Hemiplegic migraine
- E. All of the above

**403.** Which medication has the greatest risk of Stevens-Johnson syndrome (SJS) when used as monotherapy?

- A. Carbamazepine (Tegretol)
- B. Divalproex sodium (Depakote)
- C. Gabapentin (Neurontin)
- D. Topiramate (Topamax)
- E. Lamotrigine (Lamictal)

**404.** Match the cause of headache with the most appropriate treatment listed. Each answer may be used once, more than once, or not at all.

- |   |                                |
|---|--------------------------------|
| A. Tolosa-Hunt syndrome                       | 1. Acetazolamide (Diamox®)     |
| B. Herpes encephalitis                        | 2. Corticosteroids             |
| C. Giant cell arteritis (GCA)                 | 3. Verapamil (Calan)           |
| D. Idiopathic intracranial hypertension (IIH) | 4. Acyclovir (Zovirax®)        |
| E. Bacterial meningitis                       | 5. Cyclophosphamide (Cytosan®) |

**405.** Which three triptans were deemed to “provide the highest likelihood of consistent success” in a meta-analysis, published in 2001, of 53 clinical trials involving over 24,000 migraine patients?

- A. Sumatriptan (Imitrex) 50 mg, eletriptan (Relpax) 80 mg, and almotriptan (Axert) 12.5 mg
- B. Rizatriptan (Maxalt) 10 mg, eletriptan 40 mg, and naratriptan (Amerge) 2.5 mg
- C. Sumatriptan 100 mg, zolmitriptan (Zomig) 10 mg, and almotriptan 12.5 mg
- D. Rizatriptan 10 mg, eletriptan 80 mg, and almotriptan 12.5 mg
- E. Frovatriptan (Frova) 2.5 mg, eletriptan 40 mg, and sumatriptan 50 mg

**406.** New and established medications are currently under investigation for indications that may benefit headache patients. Match the listed medication with its indication that is under clinical investigation. Each answer may be used once, more than once, or not at all.

- |  |                            |
|--|----------------------------|
| A. Flibanserin (Ectris <sup>®</sup> )  | 1. Acute migraine headache |
| B. Topiramate (Topamax)                | 2. Depression              |
| C. MK-0974 (Telcagepant <sup>®</sup> ) | 3. Decreased libido        |
| D. Vigabatrin (Sabril <sup>®</sup> )   | 4. Cocaine addiction       |
| E. BIBN4096 (Olcegepant <sup>®</sup> ) | 5. Alcohol addiction       |

**407.** Which statement best describes the use of Topiramate (Topamax) in patients with chronic migraine?

- A. Clinical trials have not shown that topiramate monotherapy benefits patients with chronic migraine.
- B. Approximately a third of chronic migraine patients on topiramate complain of cognitive side effects.
- C. Topiramate benefits patients with medication overuse headache (MOH).
- D. The high treatment discontinuation rate in clinical trials obscures any therapeutic benefit.
- E. Topiramate was only of benefit when combined with other preventative medications.

**408.** The combination of riboflavin, magnesium, and feverfew for migraine prophylaxis:

- A. Generally shows a beneficial effect in 3 weeks.
- B. Should not be combined with prescription preventative medications.
- C. Is generally well tolerated for migraine prevention.
- D. Has been shown to be superior to riboflavin alone in migraine prevention.
- E. All of the above

**409.** The nonprescription migraine combination medication acetaminophen/aspirin/caffeine:

- A. Was found possibly superior to sumatriptan (Imitrex) in a head-to-head comparison in acute migraine.
- B. Is more likely to cause medication overuse headache (MOH) than a triptan.
- C. Causes a less intractable MOH than a triptan.
- D. Appears to be less effective than ibuprofen in the acute treatment of migraine.
- E. All of the above

**410.** Butterbur:

- A. Contains an active ingredient derived from the root of *Petasites hybridus*.
- B. Has dose-dependent efficacy in acute migraine.
- C. May cause increased burping.
- D. Is generally well tolerated.
- E. All of the above

**411.** Gabapentin (Neurontin):

- A. Has not been shown to be of benefit as a prophylactic agent in patients with migraine.
- B. Has somnolence and dizziness as its most common side effect.
- C. Has increased bioavailability with increasing dose.
- D. Has a half-life consistent with once-a-day dosing.
- E. All of the above

**412.** Which medication, when given to patients with preexisting treated hypothyroidism, is most likely to lead to overt hypothyroidism?

- A. Lamotrigine (Lamictal)
- B. Carbamazepine (Tegretol)
- C. Phenytoin (Dilantin)
- D. Divalproex sodium (Depakote)
- E. Gabapentin (Neurontin)

**413.** Which medication increases the half-life of lamotrigine (Lamictal)?

- A. Topiramate (Topamax)
- B. Gabapentin (Neurontin)
- C. Oxcarbazepine (Trileptal)
- D. Valproic acid (Depakene) or divalproex sodium (Depakote)
- E. Carbamazepine (Tegretol)

**414.** Which of the following statements describes clinical trials of sham versus real acupuncture?

- A. Patients with TTHs respond to both types of acupuncture.
- B. Patients with migraine headaches respond to both types of acupuncture.
- C. Acupuncture may show benefit similar to preventative medication in migraine patients.
- D. The psychological and physiologic benefits of acupuncture cannot be separated.
- E. All of the above

**415.** Which triptan is associated with the lowest headache recurrence rate after acute migraine treatment?

- A. Sumatriptan (Imitrex)
- B. Rizatriptan (Maxalt)
- C. Frovatriptan (Frova)
- D. Almotriptan (Axert)
- E. Naratriptan (Amerge)

**416.** Which of the following angiotensin II receptor blockers was found to be effective in preventing migraines in a randomized, double-blind, placebo-controlled crossover trial?

- A. Olmesartan (Benicar<sup>®</sup>)
- B. Irbesartan (Avapro<sup>®</sup>)
- C. Losartan (Cozaar<sup>®</sup>)
- D. Candesartan (Atacand<sup>®</sup>)
- E. Telmisartan (Micardis<sup>®</sup>)

**417.** Which of the following supplements has shown superiority to placebo in preventing migraine in a double-blind, randomized trial?

- A. Coenzyme Q10
- B. Gingko biloba
- C. Selenium
- D. Choline
- E. Carnitine

**418.** Which statement best describes the use of selective serotonin reuptake inhibitors (SSRIs) in the prevention of migraine and TTHs?

- A. Selective serotonin reuptake inhibitors (SSRIs) are superior to tricyclic antidepressants (TCAs) in prevention of TTH.
- B. Selective serotonin reuptake inhibitors are superior to placebo in the prevention of migraine headaches.
- C. Triptans should be avoided in patients taking SSRIs for migraine prevention because of the risk of serotonin syndrome.
- D. Selective serotonin reuptake inhibitors are shown to decrease the frequency of menstrual migraine.
- E. Selective serotonin reuptake inhibitors may decrease headaches in patients with significant depression.

**419.** Which of the following antidepressant medications is most efficacious in the prevention of migraine headache?

- A. Venlafaxine (Effexor)
- B. Fluoxetine (Prozac)
- C. Paroxetine (Paxil)
- D. Citalopram (Celexa)
- E. Sertraline (Zoloft)

**420.** Hypothalamic deep brain stimulation (DBS):

- A. Has shown efficacy in the prevention of migraine headaches.
- B. Has shown efficacy in the prevention of cluster headache (CH).
- C. Is a remote activation procedure performed in the office.
- D. Can be performed easily without morbidity.
- E. All of the above

**421.** Match the triptan with its specific characteristic. Use each answer only once.

- |                          |   |
|--------------------------|---|
| A. Sumatriptan (Imitrex) | 1. Highest oral bioavailability                 |
| B. Frovatriptan (Frova)  | 2. Lowest oral bioavailability                  |
| C. Naratriptan (Amerge)  | 3. Longest half-life                            |
| D. Almotriptan (Axert)   | 4. Second longest half-life                     |
| E. Rizatriptan (Maxalt)  | 5. Shortest time to maximum blood concentration |

**422.** What is therapeutic gain?

- A. The improvement in quality of living gained by headache relief.
- B. The percentage response for active treatment minus the percentage response for placebo.
- C. The minimum response that can be reliably expected from treatment.
- D. The percentage response with active treatment.
- E. The consistent improvement seen each time treatment is compared to placebo.

**423.** Supplementation with which of the following may improve pediatric and adolescent migraine?

- A. Choline
- B. Coenzyme Q10
- C. Magnesium
- D. Selenium
- E. None of the above

**424.** Which of the following triptans appears to have the lowest incidence of chest discomfort?

- A. Almotriptan (Axert)
- B. Subcutaneous sumatriptan (Imitrex)
- C. Intranasal zolmitriptan (Zomig)
- D. Oral sumatriptan (Imitrex)
- E. Eletriptan (Relpax)

**425.** Which of the triptans listed is available in more than one medication delivery formulation?

- A. Almotriptan (Axert)
- B. Rizatriptan (Maxalt)
- C. Frovatriptan (Frova)
- D. Naratriptan (Amerge)
- E. Eletriptan (Relpax)

**426.** Which of the following appears to be the most effective preventative medication for children and adolescents with migraine headaches?

- A. Propranolol (Inderal)
- B. Gabapentin (Neurontin)
- C. Topiramate (Topamax)
- D. Levetiracetam (Keppra)
- E. Zonisamide (Zonegran)

**427.** A patient at her first visit says that she wants to try oral sumatriptan (Imitrex) to treat her migraine headaches. Her sister uses sumatriptan for her migraine headaches, and she used a few of her pills with good response. The patient is a 50-year-old woman who has no medical illnesses except for depression, which has been well controlled on tranylcypromine (Parnate) for 30 years. What do you tell this patient?

- A. You will give her rizatriptan (Maxalt), but for no more than 10 days a month.
- B. Take the sumatriptan her sister gave her, but for no more than 10 days a month.
- C. You will give her almotriptan (Axert), but for no more than 10 days a month.
- D. She should use Midrin (acetaminophen, isometheptene, and dichloralphenazone) instead of a triptan.
- E. She should use a preventative medication, not an acute medication, to treat her four headache days a month.

**428.** For the most effective relief of an acute migraine headache, a triptan should be taken:

- A. At the onset of premonitory symptoms.
- B. At the onset of the migraine aura.
- C. At the onset of migraine headache pain.
- D. When the pain and accompanying symptoms are at their peak.
- E. When cutaneous allodynia occurs.

**429.** A 44-year-old man with significant depression and anxiety reports a headache every single day for several years. He is taking daily butalbital/aspirin/caffeine combination medication, given to him by multiple physicians, but he is evasive about his exact daily dose and how long he has been on the medication. He purports to understand the concept of the development of medication overuse headache (MOH), but insists that the combination is the only medication that allows him to function. He demands that you supply him with a prescription for 90 pills a month. What do you suggest to help him?

- A. He should be admitted to the hospital for abrupt cessation of the combination medication, treating with oral phenobarbital.
- B. He should be admitted to the hospital for abrupt cessation of the combination medication, treating with intravenous propofol and intubation.
- C. He should taper the butalbital-containing medication and start a preventative medication.
- D. He should stop taking the medication immediately.
- E. Although you are concerned about his use of the butalbital-containing medication, you will supply it to him in the quantities he desires.

**430.** Which of the following describes stratified versus stepped care?

- A. Although patient satisfaction is higher with stratified care, the benefit is offset by increased costs.
- B. Disability assessment should be used to stratify appropriate care.
- C. Clinical outcome is a function of medication use to prevent headaches.
- D. The differences between stratified and stepped care are specific to a particular triptan.
- E. All of the above



- 431.** Divalproex sodium (Depakote) in migraine headache prevention:
- A. Is dosed once a day in a delayed-release (DR) formulation.
  - B. Is dosed twice a day in an extended-release (ER) formulation.
  - C. Is better tolerated in the ER than in the DR formulation.
  - D. Has been shown to be effective at doses >1,000 mg/day.
  - E. All of the above
- 432.** Which of the following have been used to prevent a migraine by treatment during its premonitory symptoms?
- A. Domperidone (Motilium)
  - B. Naratriptan (Amerge)
  - C. Metoclopramide (Reglan)
  - D. Frovatriptan (Frova)
  - E. All of the above
- 433.** An obese woman with frequent migraine headaches had good relief of her headaches on Topiramate (Topamax). She was also pleased with weight loss on the medication; however, word-finding difficulty interfered with her job as a radio talk show host, so she asked if her medication could be switched. What would you suggest?
- A. Divalproex sodium (Depakote)
  - B. Propranolol (Inderal)
  - C. Zonisamide (Zonegran)
  - D. Gabapentin (Neurontin)
  - E. Amitriptyline (Elavil)
- 434.** What of the following is a plausible mechanism of action for botulinum toxin in the treatment of migraine?
- A. Relaxation of muscles of the neck and face
  - B. Prevention of release of nociceptive neuropeptides
  - C. Reduced anxiety about wrinkles
  - D. Calcium channel inhibition
  - E. All of the above

**435.** Which of these side effects of topiramate (Topamax) primarily involves children?

- A. Word-finding difficulty
- B. Renal stones
- C. Paresthesias
- D. Oligohidrosis
- E. Acute myopia

**436.** Which medication is associated with ciliochoroidal detachment?

- A. Gabapentin (Neurontin)
- B. Topiramate (Topamax)
- C. Divalproex sodium (Depakote)
- D. Carbamazepine (Tegretol)
- E. Vigabatrin (Sabril)

**437.** Which medication has shown benefit in treating SUNCT and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA)?

- A. Lamotrigine (Lamictal)
- B. Gabapentin (Neurontin)
- C. Topiramate (Topamax)
- D. Lidocaine
- E. All of the above

**438.** Which symptom is *most* characteristically seen in patients with serotonin syndrome?

- A. Flushing
- B. Agitation
- C. Tachycardia
- D. Hyperreflexia or clonus
- E. Hyperthermia

**439.** The following medications are used for blood pressure control and headache prevention. Match each with its mechanism of action. Use each answer once, more than once, or not at all.

- |                                       |  |
|---------------------------------------|--|
| A. Lisinopril (Prinivil, Zestril)     | 1. $\alpha_2$ Agonists                           |
| B. Candesartan (Atacand)              | 2. Angiotensin II receptor blocker               |
| C. Atenolol (Tenormin <sup>®</sup> )  | 3. Angiotensin-converting enzyme (ACE) inhibitor |
| D. Verapamil (Calan)                  | 4. $\beta$ -Blocker                              |
| E. Clonidine (Catapres <sup>®</sup> ) | 5. Calcium channel blockers                      |

**440.** Which of the following has been shown to be effective in the acute treatment of CH, but not in migraine?

- A. Serotonin receptor agonists
- B. Calcitonin gene-related peptide (CGRP) receptor antagonists
- C. Somatostatin receptor agonists
- D. Nitric oxide synthase (NOS) blockers
- E. Adenosine A<sub>1</sub> receptor agonists

**441.** Steroids:

- A. Have proven benefit in withdrawal therapy following medication overuse headache (MOH).
- B. Have proven benefit in prevention of headache relapse after acute migraine headaches.
- C. May cause aseptic osteonecrosis with short-term, intermittent pulse doses in migraine patients.
- D. Are contraindicated in acute vestibular neuritis.
- E. All of the above

**442.** Which of the following best predicts a favorable response to treatment with a triptan late into the migraine?

- A. Absence of nausea
- B. Presence of unilateral pain
- C. Absence of cutaneous allodynia
- D. Presence of photophobia
- E. All of the above

**443.** Intravenous magnesium:

- A. Is poorly tolerated in the treatment of acute migraine.
- B. Has been shown to inhibit central sensitization with acute migraine.
- C. Shows preferential benefit with migraine with aura as compared to migraine without aura.
- D. Is effective in migraine based on an antiserotonergic mechanism.
- E. All of the above

**444.** Which of the following medications has been shown to be effective in the prophylaxis of basilar-type migraine in children?

- A. Propranolol (Inderal)
- B. Topiramate (Topamax)
- C. Gabapentin (Neurontin)
- D. Lamotrigine (Lamictal)
- E. All of the above

**445.** A young woman with migraines, depression, and anxiety is seen in the emergency department (ED) complaining of headache, fever, and diarrhea. She is diaphoretic and mildly agitated, with tachycardia but normal blood pressure. Her neurology examination is remarkable only for hyperreflexia without spasticity. Her magnetic resonance imaging (MRI) scan of the brain is normal. What is her most likely diagnosis?

- A. Subarachnoid hemorrhage
- B. Serotonin syndrome
- C. Neuroleptic malignant syndrome
- D. Cocaine reaction
- E. Reaction to monoamine oxidase inhibitors

**446.** Which of the following is used to preserve vision in patients with idiopathic intracranial hypertension (IIH)?

- A. Optic nerve sheath decompression (ONSD)
- B. Intracranial venous sinus stent placement
- C. Ventriculoperitoneal shunt placement
- D. Lumboperitoneal shunt placement
- E. All of the above

**447.** Which of the following medications may be an alternative to acetazolamide for the treatment of IIH?

- A. Carbamazepine (Tegretol)
- B. Gabapentin (Neurontin)
- C. Topiramate (Topamax)
- D. Lamotrigine (Lamictal)
- E. Divalproex sodium (Depakote)

**448.** At a new-patient appointment, a 29-year-old woman reported TTHs occurring about once to twice a week. She had multiple repetitive questions about her headaches and, despite normal brain imaging in the past year, was difficult to reassure that her headaches were not due to a dread disease. At your suggestion, she considered a preventative medication; however, she was very anxious about side effects of medication. She was not sure what to do and left the appointment without making a decision. You fielded innumerable phone calls about her headaches and a multitude of nonspecific complaints in the few weeks after her appointment. When she returns to see you, what medication will you suggest?

- A. Lamotrigine (Lamictal)
- B. Divalproex sodium (Depakote)
- C. Pregabalin (Lyrica)
- D. Topiramate (Topamax)
- E. Amitriptyline (Elavil)

**449.** Overuse of which of the following medications is associated with the greatest risk of ischemic complications?

- A. Triptans
- B. Ergotamines
- C. Barbiturates
- D. Over-the-counter nonselective nonsteroidal agents
- E. All of the above

**450.** Convulsive ergotism is related to:

- A. Syncope in patients with migraines
- B. The consumption of grain contaminated with fungus
- C. The increased risk of seizures in patients taking phenytoin (Dilantin) and ergotamines
- D. Psychiatric disease in women with migraine
- E. Use of grain alcohol distilled in car batteries

**451.** Patients with nummular headache resistant to medication may respond to which of the following treatments?

- A. Vagal nerve stimulation
- B. Suppression of rapid eye movement (REM) sleep
- C. Cognitive behavioral therapy (CBT)
- D. Botulinum toxin type A
- E. Occipital nerve stimulation

**452.** Match the medication used for prevention of chronic headaches with the medical condition that may be affected by its use. Use each condition once, more than once, or not at all.

- |                                 |                                     |
|---------------------------------|-------------------------------------|
| A. Propranolol (Inderal)        | 1. Conduction block                 |
| B. Topiramate (Topamax)         | 2. Unstable asthma                  |
| C. Verapamil (Calan)            | 3. Recurrent kidney stones          |
| D. Divalproex sodium (Depakote) | 4. Polycystic ovary syndrome (PCOS) |
| E. Magnesium                    | 5. Chronic diarrhea                 |

**453.** What is the approximate headache response rate at 2 hours post-dose for zolmitriptan (Zomig) nasal spray in adults patients with migraine?

- A. 33%
- B. 44%
- C. 55%
- D. 66%
- E. 77%

**454.** Statistically significant benefit of triptan treatment is elusive in clinical trials of acute migraine in children and adolescents. Why?

- A. Pediatric migraine is of shorter duration than adult migraine.
- B. Boys are more likely to have migraines than girls.
- C. Vomiting is common in children with migraine.
- D. The therapeutic gain is small in pediatric clinical trials.
- E. All of the above

**455.** What is the approximate incidence of chest discomfort associated with oral almotriptan (Axert) treatment?

- A. <0.5%
- B. 2%
- C. 4%
- D. 6%
- E. 8%

**456.** Which of the following medications may increase carbamazepine (Tegretol) drug levels and lead to clinical drug toxicity?

- A. Erythromycin
- B. Clarithromycin (Biaxin)
- C. Quetiapine (Seroquel)
- D. Isoniazid
- E. All of the above

**457.** Which medication, used for headache or pain prevention, is the least likely to interact with other medications including antiepileptic drugs (AEDs), oral contraceptives and antibiotics?

- A. Topiramate (Topamax)
- B. Gabapentin (Neurontin).
- C. Carbamazepine (Tegretol)
- D. Divalproex sodium (Depakote)
- E. Zonisamide (Zonegran)

**458.** A 33-year-old woman came to the ED in the early morning hours with a migraine headache that had been persistent for 3 days. Along with severe unilateral throbbing pain, she had intermittent nausea and vomiting, as well as marked photophobia and phonophobia. Before going to bed, she had taken two doses of eletriptan (Relpax) to abort the migraine, without success, so her husband brought her to the ED in the morning for treatment. Which therapy for status migrainous would be most appropriate her?

- A. Subcutaneous sumatriptan (Imitrex)
- B. Intranasal zolmitriptan (Zomig)
- C. Intravenous valproate sodium (Depacon)
- D. Intramuscular dihydroergotamine and metoclopramide (Reglan)
- E. Intravenous dihydroergotamine and metoclopramide

**459.** A unique pharmacologic property makes which one of the following triptans ideal for the short-term prophylactic treatment of menstrual migraine?

- A. Zolmitriptan (Zomig)
- B. Naratriptan (Amerge)
- C. Frovatriptan (Frova)
- D. Eletriptan (Relpax)
- E. Rizatriptan (Maxalt)

**460.** Which of the following medications is appropriate for the treatment of pediatric migraine headaches in the ED?

- A. Intravenous ketorolac (Toradol)
- B. Intravenous prochlorperazine (Compazine)
- C. Intravenous valproate sodium (Depacon)
- D. Intravenous dihydroergotamine
- E. All of the above

**461.** The combination of sumatriptan succinate and naproxen (Treximet®) in the acute treatment of migraine:

- A. Is as effective as either component as monotherapy.
- B. Contains the same dose of naproxen sodium as available over the counter.
- C. Is more effective than either component as monotherapy.
- D. Results in more side effects than the combined individual medications.
- E. All of the above

**462.** Which of the following is a complication of divalproex sodium (Depakote) treatment?

- A. Peripheral neuropathy
- B. Pulmonary fibrosis
- C. Pancreatitis
- D. Prostatitis
- E. All of the above

**463.** Which of the following may be of benefit in the prophylactic treatment of trigeminal autonomic cephalgias (TACs), based on hypothalamic hormonal manipulation?

- A. Progesterone
- B. Estradiol
- C. Clomiphene
- D. Melatonin
- E. All of the above



**464.** A 68-year-old Filipina woman with diabetes, rheumatoid arthritis, and treated breast cancer reports transient sharp pain radiating from her left cheek to her ear and lower jaw. The pain is severe, lasts minutes, and occurs multiple times a day. The pain is triggered by eating, brushing her teeth, or washing her face. You diagnose trigeminal neuralgia and would like to start carbamazepine (Tegretol) for pain prevention. What should you do prior to treatment?

- A. Check her erythrocyte sedimentation rate.
- B. Check fasting cortisol level.
- C. Switch from metformin to glipizide
- D. Perform human leukocyte antigen typing.
- E. Repeat her mammogram.

**465.** Which of the following medications used for prevention of headaches is associated with hair loss?

- A. Lithium
- B. Divalproex sodium (Depakote)
- C. Carbamazepine (Tegretol)
- D. Timolol (Blocadren<sup>®</sup>)
- E. All of the above

**466.** Which of the following medications is most likely to be associated with major congenital malformation due to in utero exposure?

- A. Carbamazepine (Tegretol)
- B. Lamotrigine (Lamictal)
- C. Phenytoin (Dilantin)
- D. Divalproex sodium (Depakote)
- E. Gabapentin (Neurontin)

**467.** Which of the following is most appropriately used to suppress migraines triggered by menses?

- A. Oral progesterone
- B. Levonorgestrel/ethinyl estradiol and ethinyl estradiol tablets
- C. Bromocriptine
- D. Tamoxifen
- E. Oophorectomy

- 468.** Pregabalin (Lyrica) has been shown to be of benefit in the treatment of:
- A. Generalized anxiety disorder (GAD).
  - B. Fibromyalgia.
  - C. Trigeminal neuralgia.
  - D. Post herpetic facial pain.
  - E. All of the above
- 469.** A 26-year-old healthy woman related that 2 years ago she was diagnosed with a subarachnoid hemorrhage when she presented to an ED with the sudden onset of a severe headache, distinctly different from her usual migraines. A middle cerebral artery aneurysm was successfully coiled and follow-up angiography has shown no further aneurysms. Neurologic recovery was excellent. She has no family history of cerebral aneurysms. She is now seeking consultation for migraine headaches with and without aura that occur approximately once every few months. Treatment with over-the-counter (OTC) medications has been disappointing. What would you recommend?
- A. She should start a preventative medication.
  - B. She should be given a prescription for a butalbital–caffeine preparation for acute treatment.
  - C. She should be given a prescription for a triptan.
  - D. She should undergo catheter angiography every 6 months for 2 more years.
  - E. Her parents, siblings, and cousins should undergo screening for cerebral aneurysms.
- 470.** What is the recommended total daily dose for topiramate (Topamax) for migraine prophylaxis?
- A. 25 mg once a day
  - B. 50 mg once a day
  - C. 100 mg a day in two divided doses
  - D. 150 mg a day in three divided doses
  - E. 200 mg a day in two divided doses
- 471.** Which of the following statements about triptan therapy is true?
- A. Response to a triptan can be used to diagnose headache type.
  - B. Mixing different triptan brands has been shown to have serious clinical consequences.
  - C. Triptans should not be used in patients under age 18 years.
  - D. Lack of therapeutic benefit from one brand of triptans predicts lack of benefit from all triptans.
  - E. None of the above

**472.** A 45-year old-woman describes disabling migraine headaches, preceded by visual aura, occurring two to three times a month a year, starting about a year ago. Because her irregular menses are a major trigger of her most severe migraines with aura, her gynecologist suggests that she use continuous oral contraceptives to suppress her period. Her medical history is otherwise unremarkable but she has smoked about a pack of cigarettes a day since her twenties, and she is not interested in smoking cessation. What method of migraine headache prevention do you suggest?

- A. Continuous oral contraceptive pills, skipping the placebo week of pills
- B. Oral birth control specifically designed for daily continuous use
- C. Long-acting triptan prophylaxis prior to her menses
- D. Daily, preventative, nonhormonal medication for her migraines
- E. All of the above are reasonable treatment plans

**473.** Which statement comparing ergotamine to dihydroergotamine (DHE) is true?

- A. Both medications are available in oral and parenteral forms.
- B. Ergotamine is a more potent arterial vasoconstrictor than dihydroergotamine (DHE).
- C. Dihydroergotamine, but not ergotamine inhibit the reuptake of norepinephrine at sympathetic nerve endings.
- D. Ergotamine is less likely to produce nausea than DHE.
- E. All of the above

**474.** A 65-year-old man with hypertension presented to the ED with a headache, dizziness, nausea, and vomiting. The computed tomography (CT) scan was read as negative without hemorrhage or ischemia. His examination appeared unremarkable, without any clear focal deficit until he got up from lying on the stretcher to go to the bathroom and fell to the floor, unable to walk. What would be the most appropriate next step?

- A. Send the patient home with antiemetic and pain medications and instructions to call the family doctor within the next 2–3 days.
- B. Obtain an MRI of the brain and a magnetic resonance angiogram (MRA) of the brain and neck vessels.
- C. Admit the patient to the hospital with acute onset of vertigo and order nursing checks every 6 hours.
- D. Do a lumbar puncture to rule out subarachnoid hemorrhage (SAH).
- E. Obtain a carotid ultrasound in the emergency department (ED).

- 475.** Pregabalin (Lyrica) is *not* approved by the FDA for which indication?
- A. Partial seizures
  - B. Social anxiety disorder
  - C. Postherpetic neuralgia
  - D. Diabetic peripheral neuropathy
  - E. Fibromyalgia
- 476.** Intravenous valproate sodium (Depacon) may be used to treat:
- A. Chronic daily headache (CDH).
  - B. Medication overuse headache (MOH).
  - C. Acute migraine headache.
  - D. Status migrainous.
  - E. All of the above
- 477.** Which statement describes the use of steroids in the treatment of migraine headaches?
- A. Oral steroids are indicated in the prevention of migraine headaches.
  - B. Oral steroids are indicated in the acute treatment of migraine headaches.
  - C. Intravenous steroids are indicated in the treatment of migraine lasting more than 72 hours.
  - D. Avascular osteonecrosis occurs only after multiple doses of IV steroids.
  - E. All of the above
- 478.** Acetylsalicylic acid (aspirin or ASA):
- A. Should not be given to young children with flu-like symptoms.
  - B. Is contraindicated in patients with Dengue fever.
  - C. Has been shown to be equivalent to sumatriptan in the treatment of acute migraine headache.
  - D. Can be given to patients with an unruptured cerebral aneurysm.
  - E. All of the above
- 479.** Which of the following is a potential mechanism for topiramate (Topamax) in blocking neuronal hyperexcitability?
- A. Blockage of voltage-dependent sodium channels
  - B. Potentiation of  $\gamma$ -aminobutyric acid (GABA) activity
  - C. Blockade of  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazopropionic acid (AMPA)/ kainate
  - D. Blockage of calcium channels
  - E. All of the above

**480.** Which of the following is consistent with the stratification of headache care?

- A. The patient's disability dictates the frequency of medication dosing.
- B. Treatment of headache pain is based on age of onset of headaches.
- C. The severity of the patient's headaches dictates the intensity of their treatment.
- D. Headache treatment is always initiated with over-the-counter (OTC) medications.
- E. None of the above

**481.** Which of the following describes the mechanism of action of triptans?

- A. Selective extracerebral intracranial vasoconstriction
- B. Inhibition of trigeminal nerve terminals innervating extracerebral vessels
- C. Central neuronal inhibition in brainstem nuclei
- D. Activation of 5-hydroxytryptamine (5-HT)<sub>1D</sub> receptors
- E. All of the above

**482.** Which of the following medications, used for prevention of pain, may lead to oral contraceptive failure?

- A. Divalproex sodium (Depakote)
- B. Gabapentin (Neurontin)
- C. Zonisamide (Zonegran)
- D. Topiramate (Topamax)
- E. All of the above

**483.** Use of which of the following medications used during pregnancy is most likely to be associated with teratogenicity?

- A. Carbamazepine (Tegretol)
- B. Divalproex sodium (Depakote)
- C. Gabapentin (Neurontin)
- D. Zonisamide (Zonegran)
- E. Topiramate (Topamax)

**484.** Risk of which of the following is increased with the combination of divalproex sodium and topiramate (Topamax)?

- A. Stevens-Johnson syndrome (SJS)
- B. Metabolic acidosis
- C. Hyperammonemic encephalopathy
- D. Pancreatitis
- E. Weight gain

**485.** The nonprescription combination of acetaminophen, aspirin, and caffeine (AAC):

- A. Is more effective than placebo for menstrual migraine.
- B. Is more effective than placebo for migraine not associated with migraine.
- C. Is compared favorably with sumatriptan (Imitrex).
- D. Is compared favorably with ibuprofen.
- E. All of the above

**486.** Which of the following specifically decreases the risk of vision loss in IIH?

- A. Topiramate (Topamax)
- B. Acetazolamide (Diamox)
- C. Ventriculo-peritoneal shunt
- D. Lumbo-peritoneal shunt
- E. Optic nerve sheath fenestration

**487.** Some patients find that caffeine can abort a migraine headache. Match the source of caffeine with its approximate amount of caffeine. Use each answer only once.

- |  |               |
|--|---------------|
| A. Coca-Cola (12 oz.)                    | 1. 65 mg      |
| B. Mountain Dew (12 oz.)                 | 2. 55 mg      |
| C. Cup of black tea                      | 3. 34 mg      |
| D. Cup of brewed coffee                  | 4. 30–50 mg   |
| E. Excedrin Migraine <sup>®</sup> tablet | 5. 100–150 mg |

**488.** According to a post hoc analysis of the Spectrum Study, treatment with a triptan:

- A. Is less effective when the headache pain is mild.
- B. Is associated with more side effects when the headache pain is mild.
- C. Is not effective in patients with moderate to severe pain.
- D. Is associated with less headache recurrence with treatment of mild pain.
- E. All of the above

**489.** High-altitude headache may be prevented or treated with:

- A. Sumatriptan (Imitrex)
- B. Acetazolamide (Diamox)
- C. Ibuprofen
- D. Gabapentin (Neurontin)
- E. All of the above

**490.** A 24-year-old woman needs spinal fluid analysis as part of her evaluation for symptoms of multiple sclerosis. Because of the bad experience of a friend, she is very concerned about a headache after her lumbar puncture. You reassure her that you will use a small needle with the bevel inserted parallel to dural fibers and that the stylet will be replaced before the needle is withdrawn. She is not convinced, emphasizing her fear of any needles. What else can you offer her to decrease her risk of a post-dural puncture headache (PDPH)?

- A. Pretreat with coffee prior to puncture
- B. Treat with caffeinated beverages after the puncture
- C. Pretreat with twice daily subcutaneous sumatriptan for a day prior to the procedure
- D. Treat with frovatriptan 2.5 mg once daily for 5 days after the procedure
- E. Pretreat with high-dose aspirin before the lumbar puncture

**491.** Corticosteroids in acute bacterial meningitis:

- A. Are contraindicated in children.
- B. Are associated with improved neurologic outcome but increased systemic infections.
- C. Should be administered in conjunction with the first antibiotic dose in adults.
- D. Are of benefit only with meningococcal infections.
- E. All of the above

**492.** Headache recurrence with triptan use:

- A. Occurs rarely.
- B. Is inversely correlated with elimination half-life.
- C. Is correlated with 5-HT<sub>1D</sub> receptor potency.
- D. Is correlated with initial clinical efficacy.
- E. None of the above

**493.** A 22-year-old woman described migraine headaches occurring about three times a year. The headache are presaged by expanding peripheral visual obscuration, right-sided numbness, and right-sided weakness lasting for about 45 minutes. The headache pain is severe contralateral throbbing lasting for several hours, accompanied by nausea and vomiting. She is unaware of her family history, as she was adopted. She came to you as a headache specialist because she wanted a prescription for medication specifically designed to treat migraine headaches that she saw advertised on television.

- A. She should not take this medication, but you suggest OTC medication.
- B. She should not take this medication, but you suggest the combination of acetaminophen, caffeine, and butalbital.
- C. You explain that triptans are not approved for her headaches but that there does not appear to be increased risk associated with their use.
- D. You suggest that she try intranasal dihydroergotamine (DHE) because of the severity of her vomiting.
- E. You suggest a daily preventative medication and tell her that you cannot give her this medication.

**494.** Paroxysmal hemicrania is distinguished from SUNCT by its response to which medication?

- A. Verapamil (Calan)
- B. Lithium
- C. Indomethacin (Indocin)
- D. Lamotrigine (Lamictal)
- E. Methysergide (Sansert)

**495.** Which of the following IV treatments for an intractable migraine headache is contraindicated in patients with vascular disease?

- A. Magnesium
- B. Steroids
- C. Metoclopramide (Reglan)
- D. Divalproex sodium (Depakote)
- E. Dihydroergotamine (DHE)



**496.** Which medication is most likely to provide relief in the prevention of hypnic headaches?

- A. Lithium
- B. Lamotrigine (Lamictal)
- C. Gabapentin (Neurontin)
- D. Indomethacin (Indocin)
- E. Carbamazepine (Tegretol)

**497.** A 50-year-old operatic set designer spent most of her time in Europe but returned to New York City several times a year in order to supervise the set-up of her productions. She recounted to her New York neurologist that she was recently started on a medication that had been working well to suppress her long-standing migraine headaches. However, she had been having some embarrassing movements of her mouth. Whereas she used to go out to dinner every night with the singers after the performance, she was now less interested in socializing with the cast, and she spent much of her time in New York in her apartment sleeping and eating delivery food. Her friends were also concerned that she turned down an invitation to Bryant Park for fashion week and was missing trunk shows at Barney's because she said that she was too fat. Her neurologist was at a loss to explain her symptoms but was pleased that she finally had outgrown her migraines. What is the most likely cause of her improved headaches and strange behavior?

- A. Postmenopausal headache improvement and new onset parkinsonism
- B. Depression and tardive dyskinesia due to prior neuroleptic use
- C. Getting old
- D. Side effects of propranolol (Inderal)
- E. Side effects of flunarizine

**498.** What is the average headache response at 2 hours after placebo treatment in randomized clinical trials of analgesics in the treatment of migraine attacks?

- A. 5%
- B. 10%
- C. 20%
- D. 30%
- E. 40%

**499.** Which of the following best describes the use of preventative medication in the treatment of patients with migraine headaches?

- A. Prophylactic medication is probably overused in American migraineurs.
- B. Medication should be discontinued if efficacy is not noted in 3 weeks.
- C. Therapy should be initiated at the maximum tolerable dose.
- D. Polypharmacy decreases medication toxicity.
- E. Long-acting formulations improve adherence to the medication regimen.

**500.** Which of the following is an efficacious IV treatment of acute migraine in adults?

- A. Metoclopramide (Reglan)
- B. Prochlorperazine (Compazine)
- C. Haloperidol (Haldol)
- D. Tramadol (Ultram<sup>®</sup>)
- E. All of the above

**501.** What is the mean elimination half-life of naratriptan (Amerge)?

- A. 2 hours
- B. 3 hours
- C. 4 hours
- D. 5 hours
- E. 6 hours

**502.** What is the oldest treatment for headaches still in use?

- A. Aspirin
- B. Trephination
- C. Phlebotomy
- D. Butalbital
- E. Poultice of catfish skull

**503.** Which drug is excreted unchanged in the urine?

- A. Gabapentin (Neurontin)
- B. Pregabalin (Lyrica)
- C. Vigabatrin (Sabril)
- D. All of the above
- E. None of the above

**504.** Match the drug with its corresponding property or side effect. Each property or side effect may be used once, more than once, or not at all.

- |                               |  |
|-------------------------------|--|
| A. Lamotrigine (Lamictal)     | 1. Reverses sexual side effects of serotonin reuptake inhibitors |
| B. Phenelzine (Nardil)        | 2. May be beneficial for migraine with aura                      |
| C. Gabapentin (Neurontin)     | 3. Hyponatremia  |
| D. Oxcarbazepine (Trileptal)  | 4. Decreased bioavailability at high doses                       |
| E. Cyproheptadine (Periactin) | 5. Improved tolerability combined with amitriptyline             |

**505.** Which medication has been shown to stop migraine with allodynia through the suppression of central sensitization?

- A. Subcutaneous sumatriptan (Imitrex)
- B. Intravenous valproate sodium (Depacon)
- C. Intravenous ketorolac (Toradol)
- D. Intravenous chlorpromazine (Thorazine®)
- E. None of the above

**506.** Which medication used for headache prevention has the most concerning teratogenic potential?

- A. Divalproex sodium (Depakote)
- B. Amitriptyline
- C. Verapamil (Calan)
- D. Propranolol (Inderal)
- E. Lamotrigine (Lamictal)

**507.** Which side effect of SSRIs frequently leads to discontinuation of treatment?

- A. Hair loss
- B. Weight gain
- C. Tremor
- D. Anorgasmia
- E. Cognitive dysfunction

**508.** Which blood test in patients with treatment-resistant CH may indicate a specific treatment?

- A. Testosterone level
- B. Erythrocyte sedimentation rate (ESR)
- C. Albumin level
- D. Melatonin
- E. Follicle-stimulating hormone (FSH)

**509.** Match the complementary or alternative medicine treatment with its source, chemical name, or physiologic role. Each answer can be used once, more than once, or not at all.

- |                          |   |
|--------------------------|---|
| A. Feverfew              | 1. Electron transporter.                          |
| B. Petasties (butterbur) | 2. 5-methoxy-N-acetyltryptamine                   |
| C. Magnesium             | 3. Root of a perennial shrub                      |
| D. Riboflavin            | 4. Eye of newt                                    |
| E. Coenzyme Q10 (CoQ10)  | 5. N-methyl-D-aspartate (NMDA) receptor inhibitor |
| F. Melatonin             | 6. Dried chrysanthemum leaves                     |

**510.** Which of the following is the most effective preventative medication for CTTH?

- A. Tricyclic antidepressants
- B. Nonsteroidal anti-inflammatory agents (NSAIDs)
- C. Selective serotonin reuptake inhibitors (SSRIs)
- D. Botulinum toxin
- E. Anticonvulsant medications

**511.** What of the following describes the impact of an acute antimigraine compound on platelet and erythrocyte aggregation?

- A. Ergotamine tartrate increases platelet aggregation.
- B. Aspirin increases platelet aggregation.
- C. Ergotamine tartrate increases erythrocyte aggregation.
- D. Sumatriptan decreases erythrocyte aggregation.
- E. All of the above

**512.** Which of the following is used to treat reversible cerebral vasoconstriction syndromes?

- A. Intravenous cyclophosphamide (Cytoxan)
- B. Plasmapheresis
- C. Calcium channel blockers
- D. Intravenous immunoglobulin
- E. All of the above

**513.** Which of the following is most effective in the prevention of CTTH?

- A. Acupuncture
- B. Cognitive behavioral therapy alone
- C. Tricyclic antidepressants (TCA) alone
- D. Cognitive behavioral therapy combined with TCAs
- E. Oromandibular treatment

**514.** Which of the following medications used to treat trigeminal neuralgia can rarely cause a life-threatening reaction when large doses are abruptly discontinued?

- A. Nortriptyline (Pamelor)
- B. Carbamazepine (Tegretol)
- C. Gabapentin (Neurontin)
- D. Phenytoin (Dilantin)
- E. Baclofen (Lioresal®)

**515.** Both Bell's palsy and Ramsay-Hunt syndrome can be treated with?

- A. Famciclovir (Famvir®)
- B. Acyclovir (Zovirax®)
- C. Prednisone
- D. All of the above
- E. None of the above



# HEADACHE TREATMENT

## ANSWERS

**356. The answer is A.** The Spectrum Study, a randomized, double-blind, placebo-controlled, crossover study, evaluated the effectiveness of sumatriptan (Imitrex<sup>®</sup>), 50 mg, in treating the spectrum of headaches (migraine, migrainous, and episodic tension-type) in 249 patients who had migraine headaches. Sumatriptan was superior to placebo at 4 hours for response to all headache types (migraine, 66% versus 48%;  $p < .001$ ; migrainous, 71% versus 39%;  $p < .01$ ; tension-type, 78% versus 50%,  $p < .001$ ). Sumatriptan was also superior to placebo for pain-free response at 2 and 4 hours for migraine and tension-type headaches (TTHs). The Spectrum Study concluded that sumatriptan was effective for the full spectrum of different headache types experienced by patients who also had disabling migraines. However, patients who do not have a history of migraine headaches do not experience a treatment response with triptans used to treat a TTH. (Lipton, Stewart, Cady, et al., *Headache* 2000)

**357. The answer is A.** Because the pain of a cluster headache (CH) is both excruciating and difficult to treat acutely, finding an effective preventative medication is crucial. Verapamil (Calan<sup>®</sup>) is the preventative drug of choice in patients with CHs. Higher doses of this calcium-channel blocker than are used for cardiac indications may be needed for CH pain prevention. Patients taking higher doses of verapamil should be monitored by electrocardiogram for heart block, although, conduction abnormalities may not be dose-related. Constipation is the most common side-effect of verapamil. Lithium can be an effective agent for prevention of CH; however, it may be poorly tolerated and renal, thyroid, and peripheral nerve toxicities limit its use. Lithium levels need to be monitored. Indomethacin (Indocin<sup>®</sup>), lamotrigine (Lamictal<sup>®</sup>), and gabapentin (Neurontin<sup>®</sup>) have not shown consistent benefit in the prevention of CH. (Goadsby, Cohen, & Matharu, *Curr Neurol Neurosci Rep* 2007)

**358. The answer is B.** Most people with migraine do not seek medical care for their headaches. When they do receive migraine care, it is most often provided by primary care practitioners, not neurologists or headache specialists. Only about half of people with migraine are appropriately diagnosed with migraine headaches; common misdiagnoses include “sinus headaches” and “tension headaches.” Only a minority of patients with migraine headaches are treated with migraine-specific medications such as triptans. About 29% of migraineurs are very satisfied with their usual acute treatment. Preventative therapy for migraineurs with frequent disabling headaches is also underutilized. (Lipton & Bigal, *Headache* 2007)

**359. The answer is A 3, B 2, C 1, D 4, E 2.** Trigeminal autonomic cephalalgias (TACs) are a group of primary headache disorders (CH, paroxysmal hemicrania [PH], short-lasting unilateral neuralgiform headache with conjunctival injection and tearing [SUNCT]) characterized by unilateral head pain associated with ipsilateral cranial autonomic symptoms. Because of their transient, albeit excruciatingly painful, symptoms, preventative therapy is generally more effective than abortive therapy. High-dose verapamil (Calan) is the most effective and most easily tolerated treatment for chronic or episodic CH. The therapeutic response to indomethacin (Indocin) is unique to PHs and hemicrania continua. Multiple drugs have been used for long-term prevention of SUNCT, with variable results. However, lamotrigine (Lamictal) appears to have the most reliable response. Carbamazepine (Tegretol) is generally the initial medication of choice for patients with trigeminal neuralgia. (Cohen, Matharu, & Goadsby, *Headache* 2007)

**360. The answer is B.** Patients with fibromyalgia, who are generally middle-aged women, complain of diffuse musculoskeletal pain, sleep problems, and fatigue. All of the listed medications have been used to alleviate the symptoms of fibromyalgia, but only pregabalin (Lyrica<sup>®</sup>) on this list has been approved by the U.S. Food and Drug Administration (FDA) for its treatment. In a study of patients with fibromyalgia, pregabalin at 450 mg a day reduced symptoms of pain, disturbed sleep, and fatigue compared with placebo. The medication was well tolerated and improved global measures and health-related quality of life. In clinical trials of patients with fibromyalgia, gabapentin (Neurontin) was also found to induce rapid and sustained improvement in pain, as compared to placebo. In a randomized, double-blind, placebo-controlled, multicenter trial, gabapentin (Neurontin) (1,200–2,400 mg/day) was found to be safe and efficacious for the treatment of pain and other symptoms associated with fibromyalgia. Gabapentin may be a generic, cost-effective alternative to pregabalin in the treatment of fibromyalgia. Duloxetine (Cymbalta<sup>®</sup>), a norepinephrine and serotonin reuptake

inhibitor, at doses of 60 mg/day and 120 mg/day, is safe and efficacious in patients with fibromyalgia and the medication has been FDA approved recently for use in patients with fibromyalgia. (Arnold, Goldenberg, Stanford, et al., *Arthritis Rheum* 2007; Crofford, Rowbotham, Mease, et al., *Arthritis Rheum* 2005; Russell IJ, Mease PJ, Smith TR, et al., *Pain*)

**361. The answer is A.** Oral steroids are the most effective short-term preventative therapy for CH. They may be used while the doses of long-term preventative medications, such as verapamil (Calan) or topiramate (Topamax<sup>®</sup>), are being escalated. Methysergide (Sansert<sup>®</sup>) is a potent preventative, but it has significant side effects and is no longer available in the United States. Injectable sumatriptan (Imitrex), intranasal lidocaine, and oxygen inhalation are acute treatments for individual CHs, but are not used as preventative medications in this primary headache disorder. (Cohen, Matharu, & Goadsby, *Headache* 2007)

**362. The answer is D.** Frovatriptan's (Frova<sup>®</sup>) affinity for the migraine-specific serotonin 5-HT<sub>(1B)</sub>-receptors is highest in the triptan class, and this triptan has the longest elimination half-life in plasma at 26 hours. It has a long duration of action and low risk of interactions with other drugs. Frovatriptan has no inhibiting or inducing effects on cytochrome P450 isoenzymes and is only slightly bound to plasma proteins, thus it has a low potential for drug interactions. Frovatriptan has the lowest headache recurrence rate of all the triptans; however, onset of migraine pain relief is delayed compared to the other triptans with shorter half-lives and shorter times to maximal serum concentration, limiting its use in acute treatment of migraine headache. Acute treatment with frovatriptan is most effective in migraines with slow escalation of pain and long duration of headache. Frovatriptan's long plasma-half life makes it an ideal triptan for menstrual migraine prophylaxis, used around the time of the expected menstrual migraine headache. Patients have also reported benefit taking frovatriptan prior to known migraine triggers such as a thunderstorm, airplane travel, or getting married. (Goldstein, *Expert Opin Pharmacother* 2003; Markus & Mikko, *Expert Opin Pharmacother* 2003)

**363. The answer is B.** Topiramate (Topamax) has been shown to inhibit the activity of specific carbonic anhydrase enzymes in the kidney. This action is associated with the development of metabolic acidosis, decreased urinary citrate levels, hypercalciuria, and increased urine pH, leading to an increased risk of calcium phosphate kidney stones. The reported incidence of renal stones is 1–2%, which is a two- to fourfold increase over the estimated incidence in the general population. Patients on this medication should be encouraged to drink fluids liberally to avoid stone formation. Carbonated cola beverages are often described as tast-



ing metallic on topiramate and water without bubbles often becomes the fluid of choice for patients on the medication. The patient's profession may affect the risk of developing renal stones. Elementary school teachers and overworked residents often limit fluid intake on purpose, since they have no time to urinate, and are at risk for renal stone formation, even without this medication. (Vega, Maalouf, & Sakhaee, *Expert Opin Drug Saf* 2007)

**364. The answer is A.** Ibuprofen is recommended for the acute treatment of migraine in children. Acetaminophen is probably effective as well for the acute treatment of migraine in children. Data on the use of oral triptans and subcutaneous sumatriptan in children and adolescents are not adequate to judge their efficacy. Oral dissolving formulations of triptans (rizatriptan [Maxalt<sup>®</sup>], zolmitriptan [Zomig<sup>®</sup>]) may be appropriate in children and adolescents who have severe early nausea associated with their headaches. Intranasal formulations of zolmitriptan and sumatriptan (Imitrex) have been studied in adolescents, with evidence of efficacy. The high response to placebo treatment (low therapeutic gain) noted in clinical trials of triptans in children and adolescents limits the demonstration of triptan efficacy. Pediatric migraines tend to be of relatively short duration, with marked nausea and vomiting, making treatment with acute medication problematic. (Lewis, Ashwal, Hershey, et al., *Neurology* 2004)

**365. The answer is A.** Paroxysmal hemicrania responds dramatically to prevention with indomethacin (Indocin), distinguishing it from other TACs (SUNCT, short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms [SUNA], CH) and migraine headaches. Resolution of the headache generally starts within days of starting doses ranging from 12.5 to 300 mg daily. Gastric intolerance is the most common side effect of the medication. Hemicrania continua also responds to preventative treatment with indomethacin. A diagnostic trial of indomethacin should be considered in patients with unilateral, side-locked headaches accompanied by autonomic symptoms. Lack of response to indomethacin should lead to reconsideration of the diagnosis of PH. (Cohen, Matharu, & Goadsby, *Headache* 2007)

**366. The answer is A.** This man was recently put on the antibiotic clarithromycin (Biaxin<sup>®</sup>) for flu-like symptoms, triggering ergotamine toxicity from a drug–drug interaction. The macrolide class of antibiotics, including erythromycin and clarithromycin, is associated with clinically significant adverse drug interactions. The interaction is due to the macrolide inhibition of cytochrome P450 metabolism of numerous medications, including ergotamines, resulting in elevated serum drug levels and clinical intoxication. Vasoconstriction led to lower extremity ischemia

in this man on this particular antibiotic and an ergotamine preparation. Of note, this patient's medications indicate that he has vascular risk factors, and he probably should not be taking ergotamine preparations because of his increased risk of cardiac and cerebral ischemia. (Ausband & Goodman, *J Emerg Med* 2001)

**367. The answer is E.** Flunarizine, a calcium-channel blocker, is probably effective for the preventative treatment of migraines in children and adolescents, but it is not available in the United States. There is not sufficient evidence to evaluate the efficacy of the other agents listed in the prevention of headaches in children. Topiramate (Topamax) is effective for the prevention of migraine headaches and may be appropriate therapy in children and adolescents, when its potential for cognitive side effects is considered. Cyproheptadine (Periactin<sup>®</sup>) is an antihistaminic, antiserotonergic medication used for prevention of migraine headaches in children but, as with divalproex sodium (Depakote<sup>®</sup>) and propranolol (Inderal<sup>®</sup>), data about its efficacy are inconclusive in children. (Lewis, Ashwal, Hershey, et al., *Neurology* 2004)

**368. The answer is A 2, B 3, C 1, D 4, E 4.** Multiple formulations are currently available for sumatriptan (Imitrex; subcutaneous injection, swallowed tablet, intranasal spray), zolmitriptan (Zomig; swallowed tablet, oral dissolving tablet, intranasal spray), and rizatriptan (Maxalt; oral dissolving tablet, swallowed tablet). Eletriptan (Relpax<sup>®</sup>), almotriptan (Axert<sup>®</sup>), naratriptan (Amerge<sup>®</sup>), and frovatriptan (Frova) are available only in tablets that must be swallowed. The acuity of the pain, as well as the severity of the nausea and vomiting, dictate the indicated formulation. As the FDA has proscribed the combination treatment with different triptan brands within 24 hours, for scientifically ambiguous reasons, different formulations of the same triptan permit subcutaneous, intranasal, or orally dissolving treatment initially, followed within 24 hours by swallowed tablet dosing. (Tfelt-Hansen, De Vries, & Saxena, *Drugs* 2000)

**369. The answer is E.** Multiple medications can cause or worsen unpleasant or frightening dreams usually occurring during rapid eye movement (REM) sleep. The clinical use of pharmacologic agents affecting the neurotransmitters norepinephrine, serotonin, and dopamine are associated with nightmares. Beta-blockers appear to be most frequently associated with nightmares, with some patients on propranolol revealing disturbing dreams on direct questioning. Tricyclic antidepressants may be associated with nightmares, and even delirium, in the elderly. Agents affecting the neurotransmitters  $\gamma$ -aminobutyric acid (GABA), acetylcholine, and histamine are less likely to be associated with nightmares. (Pagel & Helfter, *Human Psychopharmacol Clin Exp* 2003)

**370. The answer is B.** Triptans, 5-HT<sub>1B/1D</sub> agonists, are effective acute medications to abort acute episodic migraines. However, they should not be used in migraine sufferers who have untreated or symptomatic vascular disease, including uncontrolled hypertension and ischemic cerebrovascular or cardiovascular disease. This woman may have perimenopausal exacerbation of her migraine headaches. She should not be put on either a short- or long-acting triptan for her migraines. Given the frequency of her headaches, she will not be comforted by lack of treatment and she is at risk of medication overuse headaches should you start frequent use of over-the-counter (OTC) medications or a butalbital/acetaminophen/caffeine combination. She should be offered a daily preventative medication to decrease the frequency and severity of her migraines. A preventative medication that is also an antihypertensive agent, such as a calcium-channel blocker,  $\beta$ -blocker or an angiotensin II receptor blocker would be appropriate. Preventative treatment of her headaches may only be needed for a few months until she experiences a postmenopausal remission of her headaches. (Olesen, Goadsby, Ramadan, et al., *Headaches*, Chapter 51, 2005)

**371. The answer is E.** Studies have failed to show that real acupuncture in adults is superior to medical treatment in the prophylaxis of migraine headaches. A blinded study compared sham acupuncture to real acupuncture in migraine patients who kept a diary to document headache symptoms. Sham acupuncture was performed into points that were felt to have no influence on headaches. Real acupuncture treatment was performed with insertion and manipulation into points related to the patient's pain topography and to principles of traditional Chinese medicine. No statistically significant difference was found between the two treatment groups in any pain measure, including migraine attack frequency and total migraine days. However, within-group comparisons found that all migraine pain parameters improved in both treatment groups, and nausea decreased in the patients with real acupuncture. The blinding was successful. The study concluded that real acupuncture was no better than sham acupuncture in preventing attacks in migraine sufferers. However, both treatments offered benefit, emphasizing the strong placebo effect that factors into migraine management. Migraine patients who believe in its benefit may obtain headache relief with acupuncture, but scientific validity for the treatment is still controversial. Acupuncture has not been shown to be of benefit in children. (Alecrim-Andrade, Maciel-Junior, Cladellas, et al., *Cephalalgia* 2006)

**372. The answer is B.** Relaxation techniques, biofeedback, stress-management training, and cognitive biofeedback can be used as alternatives or adjuncts to medication in the treatment of frequent TTHs. Minimal contact treatment formats with only a few clinical visits, but with home study materials and phone

contact, can be used in self-motivated patients. However, cognitive impairment, overuse of medication, severe chronic daily headache (CDH), nonadherence to headache diaries, psychiatric disease, and advanced age may limit success with these minimal-contact treatment programs, which work best with the self-motivated, insightful patient. (Holroyd, *Curr Pain Headache Rep* 2002)

**373. The answer is D.** SUNCT/SUNA is particularly refractory to prevention with oral medications. Some patients have responded to lamotrigine (Lamictal), with a less predictable response to topiramate (Topamax). Gabapentin (Neurontin) and carbamazepine (Tegretol) have also been tried with variable benefit. This headache does not respond to indomethacin, distinguishing SUNCT/SUNA from the PHs and hemicrania continua. The lack of response to indomethacin (Indocin) and the response to intravenous (IV) lidocaine can be used to aid in the diagnosis of SUNCT/SUNA. (Cohen, *Cephalalgia*, 2007)

**374. The answer is E.** All of the medications listed are used to prevent the episodic facial pain of trigeminal neuralgia, but carbamazepine (Tegretol), at doses from 300 to 800 mg/day, is generally most effective. The effect of the medication may decrease over time, with higher doses required to achieve pain relief. Dizziness and gastric intolerance are the most common side effects of carbamazepine; skin and hemopoietic toxicities are the most serious side effects. Oxcarbazepine (Trileptal), a derivative of carbamazepine, is generally better tolerated, with probably similar efficacy to carbamazepine. Oxcarbazepine is associated with hyponatremia, and serum sodium levels should be monitored in patients on the medication for long periods of time. (Cheshire, *Curr Pain Headache Rep* 2007)

**375. The answer is A 1, B 2, C 1, D 5, E 3.** Weight concerns often factor into the decision when choosing a preventative therapy for headaches. Obesity is a risk factor for chronification of headaches, as well as the major cause of idiopathic intracranial hypertension. Topiramate (Topamax) is either weight neutral or associated with weight loss; amitriptyline (Elavil) and divalproex sodium (Depakote), and to a lesser degree propranolol (Inderal), are associated with weight gain. Propranolol may alleviate tremors, both chronic familial and situational (as with musical auditions). Anxiety and panic attacks may be treated with  $\beta$ -blockers but they should probably be avoided in dysthymic individuals because depression may be exacerbated. Athletes may not want the fatigue and decreased heart rate associated with a  $\beta$ -blocker. Insomnia may improve with the sedation of a night time dose of a tricyclic antidepressant such as amitriptyline. Constipation with the antihypertensive calcium channel blocker verapamil (Calan) may be beneficial to some patients with the comorbid conditions of migraine and irritable bow-

el syndrome. Word-finding difficulty or other cognitive problems may be noted rarely by patients taking topiramate, especially early in the dose escalation. Side effects may be minimized by very slow dose escalation by 12.5 mg increments a week. Divalproex sodium has been linked with tremor and hair loss. Women should be advised to take folate supplementation and avoid pregnancy on divalproex sodium because of the risk of birth defects. (*Wolff's Headache and Other Pain*, Chapter 11; Ramadan, *Headache* 2007)

**376. The answer is D.** Although verapamil (Calan) is the preventative drug of choice in patients with CHs, it may require escalation of the dose over time to be effective. Likewise, lithium needs to be titrated over time to reach a therapeutic level. A short intensive course of oral corticosteroids can be highly effective in decreasing cluster attack frequency and severity while long-term preventative medication is being increased to an efficacious level or dose. Because of steroid side effects with chronic use, a short course of high-dose prednisone or dexamethasone is rapidly tapered, in conjunction with the dose escalation of a long-term preventative medication. Indomethacin (Indocin) and gabapentin (Neurontin) have not been shown of consistent benefit in prevention of CH. (Goadsby, Cohen, & Matharu, *Curr Neurol Neurosci Rep* 2007)

**377. The answer is A 1, B 3, C 5, D 4, E 2.** Most medications used for prevention of headaches have some concerns when given to pregnant women. Postmarketing experience indicates a possible association between in utero exposure to topiramate (Topamax) and hypospadias. Divalproex sodium (Depakote) is the most teratogenic of the listed medications, associated primarily with developmental anomalies of the spinal cord. Women of childbearing potential on divalproex sodium should take supplemental folate to decrease the risk of birth defects with an unexpected pregnancy. Propranolol (Inderal) is rarely associated with specific anomalies but may cause low birth weight. Methysergide (Sansert), a semisynthetic ergot alkaloid, is used in obstetrical practice as an oxytocic agent and is no longer used as a preventative for headaches in the United States. First-trimester exposure to angiotensin-converting enzyme (ACE) inhibitors such as lisinopril (Prinivil®) is associated with cardiac defects (atrial and ventricular defects, patent ductus arteriosus) and other less common congenital anomalies. Use of ACE inhibitors during the second and third trimesters of pregnancy is also contraindicated because of the association with an increased risk of fetopathy. (*Wolff's Headache and Other Pain*, Chapter 11; Ramadan, *Headache* 2007)

**378. The answer is C.** The causal relationship between patent foramen ovale (PFO) and migraine with aura awaits elucidation. The mechanism by which PFO

closure could potentially reduce migraine frequency and severity has not been explained. Trials of patients with presumed PFO-related stroke do not indicate if closure benefits headache frequency and severity. Studies of patients with PFO closure after paradoxical embolization did not have age-matched, sham-operated controls, and the collection of headache data was retrospective. Aspirin used daily in these migraine and stroke patients may decrease chronic headaches, and migraine headaches may improve after an ischemic stroke, due to an unknown mechanism. Transcatheter closure of PFOs is associated with cardiovascular and cerebrovascular adverse events, as noted in a randomized controlled trial of PFO closure in migraineurs, and is not an entirely benign procedure. The combination of antiplatelet agents (e.g., aspirin and clopidogrel [Plavix<sup>®</sup>]) used after PFO closure may increase intracranial hemorrhage risk. Until more information is available about the cause of the epidemiologic correlation between migraine with aura and PFO, and until it is clear that closure is beneficial, routine PFO closure in migraine patients cannot be recommended. (Diener, Kurth, & Dodick, *Curr Opin Neurol* 2007)

**379. The answer is C.** Ethinyl estradiol induces the main metabolic enzyme for lamotrigine (Lamictal), and levels may be reduced by up to 50% in women on oral contraceptives. When levels of the medication are critical, such as in patients with epilepsy, they should be checked before and after starting oral contraceptives. There may even be an increase in the levels of lamotrigine on placebo birth control pill days. The other drugs do not interact with oral contraceptives. (Harden & Leppik, *Neurology* 2006)

**380. The answer is B.** The pain of a CH generally lasts 15 to 180 minutes. Because of the CH's rapid build-up of pain, severe pain intensity, and relatively short duration, a triptan with rapid peak serum concentration (subcutaneous or nasal mucosal absorption) is most effective. Subcutaneous sumatriptan (Imitrex), 6 or 4 mg, is the drug of choice to abort a cluster attack. Nasal sprays are somewhat less effective but may be better tolerated than an injectable medication. Rectal administration of medication for pain relief is generally less popular. Time to pain relief may be too long with an oral agent in CH. Cluster headache sufferers, often middle-aged men, may have vascular risk factors or a history of vascular disease that can contraindicate the use of a 5-HT<sub>1B/1D</sub> agonist such as sumatriptan or ergotamine. (Goadsby, Cohen, & Matharu, *Curr Neurol Neurosci Rep* 2007)

**381. The answer is C.** Chronic tension-type headache (CTTH) is more refractory to treatment than is episodic tension-type headache (ETTH). The mechanisms by which electromyographic (EMG) biofeedback training reduces CTTH are un-

clear; biofeedback may work through control of pericranial muscle contraction, as well as other central nervous system (CNS) and psychological pain modulation. The combination of behavior therapies, such as EMG biofeedback, with medical treatment using tricyclic antidepressants (TCAs) offers additive, and more rapid, benefit over the two therapies individually. One study found that EMG biofeedback training alone was associated with better long-term headache improvement than the initial combination of medical and biofeedback treatments, at least after the medication was eventually discontinued 20–24 months after initiation of treatment. It was suggested that the patients who attributed their improvement to medication may have discontinued the behavioral treatment, with loss of the combined benefit. Long-term maintenance of therapy is important for sustained benefit, especially in patients with comorbid psychiatric disease who are likely to relapse. (Holroyd, *Curr Pain Headache Rep* 2002)

**382. The answer is C.** All of the listed agents have been used for prevention of chronic headaches, including migraines. Some data indicate that coenzyme Q10, magnesium, butterbur, and acupuncture are superior to placebo for chronic treatment of headaches. Feverfew (*Tanacetum parthenium L.*) extract is a herbal preparation used for prevention of attacks of migraine. Randomized, placebo-controlled, double-blind trials assessing the efficacy of feverfew for preventing migraine were reviewed in a Cochrane database report. Five trials (343 patients) using clinical outcome measures met the inclusion criteria. Results from these trials were mixed and did not convincingly establish that feverfew is efficacious for preventing migraine. The review concluded that evidence from randomized, double-blind trials did not indicate an effect of feverfew over and above placebo for preventing migraine. Trials of feverfew reported only mild and transient adverse events. (Pittler & Ernst, *Cochrane Database Syst Rev* 2004)

**383. The answer is B.** Primary cough headache generally responds to preventative treatment with indomethacin (Indocin) at doses ranging from 25 to 150 mg daily. The pathophysiologic mechanism to explain the distinctive response of primary cough headache to this particular medication is not clear. Headaches triggered by sexual intercourse or exercise may also be prevented with indomethacin. (Pascual, *Curr Headache Rep* 2005)

**384. The answer is A.** Currently, no triptan is FDA approved for the short-term, peri-menstrual prevention of menstrual migraine. However, two long-acting triptans (naratriptan [Amerge]) and frovatriptan [Frova]) and one short-acting triptan (zolmitriptan [Zomig]) have been shown to prevent menstrual migraine in large, randomized, placebo-controlled clinical trials. The triptan is given daily



for several days prior to the expected menstrual-related headache, continuing for several days after the time of the expected headache has passed. A small, open-label study of sumatriptan showed efficacy. Triptans for short-term menstrual migraine prevention are well tolerated without any expected side effects. The FDA recommends that different brands of triptans not be used together within 24 hours. This means that a headache that breaks through triptan menstrual migraine prophylaxis should be treated with another dose of that same triptan. Prevention of menstrual migraine with triptans is most effective for women with regular, predictable menses. (Newman, *Headache* 2007)

**385. The answer is D.** As distinct from PH and hemicrania continua, SUNCT/SUNA does not respond to indomethacin (Indocin). Although CHs may be treated acutely with inhalational oxygen or short-acting subcutaneous or intranasal triptans, these agents are not effective to abort attacks of SUNCT. Oral agents are not going to be effective for acute treatment because of the transient, albeit intense, pain of SUNCT/SUNA. Intravenous lidocaine has been noted, in some patients, to reduce attack frequency and severity for periods ranging from days to months. (Cohen, *Cephalalgia* 2007)

**386. The answer is D.** Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been associated with lamotrigine (Lamictal) therapy. Plus the combination of lamotrigine and divalproex sodium (Depakote) increases the risk of an adverse skin reaction. In a search of published and reported cases of lamotrigine-associated SJS or TEN, concomitant use of divalproex sodium was reported in 74% of the SJS cases and 64% of the TEN cases. The severe skin drug reactions generally occur early in treatment. Dose escalation of lamotrigine at the initiation of treatment should be slower in patients who are also taking divalproex sodium. (Schlienger, Shapiro, & Shear, *Epilepsia* 1998; Kocak, Girisgin, Gul, et al., *Am J Clin Dermatol* 2007)

**387. The answer is A.** Serotonin toxicity results from an excess of 5-HT in the CNS, which can be due to several pharmacological mechanisms. These include inhibition of 5-HT metabolism, prevention of its reuptake, increase in its precursors, or increase in its release. The life-threatening clinical effects may be mediated by the 5-HT<sub>2A</sub> receptors. This woman was taking phenelzine (Nardil), a monoamine oxidase inhibitor, and an occasional triptan, a 5-HT<sub>1B/1D</sub> agonist without difficulty. However, she made a poor choice when she ingested methylenedioxymethamphetamine (MDMA), popularly known as ecstasy, at a nightclub, and exceeded her body's tolerance for 5-HT. She exhibits the neuromuscular effects, autonomic effects, and mental status changes of serotonin syndrome. Her



hyponatremia is a hint that her symptoms are related to MDMA, which may produce life-threateningly low sodium levels. Fugu is a potentially fatal sashimi dish prepared from pufferfish, which contains the neurotoxin tetrodotoxin. Sherms are tobacco or marijuana cigarettes soaked in formaldehyde. Special K is a recreational form of ketamine with a short-acting hallucinogenic effect. Absinthe is a high-proof alcoholic beverage derived from wormwood. (Isbister, Buckley, & Whyte, *Med J Aust* 2007)

**388. The answer is C.** Successful and reliable options for the medical treatment of the excruciating pain of CH are limited. Surgical procedures that target the trigeminal nerve or cranial parasympathetic outflow tracts have been attempted with variable results and risk of significant complications. Deep brain stimulation of the hypothalamus, an area of activation in CH, has been shown to be effective, but the potential surgical complications make this treatment essentially inappropriate for all but the most intractable of patients. Occipital nerve stimulation has been shown to benefit patients with chronic medication-unresponsive CH, even though its mechanism of action is not clear. Occipital nerve stimulation may be especially beneficial for patients who have experienced transient headache relief from occipital nerve injections of anesthetic or steroid medications. Multiple pain pathways, including cervical, somatic trigeminal, and dural trigeminal vascular afferents, that converge on second-order neurons in the brainstem and on third-order cortical neurons, may be impacted by stimulation of the occipital nerve. The results of two recent studies showed encouraging results. The technique appears to be safe although it may be plagued by technical glitches. (Burns, Watkins, & Goadsby, *Lancet* 2007; Magis, Allena, Bolla, et al., *Lancet Neurol* 2007)

**389. The answer is E.** Benign headaches associated with sexual activity are either a dull aching pain prior to orgasm or a severe pain at orgasm. Despite the benefit of reassurance, resumption of pleasurable sexual activity may require medication for long-term daily prophylaxis, preemptive treatment prior to sexual activity, or acute treatment of the sex-induced headache. Headaches associated with sexual activity can be prevented with indomethacin (Indocin),  $\beta$ -blockers, or triptans. Frese et al. (2007) evaluated the prevention and treatment of headache associated with sexual activity, with imaging studies used to rule out underlying secondary cause of headache. Some patients responded to indomethacin for preemptive (prior to sexual activity) therapy, with other patients enjoying improvement in their sexual satisfaction with daily  $\beta$ -blocker prophylaxis. Triptans used for headaches associated with sexual activity confer benefit with either preemptive (long-acting preparations) or acute (rapid-onset preparations) treatment. Acute headache with sexual activity is rarely due to a leakage of a cerebral aneurysm;

repeated headaches associated with sexual activity are generally annoying but benign. (Frese, Gantenbein, Marziniak, et al., *Cephalalgia* 2006; Frese, Rahmann, Gregor, et al., *Cephalalgia* 2007)

**390. The answer is A.** The most common adverse effects associated with divalproex sodium are relatively benign (weight gain, tremor, and hair thinning), but serious adverse effects can occur. Zinc supplementation may decrease hair loss associated with the medication. Rare adverse effects include metabolic (hyperammonemic) encephalopathy, coagulopathy, hepatotoxicity, teratogenicity, polycystic ovaries with the potential for sterility or carcinogenesis, and pancreatitis. Acute pancreatitis in children is often drug-induced and has been associated with divalproex sodium. Pancreatitis is not generally associated with the other medications listed. (Gerstner, Büsing, Bell, et al., *J Gastroenterol* 2007; Grauso-Eby, Goldfarb, Feldman-Winter, et al., *Pediatr Neurol* 2003)

**391. The answer is A 2, B 3, C 1, D 4, E 4.** Zonisamide (Zonegran<sup>®</sup>) has shown benefit in open-label studies in the prevention of episodic migraine. It is weight-neutral or associated with weight loss and may be appropriate when cognitive side effects interfere with the use of topiramate (Topamax). It is a sulfonamide and should be avoided in patients who are allergic to sulfa medications. Monoamine oxidase inhibitors (MAOI) such as phenelzine (Nardil) have been used in patients resistant to more usual migraine preventative treatment; however, interactions with foods containing tyramine and medications such as sympathomimetics make use of MAOIs problematic. These medications should not be combined with fluoxetine (Prozac<sup>®</sup>), isometheptene (Midrin<sup>®</sup>), meperidine (Demerol<sup>®</sup>), or certain triptans. The combination of verapamil (Calan) and lithium risks lithium toxicity at standard doses, so the lithium dose should be reduced. Amitriptyline (Elavil), a TCA, inhibits the reuptake of norepinephrine and serotonin in adrenergic and serotonergic neurons, potentiating their neuronal activity. The antihistaminic and antimuscarinic effects of TCAs account for their adverse effects, and patients with a history of urinary retention, angle-closure glaucoma, or increased intraocular pressure are at particular risk. Initiation of topiramate (Topamax) treatment has precipitated acute angle-closure or acute myopia and should be avoided in patients with untreated glaucoma. (*Wolff's Headache and Other Pain's*, Chapter 11; Ramadan, *Headache* 2007)

**392. The answer is E.** Medications with predominantly hepatic metabolism may decrease the efficacy of oral contraceptives, especially when higher-than-usual doses of the medications are combined with low-dose estrogen contraceptives. To ensure maximal pregnancy prevention, women taking enzyme-inducing

medications should use oral contraceptives containing at least 50 µg of ethinyl estradiol, and low-dose estrogen formulations should be used with caution. Divalproex sodium (Depakote), gabapentin (Neurontin), levetiracetam (Keppra), tiagabine (Gabitril), vigabatrin (Sabril), zonisamide (Zonegran), and pregabalin (Lyrica) do not induce cytochrome P450 3A4 enzymes and therefore do not interact with oral contraceptives. Women who are on low-dose oral contraceptives should be warned about possible contraceptive failure at topiramate (Topamax) doses greater than 200 mg/day. (Harden & Leppik, *Neurology* 2006)

**393. The answer is A.** Antagonism of calcitonin gene-related peptide (CGRP) is a promising abortive treatment of migraine. Two CGRP antagonists, BIBN4096 (Oliceridine) and MK-0974 (Telcagepant), IV and oral agents, respectively, are being investigated in clinical trials. Antagonists of CGRP appear to inhibit the peptide's cerebral vasodilatory effect without causing cerebral or coronary vasoconstriction. Although small amounts of these agents may penetrate the brain, they inhibit peripheral neurogenic vasodilatation and inflammation. They are well tolerated, with only mild paresthesias noted with high-dose BIBN4096, and they appear to be efficacious as compared to placebo in relieving the pain of migraine. (Doods, Arndt, & Just, *Trends Pharmacol Sci* 2007; Tepper & Stillman, *Headache* 2008)

**394. The answer is B.** A randomized, double-blind, placebo-controlled multicenter trial by Friedman et al. (2007) evaluated dexamethasone (Decadron) 10 mg IV versus placebo in 205 patients evaluated in the emergency department (ED) with acute migraine. All patients also received IV metoclopramide (Reglan) as a migraine-abortive and anti-nausea medication and IV diphenhydramine (Benadryl) to prevent extrapyramidal reaction to the metoclopramide. Persistent pain-free outcome was achieved in 25% of those migraine patients randomized to IV dexamethasone and 19% of those given IV placebo ( $p = 0.34$ ). However, in patients with migraine lasting longer than 72 hours, 38% of patients on dexamethasone and 13% of patients on placebo were persistently pain-free ( $p = 0.06$ ). No differences in side effects or functional impairment were noted in either group. There may be an adjunctive role for IV steroid treatment of patients with persistent intractable migraine. (Friedman, Greenwald, Bania, et al., *Neurology* 2007)

**395. The answer is C.** The CGRP receptor antagonist MK-0974 (Telcagepant) has been studied in a randomized, double-blind, parallel-group, dose-ranging clinical trial comparing MK-0974 to rizatriptan (Maxalt) and placebo. Since CGRP receptor antagonists lack direct vasoconstrictor activity, this medication may be appropriate for acute abortive therapy in migraine patients with cardiac and cerebro-

vascular disease. Two-hour pain relief was significantly improved with MK-0974 as compared to placebo. Two-hour pain relief with higher doses of MK-0974 was comparable to rizatriptan in the 50–70% range. The CGRP receptor antagonist was well tolerated with nausea, dizziness, and somnolence noted as the most common adverse experiences. This class of acute abortive medication offers promise for pain relief in combination with triptans and in patients for whom triptans are not appropriate or efficacious. The CGRP receptor antagonists may be combined with triptans for additive efficacy. (Ho, Mannix, Fa, et al., *Neurology* 2007)

**396. The answer is A.** Topiramate (Topamax) has been studied in children with pediatric migraine with or without aura, as defined by the International Headache Society (IHS) classification. A significant benefit in reduction of mean monthly migraine days was noted, as compared to children receiving placebo. However, there was no significant difference in the percentage of patients with more than 50% reduction in mean monthly migraine days. Divalproex sodium (Depakote), verapamil (Calan), amitriptyline (Elavil), and fluoxetine (Prozac) are used with variable efficacy to prevent migraine headaches in adults; however, they have not been adequately evaluated in children. Medications to prevent chronic headaches have rarely been studied in children, and their benefit in children is generally extrapolated from data on efficacy in adults with chronic headaches. (*Wolff's Headache and Other Pain's*, Chapter 27; Lakshmi, Singhi, Malhi, & Ray, *J Child Neurol* 2007)

**397. The answer is A.** The intranasal triptans, sumatriptan (Imitrex) and zolmitriptan (Zomig), are particularly suitable to treat the relatively short-duration adolescent migraine headache, which may be accompanied by severe nausea. A multicenter, randomized, double-blind, placebo-controlled, two-way, two-attack, crossover design was used to evaluate the efficacy and tolerability of zolmitriptan nasal spray in the treatment of adolescent migraine. A total of 171 patients (mean age: 14.2 years; 57.3% female) treated one or more attack with study medication (intention-to-treat population). The onset of significant pain relief was apparent 15 minutes after treatment with zolmitriptan nasal spray. At 1 hour after the dose, zolmitriptan nasal spray produced a higher headache response rate than did placebo (58.1% versus 43.3%). Treatment with zolmitriptan nasal spray was well tolerated and effective in the acute treatment of adolescent migraine. Ibuprofen and acetaminophen are used for acute migraine treatment in children; adolescents with an acute migraine are more easily treated with intranasal, as opposed to subcutaneous, sumatriptan. Although older adolescents are rarely considered adult-like in their behavior, the usual acute and preventative medications are used to treat their increasingly adult-like headaches. (Lewis, Winner, Hershey, et al., *Pediatrics* 2007)

**398. The answer is A.** All of the answers are adverse effects noted with treatment with topiramate (Topamax), which can be used in the prevention of episodic or chronic migraine. Paresthesias (tingling sensation in the hands and feet) were the most common adverse effect noted in a recently published randomized, placebo-controlled, parallel-group, multicenter study of the efficacy and safety of topiramate (100 mg/day) as compared with placebo for the treatment of chronic migraine. Topiramate treatment resulted in a statistically significant mean reduction of migraine/probable migraine headache days (topiramate  $-6.4$  versus placebo  $-4.7$ ,  $p = 0.010$ ) and migraine headache days relative to baseline (topiramate  $-5.6$  versus placebo  $-4.1$ ,  $p = 0.032$ ). Adverse events occurred in 132 (82.5%) and 113 (70.2%) of topiramate-treated and placebo-treated subjects, respectively, and were generally of mild or moderate severity. The most commonly reported adverse event in the topiramate group was paresthesias ( $n = 46$ ; 28.8%). Foods rich in potassium, such as bananas, oranges, and tomatoes, and a slow escalation of the dose may alleviate the symptoms of paresthesias as treatment with topiramate is being initiated. (Silberstein, Lipton, Dodick, et al., *Headache* 2007)

**399. The answer is A.** Polycystic ovarian syndrome (PCOS) is characterized by clinical signs of endocrine dysfunction, such as irregular menstruation, hirsutism, and infertility, but its pathogenesis and presentation are heterogeneous. There appears to be an association between divalproex sodium (Depakote) and PCOS in young women treated for epilepsy or bipolar disorder, which may translate into increased risk in women taking divalproex sodium for migraines. Divalproex sodium is associated with other menstrual abnormalities and hyperandrogenism as well. Divalproex sodium may be used in young women for migraine prevention, but with monitoring of its endocrinologic and reproductive adverse events. The other medications listed have not been associated with PCOS. (Duncan, *Epilepsia* 2001; O'Donovan, Kusumakar, Graves, et al., *J Clin Psychiatry* 2002)

**400. The answer is E.** Generalized anxiety disorder (GAD) is often treated acutely with benzodiazepines, but these medications may be associated with the development of tolerance, psychomotor impairment, cognitive changes, physical dependence, and a withdrawal reaction on abrupt discontinuation. Medications used to treat depression may be effective in patients with GAD. The serotonin and noradrenaline reuptake inhibitors, including venlafaxine XR (Effexor XR) and duloxetine (Cymbalta), have demonstrated efficacy over placebo in randomized long-term and acute treatment trials. Paroxetine (Paxil) and other selective serotonin reuptake inhibitors (SSRIs) are effective in the treatment of GAD. Buspirone (BuSpar) is an azapirone, a group of drugs that work at the 5-HT<sub>1A</sub> receptor, which has been used for short treatment of patients with GAD. Cognitive-behavioral therapy

(CBT) shows the greatest benefit of the psychological therapies, with evidence of durable treatment gains in patients with GAD. In many patients distressed by GAD, treatment with a combination of medication and nonpharmacological intervention is necessary. (Allgulander, Bandelow, Hollander, et al., *CNS Spectr* 2003)

**401. The answer is D.** Angiotensin-converting enzyme (ACE) inhibitors lower arteriolar resistance and increase venous capacitance. Lisinopril (Prinivil, Zestril) up to 20 mg/day was evaluated in a double-blind, placebo-controlled, crossover study of migraine patients with two to six episodes a month. Hours with headache, days with headache, days with migraine, and headache severity index were significantly reduced with lisinopril compared with placebo. Lisinopril appears to have a clinically important prophylactic effect in migraine, but the other ACE inhibitors have not been evaluated in migraine patients. It is not clear if lisinopril's beneficial effect in migraine prevention is unique among the ACE inhibitors or if it represents a class effect of ACE inhibitors. Angiotensin-converting enzyme inhibitors should not be given to pregnant women because of their teratogenicity. (Schrader, Stovner, Helde, et al., *BMJ* 2001)

**402. The answer is D.** Although the triptan product labeling indicates a contraindication in patients with either familial or sporadic hemiplegic migraine because of theoretic risk of ischemic stroke, there is little evidence of increased vascular risk with triptan treatment in patients with hemiplegic or basilar-type migraine. Published reports of triptans used in patients with hemiplegic migraine, basilar-type migraine, and migraine with prolonged or prominent aura have not indicated concern about the use of these agents in these patients. Triptans are not contraindicated in the other migraine types listed. (Artto, Nissilä, Wessman, et al., *Eur J Neurol* 2007; Klapper, Mathew, & Nett, *Headache* 2001)

**403. The answer is A.** Some medications used for prevention of headaches are associated with the severe cutaneous reactions, SJS and TEN. In a case control study of patients with epilepsy, SJS and TEN were associated with phenytoin (Dilantin), phenobarbital, and carbamazepine (Tegretol) at onset of monotherapeutic treatment. The association of the cutaneous reaction with divalproex sodium (Depakote) seemed to be confounded by concomitant short-term therapy with other causal drugs. Lamotrigine (Lamictal) also had the potential for severe skin reactions, but generally in combination with divalproex sodium therapy. The period of increased risk with lamotrigine, in combination with divalproex sodium, is generally during the first 8 weeks of treatment. Dose escalation at the initiation of lamotrigine treatment is slowed when the medication is prescribed in combination with divalproex sodium. (Rzany, Correia, Kelly, et al., *Lancet* 1999)

**404. The answer is A 2, B 4, C 2, D 1, E 2.** Steroids are appropriate treatment for orbital inflammatory disease, such as Tolosa-Hunt syndrome, idiopathic orbital inflammation (formerly known as *orbital pseudotumor*), orbital myositis, Graves' disease, Wegener's granulomatosis, and sarcoidosis. They are also used in patients with giant cell arteritis (GCA) and as adjunctive therapy in acute bacterial meningitis. Although steroids have been used for short-term treatment of idiopathic intracranial hypertension (IIH), their prolonged use or abrupt withdrawal has been implicated in the production of IIH. Patients with suspected herpes simplex encephalitis should be started on empiric IV acyclovir while waiting for polymerase chain reaction (PCR) test results from the spinal fluid, although the antiviral treatment risks acute renal insufficiency. (Lutt, Lim, Phal, & Rosenbaum, *Semin Arthritis Rheum* 2007)

**405. The answer is D.** Seven different triptans, selective serotonin 5-HT<sub>1B/1D</sub> agonists, are clinically available for treatment of acute migraine. To assess the choice of triptans, Ferrari et al. (2001) requested raw patient data of all double-blind, randomized, controlled clinical trials of oral triptans in migraine, and 53 clinical trials (12 unpublished) involving 24,089 patients were reviewed. Mean results for sumatriptan (Imitrex) 100 mg were used for comparison with the other drugs. Compared with sumatriptan 100 mg data, rizatriptan (Maxalt) 10 mg showed better efficacy and consistency, and similar tolerability; eletriptan (Relpax) 80 mg showed better efficacy, similar consistency, but lower tolerability; almotriptan (Axert) 12.5 mg showed similar efficacy at 2 hours but better tolerability; naratriptan (Amerge) 2.5 mg showed lower efficacy and better tolerability. Results for zolmitriptan (Zomig) 5 mg and eletriptan 40 mg showed very similar results. The meta-analysis concluded that rizatriptan 10 mg, eletriptan 80 mg, and almotriptan 12.5 mg provided the highest likelihood of consistent success. Because of increased side effects at the 80-mg dose, eletriptan is marketed at 40 mg in the United States for treatment of acute migraines. (Ferrari, Roon, Lipton, & Goadsby, *Lancet* 2001)

**406. The answer is A 3, B 5, C 1, D 4, E 1.** Vigabatrin (Sabril) is an antiepilepsy medication available in Canada and other countries, but not yet in the United States. It is an irreversible GABA-transaminase inhibitor that is being investigated for the treatment of cocaine and methamphetamine addiction. Long-term use may lead to retinal damage in up to a quarter of patients. Flibanserin (Ectris<sup>®</sup>) has preferential affinity for serotonin 5-HT(1A), dopamine D(4k), and serotonin 5-HT(2A) receptors and was thought to have antidepressant properties. However a beneficial side-effect was noted in unsuccessful antidepressant clinical investigation. It is now in clinical trials as an enhancement of female libido and



sexual arousal. Calcitonin gene-related peptide (CGRP) is found in central and peripheral locations, including meninges, trigeminal ganglion, trigeminocervical complex, brainstem nuclei, and cortex. Elevation of CGRP occurs during migraine, resolving following migraine-specific treatment. BIBN4096 (Olcegepant) is the first CGRP antagonist for the treatment of migraine that has been tested in clinical trials, but its principal limitation is that BIBN4096 presents low oral bioavailability and has only been tested through intravenous formulation. The first oral CGRP antagonist, MK-0974 (Telcagepant), has recently been shown to be highly effective in the treatment of migraine attacks. In a multisite, 14-week, double-blind, randomized controlled trial, the effects of topiramate (Topamax) (up to 300 mg/day) were compared with placebo on physical health, obsessional thoughts and compulsions about using alcohol, and on the psychosocial well-being of 371 alcohol-dependent subjects. Topiramate compared with placebo significantly ( $p < .05$  for all comparisons) decreased obsessional thoughts and compulsions about using alcohol, increased subjects' psychosocial well-being, and improved some aspects of quality of life, thereby diminishing the risk of relapse and longer-term negative outcomes. (Borsini, Evans, Jason, et al., *CNS Drug Rev* 2002; Farinelli, Missori, & Martelletti, *Expert Rev Neurother* 2008; Johnson, Rosenthal, Capece, et al., *Arch Intern Med* 2008; Tepper & Stillman, *Headache* 2008)

**407. The answer is C.** Randomized, double-blind, placebo-controlled trials of topiramate (Topamax) in patients with chronic migraine have shown benefit and tolerability, even in patients with medication overuse headache (MOH). Diener et al. (2007) found that topiramate, at a target dose of 100 mg/day, significantly reduced the mean number of monthly migraine days ( $\pm$  SD) by  $3.5 \pm 6.3$ , compared with placebo ( $-0.2 \pm 4.7$ ,  $p < 0.05$ ). Over three-quarters of the patients in the study met the definition for acute medication overuse at baseline. Study completion rates for topiramate- and placebo-treated patients were 75% and 52%, respectively. The most common adverse events associated with topiramate use were paraesthesia, nausea, dizziness, dyspepsia, fatigue, anorexia, and disturbance in attention, with cognitive effects seen least frequently. Silberstein et al. (2007) found that topiramate treatment, at daily doses of approximately 100 mg without concomitant preventative medications, resulted in statistically significant improvement compared with placebo in mean monthly migraine/probable migraine and migraine headache days. Discontinuation rates were similar between placebo and drug treatment, and the most common adverse event with topiramate was paresthesias. Generic topiramate is now available. (Silberstein, Lipton, & Dodick, *Headache* 2007; Diener, Bussone, Van Oene, et al., *Cephalalgia* 2007)



**408. The answer is C.** A randomized double-blind trial compared a daily combined dose of riboflavin 400 mg, magnesium 300 mg, and feverfew 100 mg with a placebo containing 25 mg riboflavin. Riboflavin alone showed an effect comparable to the combination of riboflavin, magnesium, and feverfew. The placebo response was high, suggesting that the placebo, riboflavin 25 mg, may be an active comparator. There is no clear evidence of efficacy of these compounds for migraine prophylaxis, although they may be appropriate for patients who do not want prescription prophylactic medication or who want adjunctive therapy. In general, at least 6 weeks of treatment is needed with the combination of these medications to assess efficacy in an individual patient. (Maizels, Blumenfeld, & Burchette, *Headache* 2004)

**409. The answer is A.** A head-to-head comparison was made of a combination nonprescription migraine medication (acetaminophen 500 mg, aspirin 500 mg, and caffeine 130 mg) with a prescription migraine product (50 mg sumatriptan [Imitrex]) in a randomized, controlled clinical trial in which 171 subjects were treated at the first sign of a migraine attack. The combination of acetaminophen, aspirin, and caffeine was significantly more effective ( $p > .05$ ) than sumatriptan in the early treatment of migraine, as shown by superiority in summed pain intensity difference, pain relief, pain intensity difference, response, sustained response, relief of associated symptoms, use of rescue medication, disability relief, and global assessments of effectiveness. The small sample size and potential randomization bias in this study complicate the interpretation of its results. Triptans are more likely to cause MOH than are combination analgesics. There is a shorter withdrawal period when a triptan, as compared to a combination analgesic, is discontinued. Studies of the combination medication show benefit over placebo and over ibuprofen in acute treatment of migraine. (Goldstein, Silberstein, Saper, et al., *Headache* 2005)

**410. The answer is E.** *Petasites hybridus*, a perennial shrub, is commonly referred to as “butterbur” because the leaves of the plant were once used to wrap butter. Petasins, extracted from the root of the butterbur plant, are the active ingredient and have been used as a preventative treatment of migraine. A randomized trial compared *Petasites* extract 75 mg b.i.d., *Petasites* extract 50 mg b.i.d., or placebo b.i.d. in 245 patients with migraine. The proportion of patients with  $\geq 50\%$  reduction in attack frequency after 4 months was 68% for patients in the *Petasites* extract 75-mg arm and 49% in the placebo arm ( $p < 0.05$ ). The most frequently reported adverse reactions with the treatment were mild gastrointestinal events, predominantly burping. *Petasites* extract 75 mg b.i.d., but not the lower dose, appears to be more effective than placebo and is well tolerated as a preventive therapy for migraine headaches. (Agosti, Duke, Chrubasik, & Chrubasik, *Phytomedicine* 2006; Lipton, Göbel, Einhüpl, et al., *Neurology* 2004)

**411. The answer is B.** Gabapentin (Neurontin) was shown to be an effective prophylactic agent for patients with migraine in a multicenter, blinded, placebo-controlled clinical trial. Patients receiving a stable dose of 2,400 mg/day gabapentin in divided doses showed a statistically significant reduction of at least 50% in the 4-week migraine rate as compared to patients receiving placebo. Gabapentin was generally well tolerated, with mild to moderate somnolence and dizziness noted. The dose-dependent gastric absorption of gabapentin increases its pharmacokinetic variability. High doses with gabapentin result in saturation of gastrointestinal absorption, with bioavailability decreasing with increasing dosage. Gabapentin's half-life is 5–7 hours, depending on creatinine clearance, so the medication should be dosed multiple times a day. It may be used in patients with end-stage renal disease, with adjusted dosing after dialysis. (Mathew, Rapoport, Saper, et al., *Headache* 2001)

**412. The answer is B.** Enzyme-inducing antiepilepsy medications, including carbamazepine (Tegretol) and oxcarbazepine (Trileptal), can reduce serum thyroid hormone concentrations through increased conversion and metabolism. In patients without a thyroid disorder, carbamazepine causes a slight increase in thyrotropin (TSH) without clinical consequences. In hypothyroid patients taking thyroxine supplementation, carbamazepine may precipitate subclinical or overt hypothyroidism with marked increase in TSH. Subclinical changes in thyroid hormone concentration in normothyroid patients may also be seen with phenytoin (Dilantin). Subclinical hypothyroidism has also been noted in children taking divalproex sodium (Depakote). Lamotrigine (Lamictal) and gabapentin (Neurontin) are generally not associated with thyroid abnormalities. (Simko & Horacek, *Acta Neurol Scand* 2007; Pack, *Curr Treat Options Neurol* 2005; Elwes & Binnie, *Clin Pharmacokinet* 1996; Perucca, *Epilepsia* 1999)

**413. The answer is D.** Divalproex sodium (Depakote) inhibits the glucuronidation of lamotrigine (Lamictal) and increases its half-life. The dose of lamotrigine needs to be decreased, when combined with divalproex sodium, to decrease toxicity and potentially life-threatening dermatologic side-effects. (Elwes & Binnie, *Clin Pharmacokinet* 1996)

**414. The answer is E.** Traditional or real acupuncture treatment is not strikingly more effective than usual preventative medication in treating TTHs or migraine headaches. A randomized, controlled, multicenter, patient- and observer-blinded trial compared traditional acupuncture or sham acupuncture in patients with TTH. A >50% reduction in headache days/month at 6 months was found in 33% of patients treated with traditional acupuncture and 27% of sham controls

( $p = 0.18$ ), although headache days were lower with traditional treatment. A randomized, multicenter, double-blind, parallel-group, controlled clinical trial of migraine patients compared traditional (verum) acupuncture, sham acupuncture, and standard medical therapy. Primary outcome was the difference in migraine days between 4 weeks before randomization and weeks 23–26 after randomization. Patients with a reduction of migraine days by at least 50%, 26 weeks after randomization, were 47% in the verum group, 39% in the sham acupuncture group, and 40% in the standard group ( $p = 0.133$ ). The conclusion was that treatment outcomes for migraine patients were similar with sham acupuncture, traditional acupuncture, or standard medical therapy. The psychological compared to physiologic effects of acupuncture and the degree to which any physiologic effects depend on needle placement and insertion depth in headache patients are unclear. (Diener, Kronfeld, Boewing, et al., *Lancet Neurol* 2006; Endres, Böwing, Diener, et al., *J Headache Pain* 2007)

**415. The answer is C.** Frovatriptan (Frova) is a potent 5-HT<sub>1B/1D</sub> receptor agonist and has the highest 5-HT<sub>1B</sub> potency in the triptan class. Frovatriptan has the lowest headache recurrence rate of all the triptans. Frovatriptan's long half-life in plasma of 26 hours, and metabolism by multiple pathways are unique characteristics among the triptans. Frovatriptan has no inhibiting or inducing effects on cytochrome P450 isoenzymes and is only slightly bound to plasma proteins, with a low potential for drug interactions. It has the longest duration of action and a low risk of interactions with other drugs at a recommended 2.5-mg dose for acute migraine treatment. Because of frovatriptan's long half-life, it can be used for menstrual migraine prophylaxis. (Goldstein, *Expert Opin Pharmacother* 2003; Markus & Mikko, *Expert Opin Pharmacother* 2007)

**416. The answer is D.** Angiotensin II receptor blockers (ARBs) modulate the renin-angiotensin-aldosterone system and cause vasodilation, with reduction of vasopressin and aldosterone. The ARB candesartan (Atacand<sup>®</sup>) was found effective as a migraine prophylactic drug in a randomized, double-blind, placebo-controlled crossover study. In a period of 12 weeks, the mean number of days with headache was 18.5 with placebo as compared to 13.6 with candesartan ( $p = .001$ ) in the intention-to-treat analysis ( $n = 57$ ). The tolerability profile of candesartan was comparable with that of placebo. The efficacy of olmesartan (Benicar<sup>®</sup>), another ARB, as a migraine prophylactic agent was evaluated for patients with elevated blood pressure and migraine in a small open study. Migraine prophylaxis has not been studied with the other ARBs listed. (Charles, Jotkowitz, & Byrd, *Headache* 2006; Tronvik, Stovner, Helde, et al., *JAMA* 2003)

**417. The answer is A.** Coenzyme Q10 (CoQ10) or ubiquinone at 300 mg/day was compared to placebo in a double-blind, randomized, placebo-controlled trial. CoQ10 in a liquid, water-soluble formulation was superior to placebo for attack-frequency, headache-days and days-with-nausea in the third treatment month and well tolerated in 42 patients with migraines. The extrapolation of benefit to commercially available capsule formulation of CoQ10 awaits scientific investigation. The other supplements listed have not been scientifically evaluated in patients with migraine headaches. (Sándor, Di Clemente, Coppola, et al., *Neurology* 2005)

**418. The answer is E.** In general SSRIs are not effective in patients with primary headache disorders, in the absence of a significant history of anxiety or depression. They may confer benefit when a mood disorder factors significantly into the etiology of headaches. A Cochrane database review of randomized controlled trials comparing selective SSRIs with any type of control intervention in patients of either gender, over 18 years of age, with migraine or TTH found that over 2 months of treatment, SSRIs were no more efficacious than placebo in patients with migraine. In patients with chronic TTH, SSRIs were less efficacious than tricyclic antidepressants (TCAs). The combination of triptans and SSRIs, while theoretically increasing serotonin availability, is commonly used and the risk of serotonin syndrome is very small. (Moja, Cusi, Sterzi, & Canepari, *Cochrane Database Syst Rev* 2005)

**419. The answer is A.** The SSRIs have not been shown to be effective in the prevention of migraine headaches. However venlafaxine (Effexor), a combined norepinephrine and serotonin reuptake inhibitor, has been shown to be of benefit in prevention of migraine headaches. The prophylactic effects and tolerability of amitriptyline (Elavil) and venlafaxine were similar in a randomized double-blind crossover study of patients with migraine with or without aura. (Bulut, Berilgen, Baran, et al., *Clin Neurol Neurosurg* 2004)

**420. The answer is B.** Hypothalamic deep brain stimulation (DBS) has been evaluated for CH, based on the noted increase in regional cerebral blood flow in the ipsilateral posterior hypothalamic region during a CH attack. It involves an intraoperative magnetic resonance imaging (MRI)-guided stereotactic implantation of a DBS lead and pulse generator system posterior to the mammillothalamic tract. In an open-label study, the intensity, frequency, and severity of headaches throughout a 1-week period were tracked in patient diaries immediately prior to surgery and after 1 year of continuous stimulation. At the 1-year follow-up examination, DBS had produced a greater than 50% reduction in headache inten-

sity or frequency in two of four cases. The results are encouraging but do not yet justify widespread clinical application of this technique. (Starr, Barbaro, Raskin, & Ostrem, *J Neurosurg* 2007; Goadsby, *Expert Rev Neurother* 2007)

**421. The answer is A 2, B 3, C 4, D 1, E 5.** Seven different triptans have been developed for the treatment of migraine attacks. The first released triptan, sumatriptan (Imitrex), and the other newer triptans (zolmitriptan [Zomig], naratriptan [Amerge], rizatriptan [Maxalt], eletriptan [Relpax], almotriptan [Axert], and frovatriptan [Frova]) display high agonist activity at mainly the serotonin 5-HT<sub>1B</sub> and 5-HT<sub>1D</sub> receptor subtypes. There are minor pharmacodynamic differences between the five shorter-half-life triptans, although the efficacies of the oral formulations with shorter-half lives are all relatively similar. Sumatriptan has the lowest oral bioavailability (14%), whereas almotriptan has a higher oral bioavailability than any other triptan. The rate of absorption of rizatriptan is fastest, with shortest time to maximum concentration ( $t_{max}$ ); the rapid absorption of oral rizatriptan tends to produce a quicker onset of headache relief than does oral sumatriptan or zolmitriptan. The half-lives of naratriptan and frovatriptan are longest at 6 and 26 hours, respectively. (Tfelt-Hansen, De Vries, & Saxena, *Drugs* 2000)

**422. The answer is B.** Therapeutic gain is the percentage response for active treatment minus percentage response for placebo. Because the placebo rate is often high in clinical trials of headache patients, the therapeutic gain represents the presumed effect of the active treatment, independent of a placebo response. Placebo effects are more striking in studies involving children and adolescents with acute headache than in adults. (Loder, Goldstein, & Biondi, *Cephalalgia* 2005)

**423. The answer is B.** Coenzyme Q10 (CoQ10) deficiency and response to supplementation were evaluated in pediatric and adolescent patients with migraine, with indication of beneficial effect of supplementation. A third of patients with frequent headaches had low CoQ10 levels and supplementation with 1–3 mg/kg/day of CoQ10 in liquid gel capsule formulation was recommended. In a subset of patients who returned for follow-up at a mean of 3 months, the total CoQ10 level increased, while the headache frequency improved from  $19.2 \pm 10.0$  to  $12.5 \pm 10.8$  ( $p < .001$ ) and headache disability improved. As compared to other OTC supplements, daily prophylactic treatment with CoQ10 at presumed therapeutic doses is expensive. (Hershey, Powers, Vockell, et al., *Headache* 2007)

**424. The answer is A.** Chest discomfort, presumably related to pulmonary vasoconstriction and/or esophageal spasm, is lowest in oral triptan formulations. The tolerability of almotriptan (Axert) 12.5 mg is close to that of placebo, with

a low incidence of central nervous system (CNS) side effects and chest symptoms. Chest discomfort is in the range of <3% of patients with oral sumatriptan (Imitrex) and <1% of patients given almotriptan. (Dahlöf, Dodick, Dowson, et al., *Headache* 2002; Dodick, Sandrini, & Williams, *CNS Drugs* 2007)

**425. The answer is B.** Multiple formulations are currently available for sumatriptan (Imitrex; subcutaneous injection, swallowed tablet, intranasal spray), zolmitriptan (Zomig; swallowed tablet, orally dissolving tablet, intranasal spray), and rizatriptan (Maxalt: orally dissolving tablet, swallowed tablet). Eletriptan (Relpax), almotriptan (Axert), naratriptan (Amerge), and frovatriptan (Frova) are available only in tablets that need to be swallowed. (Tfelt-Hansen, De Vries, & Saxena, *Drugs* 2000)

**426. The answer is C.** Data on preventative medication for children and adolescents with migraine headaches is sparse, as noted by the American Academy of Neurology in 2004. A more recent review published in 2007 identified and evaluated the data regarding medication use for migraine prophylaxis in the pediatric population. Few controlled clinical trials regarding prophylaxis therapy are available, and no medication is approved by the FDA for prophylaxis of migraines in children. Of the drugs with available data, topiramate (Topamax), divalproex sodium (Depakene<sup>®</sup>), flunarizine, amitriptyline (Elavil), and cyproheptadine (Pariactin<sup>®</sup>) showed efficacy in decreasing migraine frequency and duration in children, without the large clinical trials necessary to validate their utility. Topiramate, divalproex sodium, and amitriptyline had the most data on their use for prophylaxis of migraines in children. Flunarizine is not available in the United States. (Eiland, Jenkins, & Durham, *Ann Pharmacother* 2007; Lewis, Ashwal, Hershey, et al., *Neurology* 2004)

**427. The answer is C.** Tranylcypromine (Parnate<sup>®</sup>), along with the antidepressant phenelzine (Nardil), is an MAOI. MAOIs decrease first-pass metabolism of all triptans except naratriptan (Amerge), frovatriptan (Frova), and almotriptan (Axert), potentiating their effect. Almotriptan would be the most appropriate rapid-onset, short-acting triptan for occasional treatment of an acute migraine in patients taking an MAOI. Administration of an MAOI and a sympathomimetic (isometheptene in Midrin) may increase the risk for a hypertensive reaction, through inhibition of norepinephrine metabolism, thus leading to an increased pressor response at receptor sites. Serotonin toxicity from excess serotonin in the central nervous system can result rarely from the combination a MAOI and other medications that increase serotonin availability. Preventative medication is not indicated for her frequency of headaches and they may dissipate after meno-

pause. (Sternieri, Coccia, Pinetti, & Ferrari, *Expert Opin Drug Metab Toxicol* 2006; *Wolff's Headache and Other Pain's*, Chapter 11, 2007)

**428. The answer is C.** Triptan use during a migraine headache's premonitory symptoms or aura has not been reliable in aborting impending head pain. There is some evidence of efficacy of long half-life triptans used during premonitory symptoms; however, triptans are generally used most effectively at the onset of pain. The efficacy of a triptan is greatest when the headache pain is mild to moderate, with less chance of headache recurrence or medication side effects. This is analogous to a fire extinguisher working better on a small fire, with greater chance of quenching the fire without the fire reigniting. Once the pain has progressed to peak intensity with the development of cutaneous allodynia, triptans are much less likely to be effective. At this point, the fire extinguisher does not work, and the fire must burn itself out. (*Wolff's Headache and Other Pain's*, Chapter 11; Bursten & Jakubowski, *Neurology* 2005)

**429. The answer is A.** This man appears to have MOHs and needs to stop taking the butalbital-containing medication to decrease his CDHs. However, abrupt cessation of butalbital-containing medication could risk seizures, especially given the uncertainty about the number of pills he is taking each day. Tapering the dose as an outpatient while covering with a preventative medication or a course of a long-acting triptan may be appropriate with some compliant and perceptive patients, but in this man, with his psychiatric disease and lack of insight, an outpatient strategy probably would not work. Inpatient treatment has the greatest chance of success, but propofol (Diprivan<sup>®</sup>) and intubation could be risky. An oral phenobarbital-loading protocol, covering him during the withdrawal with a long-half life medication (an average of 90 minutes), may be an effective and safe method of withdrawing patients from excessive use of short-acting butalbital-combination medications. (Loder & Biondi, *Headache* 2003)

**430. The answer is B.** In step care, treatment is escalated after first-line medications fail; in stratified care, initial treatment is based on measurement of the severity of illness or other factors. The Disability in Strategies of Care (DISC) study applied these strategies to migraine treatment. The three different strategies evaluated were:

1. Stratified care, in which patients with milder headache disability were treated with aspirin, 800–1,000 mg, plus metoclopramide, 10 mg; and patients with more severe headache disability were treated with zolmitriptan, 2.5 mg.



2. Step care across attacks, in which initial treatment was with aspirin plus metoclopramide, switching to zolmitriptan to treat the remaining attacks if there was no initial response.
3. Step care within attacks, in which initial treatment for all attacks was with aspirin plus metoclopramide.

Disability, as measured by the Migraine Disability Assessment Scale (MIDAS), was a marker of disease severity, and the degree of disability could be used to stratify appropriate care. Stratified care strategies provided significantly better clinical outcomes than did stepped care strategies within or across attacks, as measured by headache response and disability time. An analysis of the overall cost benefits of nonspecific analgesic treatment (step care) versus migraine-specific treatment (stratified care) found that stratified care was superior to a stepped care approach. (Lipton, Stewart, Stone, et al., *JAMA* 2000; Sculpher, *Pharmacoeconomics* 2002)

**431. The answer is C.** Divalproex sodium (Depakote) is available in twice-daily delayed-release (DR) and once-daily extended-release (ER) formulations. The recommended starting dose is 250 mg b.i.d. for the DR formulation, or 500 mg once-daily for the ER formulation, with dose escalation in increments of several days to a week. A dose of divalproex sodium of >1,000 mg has not been shown to be effective as compared to lower doses. As compared to placebo in the pivotal trials, side effects were more common with the DR formulation than with the ER formulation. The medication has been associated with alopecia, tremor, weight gain, and nausea, as well as teratogenic risk when used in early pregnancy. Zinc supplementation may decrease the medication-associated alopecia. (Kaniecki, *Headache* 2008)

**432. The answer is E.** A dopaminergic mechanism for migraine premonitory symptoms (prodrome) has been postulated, and dopamine blockers (such as domperidone [Motilium] and metoclopramide [Reglan]) have been used to abort an attack at the stage of premonitory symptoms. The longer half-life triptans, naratriptan (Amerge) and frovatriptan (Frova), have also been used to abort the headache during the premonitory phase. The efficacy of this treatment obviously depends on the accuracy of the patients' symptom recognition. (Buzzi, Cologno, Formisano, & Rossi, *Funct Neurol* 2005)

**433. The answer is C.** Zonisamide (Zonegran), like topiramate (Topamax), has properties of a carbonic anhydrase inhibitor and has been shown to decrease the frequency and severity of migraine headaches, although it has been less extensively studied than has topiramate. In a short-term study, zonisamide and a diet



decreased weight more than diet alone. Zonisamide is less likely to cause cognitive side effects or word-finding difficulties than is topiramate. Divalproex sodium (Depakote), propranolol (Inderal), gabapentin (Neurontin), and amitriptyline (Elavil) do not have the weight loss or weight neutral properties of topiramate and zonisamide. Zonisamide should not be given to a patient with a true sulfa drug allergy. (Gadde, Franciscy, Wagner, et al., *JAMA* 2003)

**434. The answer is B.** Botulinum toxin blocks acetylcholine release from motor nerve terminals and other cholinergic synapses and may reduce the release of neuropeptides involved in pain perception, including substance P and glutamate. Botulinum toxin injections have been studied in patients with TTH, chronic migraine, and CDH. Multiple randomized, double-blind, placebo-controlled trials of botulinum toxin used to treat headaches have been published with variable results. Botulinum toxin type A and placebo injections have been equally effective in some studies, and its role in the prevention of multiple headache types continues to be investigated. (Schulte-Mattler & Leinisch, *J Neural Transm* 2007; Ramadan, *Headache* 2007)

**435. The answer is D.** All of the listed side effects are noted with topiramate (Topamax), with paresthesias being the most common side effect noted in adult patients. Oligohidrosis (decreased sweating) and elevated body temperature have been reported in patients on topiramate, primarily young children. Symptomatic hyperthermia is primarily associated with increased environmental temperature and/or exercise, and generally can be prevented with adequate hydration. The risk of hyperthermia is increased when topiramate is combined with other drugs, such as carbonic anhydrase inhibitors and anticholinergic medications, which also predispose patients to heat-related disorders. The other topiramate side effects listed are not more prevalent in children. (Cerminara, Seri, Bombardieri, et al., *Pediatr Neurol* 2006)

**436. The answer is B.** Topiramate (Topamax) may cause idiosyncratic ciliochoroidal detachment and ciliary body edema, leading to anterior displacement of the lens–iris diaphragm, lens thickening, and acute angle-closure glaucoma and acute myopia. These rare visual complications of topiramate typically occur while treatment is being initiated and are usually reversible with discontinuation of the medication. Gabapentin (Neurontin) is rarely associated with blurred vision and diplopia. Vigabatrin (Sabril) is associated with retinopathy with visual field defects. Carbamazepine (Tegretol) can cause nystagmus, diplopia, and blurred vision. Vigabatrin is associated with retinopathy with visual field constriction in up to 40% of patients; therefore, visual field testing is suggested with

continued treatment with this medication. (Verrotti, Manco, Matricardi, et al., *Pediatr Neurol* 2007)

**437. The answer is E.** SUNCT and SUNA are primary headache syndromes, classified as TACs, and associated with hypothalamic activation. They respond to IV lidocaine, but not indomethacin (Indocin). Preventive treatments include lamotrigine (Lamictal), gabapentin (Neurontin), and topiramate (Topamax). (Cohen, *Cephalalgia* 2007)

**438. The answer is D.** All of the listed symptoms may be seen with serotonin syndrome, but hyperreflexia is the most common. Serotonin syndrome, due to excess 5-HT in the CNS, is characterized by generalized hyperreflexia and increased muscle tone with clonus. Serotonin toxicity can be of variable intensity, ranging from mild anxiety with increased muscle stretch reflexes to a medical emergency with severe hyperthermia, muscle rigidity, and multiple organ failure. Neuroleptic malignant syndrome may be confused with serotonin syndrome, but is associated with bradykinesia, muscle rigidity, and extrapyramidal symptoms. Other disorders with clinical presentations similar to serotonin syndrome include nonconvulsive seizures, acute baclofen withdrawal, encephalitis, anticholinergic or sympathomimetic toxicity, and malignant hyperthermia. (Isbister, Buckley, & Whyte, *Med J Aust* 2007)

**439. The answer is A 3, B 2, C 4, D 5, E 1.** Although all of the above agents have been studied in the use of migraine headaches, only atenolol (Tenormin) and verapamil (Calan) have shown efficacy in at least two placebo-controlled studies. Verapamil is most often used in the prevention of CH. Candesartan (Atacand) and lisinopril (Zestril, Prinivil) have shown benefit in single trials in which they were found to decrease headache disability with few side effects. It is not clear that the beneficial effects of these individual antihypertensive medications in headache patients extends to other medications in their same drug class. These medications may be especially useful in hypertensive migraineurs with frequent headaches. (Rapoport & Bigal, *Neurol Sci* 2004)

**440. The answer is C.** The subcutaneous somatostatin receptor agonist, octreotide, was superior to placebo in a trial of CH patients, but not in a trial of patients with migraine. Serotonin receptor agonists are the current foundation of acute migraine treatment. Early results of (CGRP) receptor antagonists in the treatment of acute migraine are encouraging and these agents are projected to be a treatment without vascular risk. The benefits from nitric oxide synthase (NOS) blockers and adenosine A<sub>1</sub> receptor agonists are still theoretical. (Goadsby, *Curr Opin Neurol* 2005)

**441. The answer is C.** The benefit of steroids in medication withdrawal in patients with CDH due to MOH is not clear. In one study, prednisolone given orally the first 6 days after medication withdrawal did not have an effect on withdrawal headaches in patients with CDH and MOH. Another proof-of-concept study showed that prednisone might be effective in the treatment of medication withdrawal headache. A recently published randomized controlled trial of IV dexamethasone to prevent relapse in acute migraine headache found that steroids failed to reduce headache relapses after ED discharge. Hussain and Young (2007) published three cases of patients who had severe migraine and developed aseptic osteonecrosis with short-term, intermittent pulse doses of corticosteroids. Early steroid treatment in vestibular neuritis may improve long-term outcome, although the routine use of steroids is still being evaluated in this condition. (Bee, Mygland, & Salvesen, *Neurology* 2007; Hussain & Young, *Headache* 2007; Pageler, Katararava, Diener, et al., *Cephalalgia* 2007; Rowe et al., *Headache* 2007; Seemungal, *Curr Opin Neurol* 2007)

**442. The answer is C.** Treating patients with triptans within 60 minutes after the onset of the migraine effectively blocks the development of cutaneous allodynia. Cutaneous allodynia cannot be reversed once it develops by late triptan treatment. Patients who do not develop cutaneous allodynia respond to triptans with resolution of pain, even when treatment is initiated well into the headache. However, patients who are prone to develop cutaneous allodynia should initiate triptan treatment early in the attack (i.e., prior to the onset of cutaneous allodynia) in order to be rendered pain free. The other accompanying symptoms of migraine and the pain location have not been shown to predict pain response as a function of treatment timing. (Burstein & Jakubowski, *Neurology* 2005)

**443. The answer is C.** Intravenous magnesium sulphate, an N-methyl-D-aspartate (NMDA) receptor inhibitor, has been used in the acute treatment of migraines with variable efficacy. It is well tolerated when given in the ED. Central sensitization has not yet been shown to be its mechanism of action. Magnesium sulphate may preferentially benefit patients with migraine with aura. A randomized, double-blind, placebo-controlled study assessed the effect of 1 g magnesium sulphate on the pain and associated symptoms in patients with migraine with and without aura. Patients with migraine without aura showed no statistically significant difference with magnesium sulphate as compared to placebo in relief of pain or nausea. Some benefit on photophobia and phonophobia was noted in patients who received magnesium sulphate. Migraine with aura patients treated with magnesium sulphate showed a statistically significant improvement of pain and of all associated symptoms as compared with controls. (Bigal, Bordini, Tepper, & Speciali, *Cephalalgia* 2002)

**444. The answer is B.** Basilar-type migraine represents up to 20% of migraine headaches in children and adolescents. This primary headache, which may be a symptom-specific type of migraine with aura, is characterized by attacks that include symptoms of dizziness, vertigo, visual disturbances, ataxia, and diplopia, followed by migraine headache. A double-blind, parallel-group, dose comparison study assessed the efficacy and safety of topiramate (Topamax) for prophylaxis of basilar-type migraine in children and adolescents. Fourteen children (4 boys, 10 girls) were randomized to treatment with either 25 mg/day or 100 mg/day of topiramate. The study found that 86% of the children and adolescents responded with a greater than 50% reduction in migraine frequency without serious adverse events. The authors concluded that preventive therapy with topiramate resulted in a reduction of the overall migraine frequency and the frequency of attacks of basilar-type migraine at both 25 mg and 100 mg doses relative to a historical baseline and prospective baseline periods. (Lewis & Paradiso, *Headache* 2007)

**445. The answer is B.** A urine toxicology screen should be obtained to look for recreational drug use in this woman but her most likely diagnosis is serotonin syndrome. She is not hypertensive, as expected with a reaction to reaction to monoamine oxidase inhibitors or with neuroleptic malignant syndrome (NMS). However, elevated serum creatinine kinase (CK) level should be ordered to rule out NMS, which is also associated with marked muscle rigidity, as opposed to hyperreflexia. The negative MRI scan and her non-neurologic symptoms make subarachnoid hemorrhage unlikely. SSRIs in combination with other antidepressants such as the TCAs and MAOIs may risk serotonin syndrome, a rare but potentially life-threatening complication of enhanced CNS serotonergic activity. Serotonin syndrome is characterized by altered mental status (disorientation, confusion, agitation, restlessness), autonomic dysfunction (fever, shivering, diaphoresis, abdominal pain, diarrhea), and neurologic abnormalities (ataxia, hyperreflexia, myoclonus). A search of this woman's purse revealed a package of triptans and bottles of a SSRI, fluoxetine (Prozac), and a TCA, doxepin (Sinequan). During her hospitalization, she was given IV fluids and antipyretics and, over the next days, her symptoms resolved and her mental status and reflexes normalized. Although patients generally improve with only supportive care, treatment with cyproheptadine, chlorpromazine, or propranolol may be used for patients with life-threatening symptoms. (Lane & Baldwin, *J Clin Psychopharmacol* 1997) (Isbister, Buckley, & Whyte, *Med J Aust* 2007)

**446. The answer is E.** Optic nerve sheath decompression (ONSD), which is also called optic nerve sheath fenestration, as well as intracranial venous sinus stent placement, ventriculoperitoneal shunt placement, and lumboperitoneal shunt

placement, are all surgical techniques used for the management of visual loss in IIH, which is unresponsive to usual medical treatment and weight loss. In one study of the techniques, visual outcomes from ONSD appeared to be superior to other surgical techniques for management of IIH. However, ONSD was the most commonly used technique in IIH with the most follow-up data in treated patients. Less information is available on visual outcomes after intracranial venous stent placement and cerebrospinal fluid (CSF) diversion procedures for IIH. (Feldon, *Neurosurg Focus* 2007)

**447. The answer is C.** Topiramate (Topamax) can be used to treat IIH with efficacy that is probably comparable to acetazolamide (Diamox). Weight reduction and decreased CSF formation are possible mechanisms of action for topiramate in the treatment of IIH. Aggressive weight loss, which may be enhanced by topiramate, is indicated for the obesity characteristically seen in patients with IIH. (Celebisoy, Gökçay, Sirin, & Akyürekli, *Acta Neurol Scand* 2007)

**448. The answer is C.** This woman appears have generalized anxiety disorder (GAD), which is confirmed on questioning about other aspects of her life. Pregabalin (Lyrica) has been shown to be of benefit in patients with GAD. Its benefit in patients with primary headache disorders is not evident but, in a woman with headaches in the setting of GAD, pregabalin may be a reasonable choice for prevention of chronic headaches. Pregabalin is a GABA analogue closely related to gabapentin (Neurontin). The side effects of gabapentin and pregabalin are similar and include dizziness, drowsiness, and weight gain, as well as peripheral edema in older patients. Pregabalin, like gabapentin, is eliminated unchanged in urine, limiting interactions with drugs metabolized by the cytochrome P450 system. The other medications listed have not been shown to be effective in treating GAD. Selective serotonin reuptake inhibitors, as well as combined norepinephrine and serotonin reuptake inhibitors, are effective in treatment of GAD. (Feltner, Wittchen, Kavoussi, et al., *Int Clin Psychopharmacol* 2008)

**449. The answer is B.** The vasoconstrictive effects of ergotamines are mediated by their effects on vascular 5-HT<sub>1B</sub> receptors. Ergots may increase risk of vascular events, especially with frequent, prolonged use. A retrospective, nested, case-control study investigated whether excessive use of triptans and ergotamines was associated with a risk of ischemic complications, using a pharmacologic database. Triptan overuse was not associated with an increased risk of ischemic complications (odds ratio [OR] 0.96; 95% confidence interval [CI]: 0.49 to 1.90). Overuse of triptans in patients on cardiovascular drugs did not increase vascular risk. Overuse of ergotamine turned out to be a risk factor for ischemic complications

(OR 2.55; 95% CI: 1.22 to 5.36). Overuse of ergotamine appears to increase the risk of ischemic complications, especially in patients using cardiovascular drugs. Ergotamine use is also associated with cardiac valvular disease. Barbiturates are not associated with increased vascular risk. Studies on the effect of nonselective nonsteroidal anti-inflammatory agents (NSAIDs) on blood pressure elevation have not shown consistent association, and there is no clear vascular risk. The major risk with excess NSAID use is gastrointestinal hemorrhage and acute renal failure. (Wammes-van der Heijden, *Neurology* 2006)

**450. The answer is B.** In the Middle Ages, epidemics of “convulsive ergotism” or “St. Anthony’s Fire” were widespread in Europe. The disorder was related to consumption of rye bread made from grain contaminated with ergot, produced by the fungus *Claviceps purpurea*. The clinical features of convulsive ergotism include uncontrollable muscle twitching and spasms, changes in behavior and cognition, hallucinations, sweating, and fever lasting for several weeks. Serotonergic overstimulation similar to that described as serotonin syndrome may be an explanation for the variable symptoms. (Eadie, *Lancet Neurol* 2003; van Dongen & de Groot, *Eur J Obstet Gynecol Reprod Biol* 1995)

**451. The answer is D.** Nummular headache is relatively rare primary headache disorder characterized by unilateral, circumscribed round or elliptical areas of variable mild-to-moderate head pain in a chronic or remitting pattern. Nummular headaches are relatively resistant to treatment with local anesthetic agents or with medications that are generally used for treatment of other primary headache types. A study evaluated botulinum toxin type A (BoNTA) in four patients who had nummular headaches resistant to treatment with usual medications. They were given 25 units of BoNTA divided among 10 injection sites in and around the circumscribed areas of pain, paresthesia, and allodynia. Six to 10 days following BoNTA treatment, all patients experienced a reduction in nummular headache symptoms. Pain relief lasted approximately 14 weeks on average. Repeat injections of BoNTA gave the same degree of improvement in nummular headache symptoms. No treatment-related adverse events were reported with BoNTA. The other treatments listed have not been shown to be of benefit in patients with intractable nummular headaches. (Mathew, Kailasam, & Meadors, *Headache* 2007)

**452. The answer is A 2, B 3, C 1, D 4, E 5.** Topiramate (Topamax), through its carbonic anhydrase properties, has been associated with recurrent kidney stones, especially with dehydration. Nonselective  $\beta$ -blockers may be contraindicated in congestive heart failure (decreases cardiac output with sympathetic blockade), asthma (exacerbates breathing difficulties and counteract  $\beta_2$ -agonist

therapy), and insulin-dependent diabetes (prolongs hypoglycemic effect of insulin). Magnesium is associated with diarrhea, and verapamil (Calan) is associated with constipation and conduction block. Divalproex sodium has been associated with PCOS with hyperandrogenism, ovarian cysts, and obesity. Patients on divalproex sodium most commonly report tremor, hair loss, and weight gain. (*Wolff's Headache and Other Pain*, Chapter 11; Ramadan, *Headache* 2007)

**453. The answer is D.** In a multicenter, randomized, double-blind, placebo-controlled study of adult patients with migraine with or without aura, zolmitriptan (Zomig) 5 mg nasal spray was used to treat up to two migraine attacks within 15 minutes of headache pain becoming moderate or severe. The primary end-point was headache response (defined as reduction in migraine pain from severe to moderate to mild or none) at 2 hours. The headache response rate at 2 hours post-dose was 66.2% for the zolmitriptan group versus 35.0% for the placebo group ( $p < 0.001$ ). Headache response rates starting at 15 minutes post dose were significantly higher with zolmitriptan nasal spray than with placebo ( $p < 0.001$ ). (Dodick, Brandes, Elkind, et al., *CNS Drugs* 2005)

**454. The answer is D.** All of the statements are true, but the reason for the difficulty in establishing efficacy for triptans in children and adolescents is that the therapeutic gain (the difference between the placebo effect and the therapeutic effect) is small. The placebo response is increased, as compared to adults, in children and adolescents in headache clinical trials. (Lewis, Ashwal, Hershey, et al., *Neurology* 2004)

**455. The answer is A.** Treatment with a triptan may result in nonischemic chest discomfort, which may also be a migraine-associated symptom independent of triptan therapy. In a review of studies of almotriptan, an oral 5-HT<sub>1B/1D</sub> receptor agonist, at the recommended therapeutic dose of 12.5 mg, the incidence of chest symptoms (pressure, warmth, and other unpleasant sensations) was 0.2%. Sumatriptan has been associated with chest symptoms, with an incidence of 3–5%, more common with the subcutaneous formulation. Triptan-associated chest pain is not due to cardiac ischemia, but may be related to esophageal spasm or pulmonary vasoconstriction. (Dodick, *Headache* 2001; Dodick, *Cephalalgia* 2004)

**456. The answer is E.** Carbamazepine (Tegretol) is associated with clinically relevant drug interactions especially with macrolide antibiotics such as clarithromycin (Biaxin) and erythromycin, the antitubercular agent isoniazid, and the antipsychotic quetiapine (Seroquel). These medications are metabolized by cytochrome P450 enzymes, especially CYP3A4 and can inhibit the metabolism of car-



bamazepine. In patients receiving carbamazepine alone or in combination with other drugs, administration of these enzyme-inducing drugs can lead to symptoms of an overdose (ataxia, dizziness, diplopia, nausea, vomiting, drowsiness). Clarithromycin, a macrolide antibiotic similar to erythromycin, is widely used to treat respiratory tract infections and is used for the treatment of atypical mycobacterial infections and *Helicobacter pylori*-associated peptic ulcer disease. (Gé-lisse P, Hillaire-Buys D, Halaili, et al., *Rev Neurol [Paris]* 2007; Grimm, Richtand, Winter, et al., *Br J Clin Pharmacol* 2006)

**457. The answer is B.** Clinically important drug interactions may occur when patients are treated with multiple medications for headache or seizure prevention. Older-generation antiepileptic drugs (AEDs) often exhibit significant pharmacokinetic interaction potential. Carbamazepine (Tegretol), phenytoin (Dilantin), and phenobarbital induce cytochrome P450 (CYP) and uridine glucuronyl transferase (GT) enzyme systems and can reduce the serum concentration of other drugs that are substrates of the same enzymes, such as lamotrigine (Lamictal). Divalproex sodium may cause clinically relevant drug interactions by inhibiting the metabolism of phenobarbital and lamotrigine. The newer AEDs are less likely to induce or inhibit the activity of CYP or GT enzymes. Oxcarbazepine (Trileptal), lamotrigine, and topiramate (Topamax) (at high doses) may stimulate the metabolism of oral contraceptive steroids. Zonisamide (Zonegran) is principally inactivated by CYP3A4-dependent reduction and carbamazepine, phenytoin, and phenobarbital all increase its clearance. Levetiracetam (Keppra), gabapentin (Neurontin), and pregabalin (Lyrica) are unlikely to cause or be a target for clinically relevant interactions with other medications used for headache or seizure prevention. (Perucca, *Br J Clin Pharmacol* 2006; Sills & Brodie, *Epilepsia* 2007)

**458. The answer is C.** This woman took a triptan for her migraine before she came to the ED, and she should not be given another brand of triptan or an ergotamine within 24 hours. Intravenous valproate sodium (Depacon) is an appropriate treatment to break her migraine headache. Other therapies that can be added to her treatment include IV magnesium, IV steroids, IV ketorolac and antiemetic medications. (*Wolff's Headache and Other Pain*, Chapter 11, 2007)

**459. The answer is C.** Frovatriptan's (Frova) long half-life in plasma (26 hours) translates into a long duration of action. It is ideal for the short-term prophylaxis of menstrual migraine, either with once-daily or twice-daily dosing. Naratriptan (Amerge) and zolmitriptan (Zomig) have also been studied for menstrual migraine prevention. Naratriptan has the second longest half-life, but its use in menstrual migraine prevention has been supplanted by frovatriptan. Zolmitrip-



tan's short half-life is not as well suited to menstrual migraine prevention, as is the case with eletriptan (Relpax) and rizatriptan (Maxalt). Frovatriptan has a slower onset of acute headache relief, making it less commonly used for acute migraine treatment. (Markus & Mikko, *Expert Opin Pharmacother* 2007)

**460. The answer is E.** All of the listed medications, used for intractable headaches in adults, are also used for the acute treatment of migraine headaches in children and adolescents with varying efficacy. In one study, IV prochlorperazine (Compazine®) (0.15 mg/kg; maximum 10 mg) was found to be superior to intravenous ketorolac (Toradol®) (0.5 mg/kg; maximum 30 mg) in the acute treatment of pediatric migraine headaches. Reviews of the use of a rapid or continuous infusion of IV valproate sodium (Depacon) in acute adolescent migraine found that the treatment was generally well tolerated and efficacious. A study of pediatric patients with migraine without aura treated with IV dihydroergotamine mesylate (DHE) at 0.1–0.5 mg, at an average of five doses, in combination with oral metoclopramide (Reglan), found that 80% of the pediatric patients responded to the protocol with only minimal side effect. (Reiter, Nickishch, & Merritt, *Headache* 2005; Brousseau, Duffy, Anderson, & Linakis, *Ann Emerg Med* 2004; Linder, *Headache* 1994; Kabbouche & Linder, *Curr Pain Headache Rep* 2005)

**461. The answer is C.** Two randomized, double-blind, single-attack, parallel-group studies evaluated the efficacy and safety of a fixed-dose tablet containing both sumatriptan succinate 85 mg and naproxen sodium 500 mg, relative to efficacy and safety of each medication as monotherapy and placebo for the acute treatment of migraine. The sumatriptan–naproxen sodium single-pill combination was more effective than placebo for headache relief and absence of photo-/phonophobia at 2 hours after dosing. For sustained pain-free response, sumatriptan–naproxen sodium was superior to monotherapy with either medication or to placebo. The incidence of adverse events was similar between sumatriptan–naproxen sodium and sumatriptan monotherapy. The combination pill, Treximet, is now available in the United States. Naproxen sodium (Anaprox®) can be prescribed in 275-mg and 550-mg dosages and is available at 220 mg as an OTC medication (Aleve®). Generic sumatriptan, initially injectable and then oral, should be available within the next year. (Brandes, Kudrow, Stark, et al., *JAMA* 2007)

**462. The answer is C.** The most common side effects associated with divalproex sodium (Depakote), tremor, weight loss, and hair loss, are typically benign. However, less common but more serious adverse events may occur. These include hepatotoxicity, hyperammonemic encephalopathy, bone marrow suppression, and pancreatitis. Divalproex sodium–induced pancreatitis is rare but has been

reported in the medical literature. Side effects of divalproex sodium, including hyperammonemic encephalopathy and hepatotoxicity, may be accentuated with the combined use of topiramate. Hepatotoxicity with divalproex sodium is more common in young children than in older individuals. (Gerstner, Büsing, Bell, et al., *J Gastroenterol* 2007)

**463. The answer is C.** Clomiphene (Clomid<sup>®</sup>) is used to treat infertility due to failure to ovulate. In men who use anabolic steroids, it can bind estrogen receptors to decrease the steroids' feminizing side effects. It acts by inhibiting the effect of estrogen on the gonadotrope cells in the anterior pituitary gland, leading to the release of gonadotropin-releasing hormone from the hypothalamus. The pituitary secretes follicle-stimulating (FSH), increasing the chance of ovulation. Reports of patients with treatment-refractory chronic CH and SUNCT who responded to treatment with clomiphene citrate indicate that hypothalamic hormonal modulation may be a new preventive therapy for TACs. Melatonin has been evaluated as a preventative treatment for CHs, with generally disappointing results. (Rozen, *Headache* 2007; Rosen, Saper, Sheftell, & Dodick, *Headache* 2005)

**464. The answer is D.** Human leukocyte antigen (HLA) typing should be performed to assess this woman's risk with carbamazepine (Tegretol) treatment. Specific HLA alleles are major histocompatibility genes that can indicate specific drug hypersensitivities. HLA-B\*1502 has been associated with carbamazepine-induced SJS and TEN (SJS/TEN). The genetic association is phenotype-specific, as HLA-B\*1502 is associated with carbamazepine-SJS/TEN but not with maculopapular eruption or hypersensitivity syndrome induced with carbamazepine. The genetic association appears to be ethnicity-specific, as carbamazepine-induced SJS/TEN associated with HLA-B\*1502 is found in patients from southeast Asia but not other areas of the world. The ethnic-specific genetic association may be explained by the different allele frequencies. Other HLA types have been associated with carbamazepine-associated skin reactions in patients from other Asian countries. Asian patients should have HLA genotyping before prescribing carbamazepine in order to prevent carbamazepine-induced SJS/TEN. The other answers are nonspecific distracters. (Chung, Hung, & Chen, *Curr Opin Allergy Clin Immunol* 2007)

**465. The answer is E.** Hair loss is a common complaint in middle-aged women who have chronic headaches. Causes of alopecia include increasing age, thyroid disorders, iron-deficiency anemia, stress, and childbirth. Some medications used for headache prevention may also increase the risk of alopecia. Lithium, timolol (Blocadren<sup>®</sup>), and divalproex sodium (Depakote) (estimated incidence >5%); car-

bamazepine (Tegretol) and lamotrigine (Lamictal) (estimated incidence 1–5%); and amitriptyline (Elavil), paroxetine (Paxil), sertraline (Zoloft), venlafaxine (Effexor), and verapamil (Calan) (estimated incidence <1%) are associated with telogen effluvium, with loss up of more than 300 hairs a day as compared to the normal loss of 100 hairs a day. The loss may begin 2–3 months after treatment and continue up to 6 months after the medication is discontinued. (Shapiro, *N Engl J Med* 2007)

**466. The answer is D.** Of all the drugs in use for prevention of migraines and seizures, divalproex sodium (Depakote) and valproic acid/valproate (Depakene) have the highest risk of congenital fetal abnormalities including spinal cord dysraphism, and autism spectrum disorders. The teratogenic effect of divalproex sodium is dose-dependent. A prospective observational study enrolled pregnant women with epilepsy from 1999 to 2004 to determine the frequency of major congenital malformations or fetal death that could be attributed to the four most commonly used AEDs. A total of 333 mother–child pairs were analyzed for monotherapy exposures: carbamazepine ( $n = 110$ ), lamotrigine ( $n = 98$ ), phenytoin ( $n = 56$ ), and valproate ( $n = 69$ ). The frequency of pregnancies resulting in serious adverse outcomes for each AED were: carbamazepine (Tegretol) 8.2%, lamotrigine (Lamictal) 1.0%, phenytoin (Dilantin) 10.7%, and valproate 20.3%. Gabapentin (Neurontin) has not been clearly associated with teratogenicity. (Meador, Baker, Finnell, et al., *Neurology* 2006)

**467. The answer is B.** Oral progesterone does not appear to be effective in the prevention of menstrual migraine or premenstrual symptoms. A dopamine receptor agonist that inhibits prolactin release may be considered, although the long-term benefit and tolerability are uncertain. Tamoxifen is a selective estrogen receptor modulator that binds to a cytosol estrogen receptor; it may be effective treatment for menstrual migraine. Again, the long-term benefit and tolerability are uncertain. Oophorectomy is not a safe, effective, or appropriate treatment for menstrual migraine. Seasonique® is a continuous estrogen birth control pill that can be used for menstrual migraine suppression. The package consists of 84 days of levonorgestrel/ethinyl estradiol tablets, 0.15 mg/0.03 mg followed by 7 days of low-dose estrogen (ethinyl estradiol tablets) 0.01 mg in place of placebo. A light menstrual period occurs every 3 months during the last week of pills. Breakthrough bleeding may occur between the four periods a year. (Loder, Rizzoli, & Golub, *Headache* 2007)

**468. The answer is E.** Pregabalin (Lyrica) has shown benefit for multiple pain-producing conditions, although it has only been approved by the FDA for pos-

therapeutic neuralgia, diabetic neuropathy, and fibromyalgia. Pregabalin is also indicated as adjunctive therapy for adult patients with partial onset seizures. It has also shown benefit in GAD, and trigeminal neuralgia, as unapproved uses. In a prospective, open-label study, patients suffering from trigeminal neuralgia with and without concomitant facial pain were treated with pregabalin 150–600 mg/day. About three-quarters of patients had some improvement in pain (one-quarter with complete relief and one-half with pain reduction) after 8 weeks with a mean dose of around 300 mg/day. Patients without concomitant facial pain showed better response rates compared with patients with concomitant chronic facial pain. The efficacy of pregabalin in the prevention of episodic migraine headache has not been proven but, given its similarity to gabapentin (Neurontin), pregabalin may be appropriate in some patients with migraine. (Obermann, Yoon, Sensen, et al., *Cephalalgia* 2007)

**469. The answer is C.** This woman does not need a preventative medication for a migraine occurring every few months. Although a butalbital combination medication could be considered, a triptan would be more likely to give symptomatic relief of her headaches and accompanying symptoms. A past history of an aneurysm that has been completely clipped or coiled is not a contraindication to triptan therapy. Occult cerebral aneurysms of varying size are relatively common, present in approximately 5% of individuals. The exact prevalence of incidentally discovered aneurysms varies, depending on the method of detection (autopsy, imaging for various indications) and the size of the aneurysm. Triptans are given, without apparent risk, to migraine patients with unsuspected aneurysms. This woman's cerebral vasculature has been vetted, as compared to the unknown vascular provenance of most patients taking triptans. Although follow-up catheter angiography is warranted after coiling, every 6 months is excessive. The benefits of early detection versus the risks of morbidity/mortality associated with asymptomatic intervention are unclear, so routine screening of multiple first- and second-degree asymptomatic family members is not warranted. The chance of detecting an asymptomatic cerebral aneurysm is greatest for siblings of the patient with aneurysmal subarachnoid hemorrhage. (Wardlaw & White, *Brain* 2000)

**470. The answer is C.** Although some patients achieve satisfactory migraine prevention on even very low doses of topiramate, and others require many times the recommended dose, most patients who benefit from the medication respond to 50 mg twice a day. A slow titration schedule, with weekly increases of a whole to a half of a 25-mg pill, is tolerated better than a more rapid dose escalation. Detailed explanation of potential side effects and their management improves patient compliance with this medication. (Kaniecki, *Headache* 2008)

**471. The answer is E.** The above statements represent the headache medicine equivalent of urban legends. The pain of nonmigraine headaches, including TTHs and even headaches due to subarachnoid hemorrhage or meningitis may be alleviated by triptans. Response to a test triptan should not be used as the sole or major criteria used to diagnose a migraine. The FDA recommendation proscribing the prescribing of different triptans simultaneously notwithstanding, mixing of triptan brands appears to carry the same risk as swimming after eating. You are told not to do it but you are not really sure why and you suspect people do it and get away with it. Early triptan trials excluded adolescents and children, but triptans can be used safely even in young children. Lack of response to one triptan does not predict lack of response to another brand, as many triptan nonresponder trials have shown. There are some patients with a clear migraine diagnosis who seem not to respond to any brand of triptan. These patients are particularly appropriate for preventative therapy in order to avoid excess use of OTC medications or controlled substances. (*Wolff's Headache and Other Pain*, Chapter 11, 2007)

**472. The answer is D.** A preventative medication to decrease the frequency and severity of this woman's migraines with aura is the most reasonable therapeutic choice. Her menses are irregular, making triptan prevention tricky, and her vascular risk is increased by her longstanding smoking. Cigarettes and oral contraceptives increase the risk of ischemic stroke in young women with migraine with visual aura, although their absolute ischemic stroke risk is still small. Women with migraine with aura have about a 1.5 greater odds of ischemic stroke, without association with hypertension, diabetes, or myocardial infarction, as compared with women with no migraine headaches. The risk is particularly increased with recent onset of migraines with aura, such as in this scenario. Women with migraine with aura who are current cigarette smokers and current users of oral contraceptives have about a sevenfold higher odds of having an ischemic stroke than do women with migraine with visual aura who do not smoke or use oral contraceptives. (MacClellan, Giles, Cole, et al., *Stroke* 2007)

**473. The answer is B.** Ergotamine is available in an oral form, including a preparation in combination with caffeine, as well as in a rectal formulation. Dihydroergotamine is only available for parenteral or intranasal use. Dihydroergotamine has less of an emetic effect than does ergotamine. Both ergotamine and DHE are serotonin agonists (5-HT<sub>1A</sub>, 5-HT<sub>1B</sub>, 5-HT<sub>1D</sub>, 5-HT<sub>1E</sub>, 5-HT<sub>1F</sub>) and possess  $\alpha$ -adrenergic properties. Dihydroergotamine and ergotamine both inhibit the reuptake of norepinephrine at sympathetic nerve endings. Ergotamine is a more potent vasoconstrictor on arteries than DHE, but the venoconstrictor effect on venous capacitance vessels is equivalent. (*Wolff's Headache and Other Pain*, Chapter 11, 2007)

**474. The answer is B.** This man presents with posterior circulation symptoms suggestive of an acute cerebellar infarct. Although his symptoms could be due to an acute vestibular disorder, such as benign positional vertigo, his age and medical history make vertebrobasilar disease the first concern. An MRI with diffusion-weighted imaging (DWI) to look for an acute lesion and a magnetic resonance angiogram (MRA) of the posterior circulation would establish the diagnosis in the face of a negative CT scan. An ultrasound study of the neck would not give adequate visualization of the vertebrobasilar system from arch to intracranial vessels. This patient has a risk of edema formation around the area of cerebellar infarction, with risk of obliteration of perimesencephalic cisterns and the fourth ventricle. Close monitoring by the nursing staff, more frequently than every 6 hours, should pick up change in mental status from obstructive hydrocephalus. This man does not have symptoms suggestive of subarachnoid hemorrhage (SAH), and a lumbar puncture in the face of possible posterior fossa obstruction increases the risk of herniation of the edematous cerebellum through the foramen magnum. (Savitz & Caplan, *N Engl J Med* 2005)

**475. The answer is B.** The FDA approved pregabalin (Lyrica), a novel GABA analogue, for the treatment of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia. It is also an FDA-approved treatment for fibromyalgia and as an adjunctive treatment in adults with partial seizures. It is not yet approved as adjunctive therapy in adults with GAD or social anxiety disorder. The most commonly reported adverse effects include somnolence, dizziness, weight gain, peripheral edema, and headache. (Tassone, Boyce, Guyer, & Nuzum, *Clin Ther* 2007)

**476. The answer is E.** Intravenous valproate sodium (Depacon) is effective in treatment of an intractable acute migraine headache and has been used to bridge the withdrawal of acute medication and the initiation of preventative medication in patients with CDH due to medication overuse. Intravenous valproate sodium is indicated in the ED for a patient with an intractable migraine headache in the setting of vascular risk factors or recent (within 24 hours) use of triptans, contraindicating the use of parenteral DHE. A study investigated the use of IV valproate sodium at loading dose of 15 mg/kg, followed by 5 mg/kg every 8 hours in the treatment of CDH or MOH. All analgesics and triptans were discontinued prior to treatment, and preventative medications for migraine were begun or continued. Improvement in headache was noted by 80% of patients treated with valproate sodium, which was generally well tolerated. (Schwartz, Karpitsky, & Sohn, *Headache* 2002)

**477. The answer is C.** Oral steroids are not shown to be effective in the prevention of migraine headaches or in the acute treatment of a migraine headache. However, there may be a role for IV steroids for treatment of acute migraine headaches in the ED. A randomized, double-blind, placebo-controlled multicenter trial evaluated the efficacy of 10 mg of IV dexamethasone (Decadron) as adjuvant therapy for patients who presented to an ED with acute migraine. All subjects also received IV metoclopramide (Reglan). Of the 205 migraine patients randomized, persistent pain-free outcome was achieved in 25% of those randomized to dexamethasone and 19% of placebo ( $p = 0.34$ ). In the subgroup of subjects with migraine lasting longer than 72 hours, 38% of those randomized to dexamethasone were persistently pain-free as compared to 13% of migraine patients treated with placebo ( $p = 0.06$ ). The investigators concluded that a moderate dose of IV dexamethasone should not be administered routinely for the ED-based treatment of acute migraine, although it might be useful for patients with migraine lasting longer than 72 hours. Avascular osteonecrosis at multiple sites, including the femoral head and capitates, has been reported after oral, nasal, topical, and intra-articular steroids. An osteonecrotic effect has also been found rarely after the relatively short-term use of IV steroids. (Friedman, Greenwald, Bania, et al., *Neurology* 2007)

**478. The answer is E.** Acetylsalicylic acid (aspirin or ASA) is an analgesic, antipyretic, and anti-inflammatory drug that is effective in the acute treatment of migraine headache. It has been associated with Reye's syndrome in young children with viral syndromes and with a hemorrhagic exanthema due to the Dengue virus. Despite concern about the hemorrhagic risk of ASA in the setting of an unruptured cerebral aneurysm, a study of patients with SAH found no deleterious effect on long-term outcome associated with the pre-hemorrhage use of aspirin. High-dose aspirin may be effective in the acute treatment of migraine. The efficacy and safety of 1,000 mg effervescent highly buffered preparation of aspirin (eASA) was compared to 50 mg sumatriptan and placebo in an individual patient data meta-analysis of three randomized, placebo-controlled, single-dose migraine trials. The treatment effect of eASA and sumatriptan were significantly different from placebo ( $p < 0.001$ ), but differences between eASA and sumatriptan were not significant. The individual patient data meta-analysis indicated that eASA 1,000 mg is as effective as sumatriptan 50 mg for the treatment of acute migraine attacks, including moderate and severe headaches, and has a better side-effect profile. Aspirin's propensity to cause occult and symptomatic bleeding, because of its platelet inhibitory effect, limits the frequent use of high-dose ASA. Many patients are also gastric-intolerant of high aspirin doses. (Diener, Lampl, Reimnitz, & Voelker, *Expert Rev Neurother* 2006; Lampl, Voelker, & Diener, *J Neurol* 2007; Toussaint, Friedman, Wijdicks, et al., *J Neurosurg* 2004)



**479. The answer is E.** Topiramate (Topamax) suppresses cortical neuronal excitability, a pathophysiological basis for migraine, by multiple mechanisms. The other listed mechanisms, as well as inhibition of carbonic anhydrase, contribute to its efficacy in prevention of acute migraine and suppression of CDH. (Ramadan, *Headache* 2007)

**480. The answer is C.** Stratification of care pairs the severity or risk of the medical condition with the intensity of the intervention and should be the inspiration for management of headache patients. The choice of treatment of a patient's headaches should be based on headache characteristics, as well as the extent of headache-related disability, the patient's comorbid conditions, individual preference, and response to prior treatment. The Migraine Disability Assessment (MIDAS) Questionnaire can be used to stratify patients into groups with different treatment needs based on the degree of headache-related disability. Stratified care is an alternative to stepped care, which dictates initiation with nonspecific pain medication with a stepwise increase in specificity of headache medication and intervention until satisfying headache relief is obtained. (Lipton & Silberstein, *Neurology* 2001)

**481. The answer is E.** Triptans activate serotonergic, 5-HT<sub>1B</sub> receptors on blood vessels, through which they mediate vasoconstriction and neuronal inhibition. They also activate 5-HT<sub>1D</sub> receptors. Some triptans stimulate 5-HT<sub>1F</sub> receptors, although their therapeutic relevance is not clear. Triptans, with variable central penetration, have an unclear role in aborting an acute migraine by central 5-HT<sub>1</sub> receptor activation; however, penetrability of the blood-brain barrier may change during a migraine attack. (Humphrey, *Headache* 2007)

**482. The answer is D.** Induction of the hepatic cytochrome P450 enzymes, specifically the 3A4 isoenzyme system, contributes to the failure of oral contraceptives by increasing the metabolism of estrogens and progestins and decreasing their circulating levels up to 50%. Carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin) are potent inducers; topiramate (Topamax) and oxcarbazepine (Trileptal) are less potent inducers. Dose-dependent reduction of ethinyl estradiol with topiramate is significant at doses higher than 200 mg. Medications that do not induce this enzyme system and thus would not lead to contraceptive failure include divalproex sodium (Depakote), gabapentin (Neurontin), levetiracetam (Keppra), tiagabine (Gabitril), vigabatrin (Sabril), zonisamide (Zonegran), and pregabalin (Lyrica). (Harden & Leppik, *Neurology* 2006)

**483. The answer is B.** The exact teratogenic risk of medications used to treat seizures and headaches is difficult to determine, but valproate sodium (Depakene)



or divalproex sodium (Depakote) appears to have the greatest risk of the medications listed. The estimated risk of spina bifida is estimated to be 1–2%, and divalproex sodium is pregnancy category D. The risk for birth defects, including notochord anomalies and cognitive deficits, with divalproex sodium appears to be dose-related. Drug level monitoring, monotherapy, and folate supplementation may decrease the risk when divalproex sodium therapy during pregnancy cannot be avoided. (Kalviainen & Tomson, *Neurology* 2006; Kaniecki, *Headache* 2008)

**484. The answer is C.** Hyperammonemia, generally asymptomatic, has been associated with divalproex sodium (Depakote) treatment alone. The risk of hyperammonemia and hyperammonemic encephalopathy is increased with divalproex sodium in combination with topiramate (Topamax). Metabolic acidosis may be associated with topiramate use. Weight gain and pancreatitis are associated with divalproex sodium. The combination of lamotrigine (Lamictal) and divalproex sodium increases the risk of skin toxicity including SJS. (Kaniecki, *Headache* 2008)

**485. The answer is E.** The nonprescription combination of acetaminophen, aspirin, and caffeine is widely used by patients with migraine headache, with a significant risk of MOH. A retrospective study of the benefits of the combination of analgesics found that for both menstruation-associated migraine and migraine not associated with menses, the proportion of subjects with pain intensity reduced to mild or none was significantly greater with the combination than with placebo at all postdose time points ( $p \leq 0.05$ ). The combination was highly effective in treating the pain, disability, and associated symptoms of both menstruation-associated migraine and migraine not associated with menses. The ASSET trial compared acetaminophen 500 mg, aspirin 500 mg, and caffeine 130 mg with sumatriptan (Imitrex) 50 mg in a randomized, controlled clinical trial in which subjects were treated at the first sign of a migraine attack. The combination was significantly more effective ( $p > .05$ ) than sumatriptan in the early treatment of migraine, as shown by superiority in summed pain intensity difference, pain relief, pain intensity difference, response, sustained response, relief of associated symptoms, use of rescue medication, disability relief, and global assessments of effectiveness. A study comparing acetaminophen 250 mg, aspirin 250 mg, and caffeine 65 mg per tablet to ibuprofen 200 mg found that they are both safe, cost-effective treatments for migraine but the combination provided significantly superior efficacy and speed of onset as compared with ibuprofen. (Goldstein, Silberstein, Saper, et al., *Headache* 2005; Goldstein, Silberstein, Saper, et al., *Headache* 2006; Silberstein, Armellino, Hoffman, et al., *Clin Ther* 1999)

**486. The answer is E.** All the listed interventions are used to treat IIH. Decreased cerebral spinal fluid production through inhibition of carbonic anhydrase

may explain the benefit of topiramate (Topamax) and acetazolamide (Diamox) in IIH. Ventriculo-peritoneal and lumbo-peritoneal shunts divert spinal fluid and decrease intracranial pressure (ICP). Medication and CSF diversion to decrease ICP improve the chronic headaches and indirectly decrease the risk of vision loss with IIH. Optic nerve sheath fenestration, a relatively straightforward surgical procedure, specifically arrests the progression of vision loss by decompressing the pressure on the optic nerve. (Skau, Brennum, Gjerris, & Jensen, *Cephalalgia* 2006)

**487. The answer is A 3, B 2, C 4, D 5, E 1.** Caffeine is a stimulant that is found in coffee, tea, chocolate, carbonated soft drinks, and medications. Patients report that headache pain may be decreased after treatment with caffeine; however, excess use of caffeine may contribute to chronic headaches or headaches may occur with a precipitous decrease in caffeine intake. Patients may misjudge the amount of caffeine ingested and not link their use of caffeine with changes in behavior or sleep. A study that analyzed the caffeine contents of carbonated beverages using high-performance liquid chromatography found caffeine contents of the following: Coca-Cola (33.9 mg/12 oz), Diet Coke (46.3 mg/12 oz), Pepsi (38.9 mg/12 oz), Diet Pepsi (36.7 mg/12 oz), Dr Pepper (42.6 mg/12 oz), Diet Dr Pepper (44.1 mg/12 oz), Mountain Dew (54.8 mg/12 oz), and Diet Mountain Dew (55.2 mg/12 oz). Caffeine content in cups of black tea (range of 30 to 50 mg) and brewed coffee (range of 100 to 150 mg) are variable. A brewed Starbucks Grande (16 oz) coffee contains 320 mg of caffeine. The increasingly popular energy drinks are highly caffeinated; an 8.3 oz can of Red Bull contains 80 mg of caffeine and other brands have up to 300 mg in about 8 oz. Excedrin Migraine<sup>®</sup> contains acetaminophen 250 mg, aspirin 250 mg, and caffeine 65 mg. A caplet of Extra Strength Excedrin<sup>®</sup> also contains acetaminophen 250 mg, aspirin 250 mg, and caffeine 65 mg. A tablet of Excedrin Tension Headache<sup>®</sup> contains acetaminophen 500 mg and caffeine 65 mg. (Chou & Bell, *J Food Sci* 2007)

**488. The answer is D.** A post hoc analysis of the Spectrum Study evaluated a subgroup of patients who treated headaches with sumatriptan (Imitrex) 50 mg while pain was mild. Twenty-six patients with disabling headaches treated 46 mild and 166 moderate or severe headaches. Across all headaches treated while the pain was mild, pain-free responses were higher for sumatriptan than for placebo at 2 and 4 hours. When patients treated headaches while pain was moderate or severe, pain-free rates were lower than when the patients initiated treatment during mild headache pain. Headache recurrence tended to be less when mild headache pain was treated, compared to when moderate or severe headache pain (13% versus 18%) was treated. Adverse events related to sumatriptan were less when the headaches were treated while pain was mild than when pain was more severe. (Cady, Lipton, Hall, et al., *Headache* 2000)

**489. The answer is E.** Symptoms of acute mountain sickness (headache, anorexia, nausea, fatigue, dizziness, insomnia) develop in unacclimatized individuals within days of arrival at a high altitude. Cerebral edema and pulmonary syndromes can develop if treatment is not initiated when symptoms start. Acetazolamide (Diamox) and steroids, either individually or in combination, can be used to prevent high-altitude headache and the development of acute mountain sickness. Headaches associated with acute mountain sickness can be treated or prevented with NSAIDs, acetaminophen, oral sumatriptan (Imitrex), or low-dose gabapentin (Neurontin) in combination with ibuprofen. (Jafarian, Gorouhi, Salimi, & Lotfi, *Cephalalgia* 2007; Jafarian, Gorouhi, Salimi, & Lotfi, *Ann Neurol* 2007; Queiroz & Rapoport, *Curr Pain Headache Rep* 2007)

**490. The answer is D.** A long-acting oral triptan, such as frovatriptan (Frova), would appear to be a reasonable medication for the prevention of post-dural puncture headache (PDPH). A nonrandomized open-label study suggested efficacy of 5-day treatment with frovatriptan 2.5 mg/day for the prophylaxis of PDPH. A mild headache occurred in seven (14%) patients for a total of 9 days ( $p < 0.01$  versus no PDPH). The rate of PDPH was compared to a literature-reported rate of PDPH of up to 40%. Data on the use of subcutaneous sumatriptan in the acute treatment of PDPH is inconclusive, and this woman does not like needles. A review by Halker et al. of the available clinical trials of PDPH found that they were scant, small in sample size, methodologically flawed, and demonstrated either lack of benefit or contradictory results. The review determined that there was no pharmacologic rationale for caffeine as an antinociceptive agent for PDPH. High-dose aspirin is unlikely to confer much specific benefit in the treatment of PDPH, and its antiplatelet effect would not be beneficial after a traumatic puncture. (Bussone, Tullo, d'Onofrio, et al., *Cephalalgia* 2007; Halker, Demaerschalk, Wellik, et al., *Neurologist* 2007)

**491. The answer is C.** Treatment with corticosteroids in acute bacterial meningitis can reduce the inflammatory process in the subarachnoidal space. A meta-analysis of randomized controlled trials of adjuvant corticosteroids used in the treatment of acute bacterial meningitis found that adjuvant corticosteroids were associated with decreased mortality (relative risk [RR] 0.83, 95% CI 0.71–0.99), lower rates of severe hearing loss (RR 0.65, 95% CI 0.47–0.91), and less long-term neurologic sequelae (RR 0.67, 95% CI 0.45–1.00). In adults with community-acquired bacterial meningitis, corticosteroid therapy should be administered in conjunction with the first antibiotic dose. In children, corticosteroids reduced severe hearing loss after bacterial meningitis. Steroids improved outcome with meningitis due to *Streptococcus pneumoniae* and *Haemophilus influenzae*, but benefit was

less clear with meningococcal meningitis. The use of corticosteroids in the meta-analysis in acute bacterial meningitis was not associated with adverse events. (van de Beek, de Gans, McIntyre, & Prasad, *Cochrane Database Syst Rev* 2007)

**492. The answer is B.** Headaches recur after triptan use at a rate ranging from 17% to 40%, influenced by the pharmacologic and pharmacokinetic properties of the individual triptans. The triptans with longer half-lives and greater 5-HT<sub>1B</sub> receptor potency had the lowest rates of headache recurrence. Although half-life and 5-HT<sub>1B</sub> receptor potency are inversely correlated with headache recurrence, 5-HT<sub>1D</sub> receptor potency, as well as the binding affinities for the 5-HT<sub>1B</sub> and 5-HT<sub>1D</sub> receptors, are not correlated with headache recurrence. Initial clinical efficacy is not correlated to headache recurrence. (Géraud, Keywood, & Senard, *Headache* 2008)

**493. The answer is C.** This woman has either familial or sporadic hemiplegic migraine for which triptans are not indicated. However, studies have not shown risk with the treatment. In one study, 76 subjects with familial or sporadic hemiplegic migraine used triptans at least once as an abortive treatment. The headaches responded to the triptan without any cerebrovascular or cardiovascular events. Over-the-counter medication and combination medication may not be as effective as a triptan. An ergotamine would not be appropriate for this woman, but a triptan is most likely to treat her headaches without vascular risk. (Artto, Nissilä, Wessman, et al., *Eur J Neurol* 2007)

**494. The answer is C.** The therapeutic response to indomethacin (Indocin) defines PH and distinguishes this TAC from CH and SUNCT, which do not respond to this specific prescription NSAID. Hemicrania continua also responds to indomethacin. (Goadsby, Cohen, & Matharu, *Curr Neurol Neurosci Rep* 2007)

**495. The answer is E.** All of these agents can be used in patients with a severe migraine headache that lasts longer than 72 hours and is refractory to usual oral migraine therapies. They are all safe for use in patients with vascular disease, except for DHE. This ergot derivative is a vasoconstrictor that has an effect on arteries, including those in the carotid and coronary beds, and on veins. Ergot alkaloids, including DHE and ergotamine, should not be used in patients with known or symptomatic vascular disease. (Oleson, Goadsby, Ramadan, et al., *Headaches*, 2006)

**496. The answer is A.** Hypnic headaches are moderate-severity headaches noted by elderly individuals on awakening. Multiple medications and caffeine have been tried to prevent hypnic headaches, with variable success. Topiramate (To-

pamax), pregabalin (Lyrica), melatonin, and indomethacin (Indocin) are among some of the medications noted to be of benefit, but the greatest relief is noted with lithium. (Evers & Goadsby, *Neurology* 2003)

**497. The answer is E.** Flunarizine is a calcium-channel blocker that is efficacious for the prevention of migraine headaches in both children and adults. It is not available in the United States, but can be obtained in Europe. The most common side effects associated with its use in adults are depression, weight gain, and extrapyramidal symptoms, which this woman exhibits. Other side effects include sedation and abdominal pain. (Verspeelt, De Locht, & Amery, *Cephalalgia* 1996)

**498. The answer is D.** The efficacy of an acute pain medication must be judged against the natural history of migraine headaches, as the headache pain may be self-limited and responsive to nonpharmacologic treatment. The placebo response in randomized clinical trials of analgesics in the treatment of migraine attacks was assessed in an analysis of 11 studies. Headache response at 2 hours occurred after placebo treatment in 7–50% of the migraineurs, with an average placebo response rate of 30% (95% CI 23–36). Two hours after treatment with placebo an average of 9% (95% CI 7–12, range 7–17%) of the patients were found to be pain free. Placebo response rates vary with the choice of primary efficacy measure as well as patient characteristics (increased in children) and study design (decreased in random crossover studies). (Bendtsen, Mattsson, Zwart, & Lipton, *Cephalalgia* 2003)

**499. The answer is E.** The American Migraine Prevalence and Prevention (AMPP) study concluded that a substantial percentage of migraine sufferers who might benefit are not receiving preventative therapy. Preventative medication should be initiated at a low dose, in a long-acting formulation if available, with a gradual escalation of the dose. A therapeutic dose should be maintained for at least 2–3 months in order to judge efficacy. The drug dose may be increased to toxicity or intolerability before it is determined to be ineffective. Drug interactions, with potential for toxicity, increase with polypharmacy. (Kaniecki, *Headache* 2008)

**500. The answer is E.** In a comparison study of patients in the ED, either prochlorperazine (Compazine) 10 mg intravenously or metoclopramide (Reglan) 20 mg intravenously, combined with diphenhydramine (Benadryl) 25 mg intravenously, was found to be an efficacious and well-tolerated treatment for patients with acute migraine. Intravenous haloperidol (Haldol) has been shown to be an effective rescue medication for intractable acute migraine. However, the study evaluating haloperidol in the ED found that, although relapses were rare, side

effects were common, limiting its use in some patients. Tramadol (Ultram<sup>®</sup>), an atypical opioid, is a centrally acting narcotic analgesic generally used for oral pain management. It is a synthetic analogue of codeine, often combined with acetaminophen (Ultracet<sup>®</sup>), and it is felt to have a lower habituation potential than other narcotic analgesics. A study of adults with migraine found that a slow IV infusion of tramadol 100 mg in 100-mL saline solution was more effective than placebo in pain response rate at the end of the first hour; it was also well-tolerated in the ED. (Alemdar, Pekdemir, & Selekler, *Clin Ther* 2007; Friedman, Esses, Solorzano, et al., *Ann Emerg Med* 2007; Honkaniemi, Liimatainene, Rainesalo, & Sualvuori, *Headache* 2006)

**501. The answer is E.** Naratriptan (Amerge) has an elimination half-life intermediate between the short-acting triptans and frovatriptan (Frova), the triptan with the longest half-life. Its peak concentration is between 2 and 3 hours, delaying onset of clinical efficacy as compared to the short-acting triptans. It has been used in the prevention of menstrual migraine. In a study of the prevention of menses-related migraine, women were randomized to receive either naratriptan 1 mg twice daily or placebo beginning 3 days before the predicted onset of menses-related migraine for a total of 6 days. The preventative use of naratriptan for menses-related migraine was efficacious and well tolerated. However, frovatriptan is used more frequently than naratriptan for menstrual migraine prophylaxis. (Mannix, Savani, Landy, et al., *Headache* 2007)

**502. The answer is B.** Trephination of the skull, with perforation by a surgical instrument, is one of the oldest therapeutic procedures used for the treatment of headache. A trephined skull, dating back thousands of years, showed new bone growth indicating some postoperative survival, although no correlating ancient headache diaries showing therapeutic benefit with the procedure have yet been found. Trephination in Africa dates back to the time of Herodotus and continues to be practiced there. A burr-hole, a small opening in the skull made with a surgical drill, is currently used to evacuate a subdural hematoma causing neurological deficits and headache and is contemporary trephination. A poultice made from the skull of catfish or other animals, boiled in oil, is mentioned in ancient Egyptian medical papyri but is not in current use. Phlebotomy has been used for headache due to hereditary hemochromatosis. Aspirin and butalbital, while still in use, are more modern inventions. (Rawlings, *Surg Neurol* 1994)

**503. The answer is D.** Gabapentin (Neurontin), pregabalin (Lyrica), and vigabatrin (Sabril) are excreted unchanged in the urine. The dosages should be adjusted in patients with renal disease, based on creatinine clearance. Levetiracetam (Kep-

pra) has linear kinetics and is eliminated partly in unchanged form by the kidneys and partly by hydrolysis to an inactive metabolite, without involvement of oxidative and conjugative enzymes. (Elwes & Binnie, *Clin Pharmacokinet* 1996)

**504. The answer is A 2, B 5, C 4, D 3, E 1.** High doses of gabapentin (Neurontin) result in saturation of gastrointestinal absorption; bioavailability decreases with increasing dosage above 1,800 mg. Lamotrigine (Lamictal) and gabapentin have a predominantly renal excretion and are not metabolized through the cytochrome P450 system. Lamotrigine has not been particularly useful with migraine prophylaxis, but some small studies indicate that lamotrigine may be particularly effective in migraine with aura. Oxcarbazepine (Trileptal) is immediately metabolized to a hydroxy metabolite and could be considered a prodrug. It appears to have fewer pharmacokinetic interactions than carbamazepine (Tegretol), but it is associated with clinically significant hyponatremia. The combination of an MAOI, such as phenelzine (Nardil), and amitriptyline (Elavil) may decrease the food-related hypertensive risk of MAOIs alone. Cyproheptadine (Periactin), with its serotonergic antagonist effect, reverses the sexual dysfunction associated with serotonin reuptake inhibitors. (Wolff's *Headache and Other Pain*; Elwes & Binnie, *Clin Pharmacokinet* 1996)

**505. The answer is C.** In a study comparing treatment with subcutaneous sumatriptan (Imitrex) (6 mg) and IV ketorolac (Toradol) (total 30 mg bolus) in patients with migraine with allodynia, treatment with ketorolac was more likely to render the patients free of pain and allodynia. A history of opioid treatment predicted lack of response to treatment. In a rat model, infusion of cyclooxygenase (COX1/COX2) inhibitors (ketorolac or indomethacin [Indocin]) blocked sensitization in meningeal nociceptors and suppressed ongoing sensitization in spinal trigemino-vascular neurons. Migraine with ongoing allodynia was treated by COX1/COX2 inhibition through suppression of central sensitization. Parenteral DHE may be effective for migraine-related allodynia, although further investigation is needed. (Jakubowski, Levy, Goor-Aryeh, et al., *Headache* 2005)

**506. The answer is A.** A prospective observational study of epilepsy centers determined if differential long-term cognitive and behavioral neurodevelopmental effects exist with epilepsy medications. Percentages of serious adverse outcomes associated with fetal exposure to the medications were as follows: carbamazepine (Tegretol) 8.2%, lamotrigine (Lamictal) 1.0%, phenytoin (Dilantin) 10.7%, and divalproex sodium (Depakote) 20.3%, with a dose-dependent effect. Divalproex sodium poses the highest risk to the fetus, with in utero exposure potentially leading to disruption of notochord development, resulting in spina bifida. Di-



valproex sodium has also been associated with neurodevelopmental delay and autistic spectrum disorders in the children of women exposed to the drug during pregnancy. Folate supplementation initiated prior to pregnancy may decrease the risk of teratogenicity when the drug is given to women of reproductive age. (Duncan, *Curr Opin Neurol* 2007; Meador, Baker, Finnell, et al., *Neurology* 2006)

**507. The answer is D.** Although reduced sexual functioning is a common depressive symptom, anorgasmia and ejaculatory dysfunction may be reported, often only on direct questioning, in patients treated with SSRIs. Drugs that have been tried to counteract the sexual side effects of SSRIs include serotonin receptor antagonists,  $\alpha_2$ -adrenergic receptor antagonists, and dopaminergic agents. Sildenafil (Viagra) may also have a role in the treatment of antidepressant-associated sexual side effects. (Fava & Rankin, *S Clin Psychiatry* 2002)

**508. The answer is A.** Hypothalamic dysfunction, with increased metabolic activity in the suprachiasmatic nucleus, appears to be an important pathophysiologic mechanism of CHs. Some male CH patients have been reported to be overmasculinized. Recent neuroendocrine and sleep studies point to an association between gonadotropin and corticotropin levels and the pineal secretion of melatonin. However, clinical response to melatonin has been inconsistent, and melatonin levels do not appear to be of clinical import in CH patients. Seven male and two female patients, with treatment-resistant CH and decreased serum testosterone levels were supplemented with either pure testosterone in five of seven male patients or combination testosterone–estrogen therapy in the female patients. The patients achieved CH freedom for the first 24 hours after treatment. Four male testosterone-deficient patients achieved remission of their chronic CHs. The author of the study concluded that abnormal testosterone levels in patients with refractory CH may predict a therapeutic response to testosterone replacement therapy. (Stillman, *Headache* 2006)

**509. The answer is A 6, B 3, C 5, D 1, E 1, F 2.** Feverfew (*Tanacetum parthenium*) is a species-specific preparation of dried chrysanthemum leaves. Reports of its efficacy in prevention of migraine headache have been underwhelming, and there is a very large variation in the percentage of active ingredient in the available commercial preparations. *Petasties hybridus* (butterbur) is prepared from the root of a perennial shrub that grows wild on German riverbanks. Early reports of efficacy are encouraging but await further study. Magnesium is an NMDA receptor inhibitor with putative neuroprotective effect that is being studied in acute ischemic stroke trials. Variable benefit has been found in randomized clinical trials of headache prevention using oral preparations, although there may be benefit with



IV magnesium with acute intractable migraine. Riboflavin (vitamin B<sub>2</sub>) and coenzyme Q10 are both electron transporters within the Krebs cycle. Encouraging results have been seen with these supplements in scanty clinical trials. Melatonin, 5-methoxy-N-acetyltryptamine, is secreted by the pineal gland with oversight by the suprachiasmatic nucleus of the hypothalamus. While a potential role for melatonin has been postulated for hypothalamically mediated CH, there does not appear to be a role for treatment with melatonin in migraine headaches. (Evans & Taylor, *Headache* 2006)

**510. The answer is A.** Tricyclic antidepressants are the most widely used and most effective medication for prevention of chronic tension-type headache (CTTH). Nighttime dosing of the TCA may benefit patients who also have difficulty with initiation or maintenance of sleep. Patients may note increased appetite with TCAs, with resultant weight gain. Nonsteroidal anti-inflammatory agents, especially ibuprofen and naproxen, are effective for acute treatment but NSAIDs are not generally used for daily preventative therapy. Long-term use may be complicated by renal or gastric complications. Selective serotonin reuptake inhibitors (SSRIs) are not convincingly effective for prevention of CTTH in the absence of significant underlying depression. Botulinum toxin has been used as a treatment for chronic headache, including CTTH, without convincing scientific proof of efficacy. Anticonvulsant medications, particularly topiramate (Topamax) and divalproex sodium (Depakote), are effective for prevention of migraine headaches, but evidence for efficacy in prevention of CTTH is less clear. (Fumal & Schoenen, *Lancet Neurol* 2008)

**511. The answer is A.** A study evaluated the impact of placebo, ASA, ergotamine tartrate, zolmitriptan (Zomig), and sumatriptan (Imitrex) on platelet and erythrocyte aggregation in a human ex vivo experimental design. Ergotamine tartrate induced a significant increase of platelet aggregation, whereas ASA induced a significant decrease platelet aggregation. Placebo, sumatriptan, and zolmitriptan did not alter platelet aggregation or erythrocyte aggregation. Platelet aggregation, but not erythrocyte aggregation, was increased by ergotamine tartrate. The role that platelet aggregation contributes to the vascular side effects of ergotamine is not clear. (Evers, Heuel, Frese, et al., *Cephalalgia* 2006)

**512. The answer is C.** Reversible cerebral vasoconstriction syndromes (RCVS) are a set of disorders, of multiple etiologies, which are characterized by vasoconstriction on angiography. They are distinct from primary angiitis of the central nervous system (PACNS) in that they are usually self-limited, with resolution of the headache, focal neurologic deficits, and angiographic evidence of vasospasm

within days to weeks. No treatment is of proven value in RCVS but empiric treatments include calcium channel blockers, steroids, blood pressure manipulation, and rarely endovascular therapy. Calcium channel inhibitors appear to be the most effective therapy for segmental cerebral arterial vasoconstriction. Steroids are generally not indicated, although a short course of steroids may be tried when the presentation overlaps that of PACNS. (Bernstein, *Curr Treat Opt Cardiovasc Med* 2006)

**513. The answer is D.** The combination of cognitive behavioral therapy (such as stress management programs) and a TCA (such as amitriptyline [Elavil] or nortriptyline [Pamelor<sup>®</sup>]) is more effective and more durable in the prevention of CTTH than either therapy alone. Biofeedback and relaxation therapies alone and in combination are useful in the treatment of TTH. When combined with cognitive behavioral therapy and preventative medications, they are especially effective. The scientific basis for acupuncture or oromandibular treatment (occlusal splints or adjustment, masticatory muscle exercises) in CTTH has not been established. (Fumal & Schoenen, *Lancet Neurol* 2008)

**514. The answer is E.** Baclofen (Lioresal<sup>®</sup>) is a muscle relaxant and antispasmodic medication that is used for pain control in patients with trigeminal neuralgia. Continuous baclofen delivered by an intrathecal pump is used for severe spasticity. Acute withdrawal from baclofen can precipitate a potentially life-threatening condition with hallucinations, hyperpyrexia, autonomic instability, muscle spasms, rigidity, and seizures. This rare complication of baclofen, which is seen more frequently with an intrathecal as compared to an oral formulation, can be prevented by tapering the medication, as opposed to abrupt cessation of use. The clinical presentation of acute baclofen withdrawal may resemble serotonin syndrome but the withdrawal syndrome may be due to acute changes in glutamatergic NMDA, GABA<sub>A</sub>, and GABA<sub>B</sub> receptor response, leading to increased excitability and spontaneous activity. (D'Aleo, Cammaroto, Rifici, et al. *Funct Neurol* 2007;22(2):81–88)

**515. The answer is D.** Ramsay-Hunt syndrome is peripheral facial nerve weakness with a vesicular rash on the ear or in the mouth; the syndrome is caused by a varicella zoster virus infection, which should be treated with antiviral medication. Bell's palsy is idiopathic facial weakness that generally resolves without any treatment. Bell's palsy may be associated with a herpes simplex virus infection for which antiviral medication may be indicated. Early treatment of patients with Ramsay-Hunt syndrome or Bell's palsy with a 7–10 day course of the antiviral medications famciclovir (500 mg, three times daily) or acyclovir (800 mg, five

times daily), as well as oral prednisone (60 mg daily for 3–5 days) can be considered. Other data suggest however that early treatment with steroids alone may be sufficient for patients with Bell's palsy. Facial physical therapy and acupuncture have not shown benefit in the treatment of Bell's palsy. Unilateral lower motor neuron facial weakness may also be associated with pregnancy, Lyme disease, sarcoidosis, diabetes, mass lesions, and peripheral demyelination. (Sweeney & Gilden, *J Neurol Neurosurg Psychiatry* 2001)

# 6

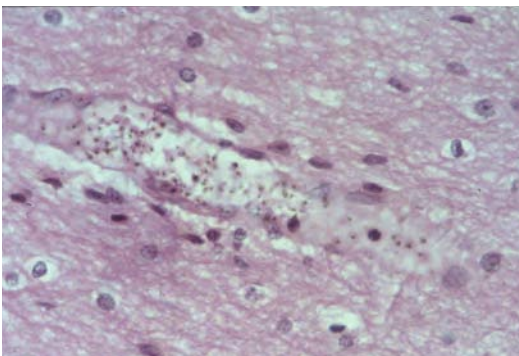
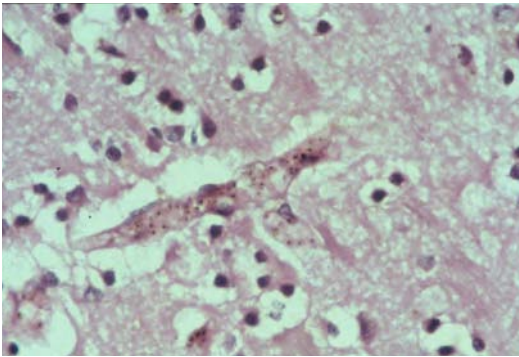
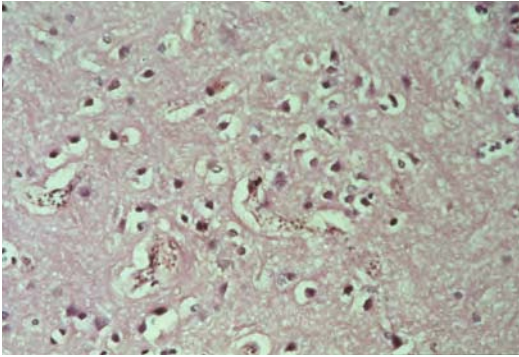
## CLINICAL HEADACHE SCENARIOS

### SCENARIO 1

A 19-year-old college student went to West Africa for a semester abroad. She did not have a history of headaches but she was treated for depression and generalized anxiety disorder. When she came back to the United States, she developed headaches, fever and lethargy but attributed her symptoms to jet lag. After being home for a week, she had a generalized tonic-clonic seizure and was brought to an emergency department. She was found to be somnolent, febrile and hypotensive. On neurologic examination, she was uncooperative but was noted to be hypertonic with brisk tendon reflexes bilaterally. Laboratory examination revealed severe anemia, hypoglycemia, and elevated liver, and renal function tests. In spite of treatment she died a few days later.

1. Which infectious disease, which causes headache and fever in international travelers, led to this woman's death?
- A. Hantavirus infection
  - B. Dengue fever
  - C. Malaria
  - D. Q fever
  - E. Brucellosis

2. What do these pathologic images show?



- A. Parasitized red blood cells in the capillaries
- B. Perivascular white blood cell infiltration
- C. Diffuse gliosis
- D. Foci of cerebral necrosis
- E. Demyelination

3. How could her disease have been prevented most effectively?

- A. Prophylaxis with mefloquine (Lariam)
- B. Prophylaxis with the combination of atovaquone and proguanil (Malarone)
- C. Use of a mosquito net over the bed at night
- D. Use of an anti-mosquito spray before going outside
- E. Avoidance of perfumes and scented body products

**1. The answer is C.** Malaria, the world's most important parasitic infection, remains a major cause of morbidity and mortality in tropical countries. Cerebral malaria should be considered in international travelers and inhabitants of tropical countries who develop headache and rapid neurological and multisystem deterioration. Malaria is caused by the *Plasmodium* species, which is acquired in sporozoite form when inoculated through the skin during a blood meal by a female *Anopheles* mosquito. The merozoites forms are erythrocytic parasites. Although infections with *P. vivax*, *P. ovale*, or *P. malariae* are rarely fatal, an infection with *P. falciparum* may cause a rapidly progressive or fatal disease.

Infection with hantaviruses, RNA viruses carried by rodents, can present with fever, headache, gastrointestinal symptoms, impaired renal function, and blurred vision. Q fever, due to a *Coxiella burnetii* infection, should be considered in recent travelers from the tropics who present with fever, headache, elevated liver enzymes, leukopenia, and thrombocytopenia. Neurobrucellosis presents with fever, headache, confusion, and gait disorders after exposure to infected animals or ingestion of unpasteurized milk products. Dengue is a mosquito-borne viral infection; patients may exhibit fever, nausea, headache, cough, diarrhea, macular rash and thrombocytopenia.

**2. The answer is A.** This brain specimen from the autopsy of this woman shows the preferential sequestration of parasitized red blood cells in the cerebral microvasculature. The brain sections reveal an edematous brain parenchyma with numerous small dot-like inclusions within red blood cells in the lumen of multiple capillaries. This morphology is consistent with merozoites forms (erythrocytic parasites) of the *Plasmodium* species of malaria. Other neuropathologic features of cerebral malaria include petechial hemorrhages in the brain parenchyma, ring hemorrhages, and Dürck's granulomas (astrocyte and microglial aggregates characteristic of cerebral malaria).

**3. The answer is B.** All of the listed choices can be used to prevent malaria, but travelers into areas with endemic malaria should take appropriate prophylactic medication given the high likelihood that they will be bitten by an infected mosquito. Prophylaxis initiated prior to travel with the combination of atovaquone

and proguanil (Malarone) could have prevented this woman's infection, as the medication is 95–100% effective against chloroquine-resistant and multidrug-resistant strains of *P. falciparum*. The medication is contraindicated in pregnancy or severe renal disease. Prophylaxis with mefloquine (Larian) is not appropriate in people with a history of psychiatric disease including depression and generalized anxiety disorder. Mefloquine has been associated with psychosis and seizures at prophylactic dosages. (Turner, *Brain Pathol* 1997; White, *N Engl J Med* 1996)

## SCENARIO 2

R. C. is 45-year-old woman without a past history of headaches. She has complained of intermittent holocephalic headaches and dizziness for 3 weeks. The head pain was worse in the morning and in the late evening after she got home from work. She had just separated from her husband and had moved into an old house she was renovating; she attributed her headache to stress and sleep deprivation. Her family doctor gave her a selective serotonin reuptake inhibitor (SSRI) because she found her beloved cat dead in the basement a week ago. She was given a triptan for her headaches and told to keep a diary. The next day R.C. came into the emergency department unresponsive. She appeared flushed with pink skin.

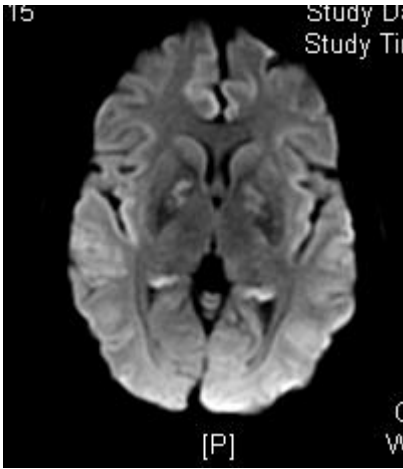
1. What test is most likely to diagnose the cause of this woman's headaches?
  - A. CT scan of the brain
  - B. Spinal fluid analysis
  - C. Liver function tests
  - D. Renal function tests
  - E. Serum carboxyhemoglobin level
2. Which treatment is should be considered?
  - A. Plasmapheresis
  - B. Renal dialysis
  - C. Hyperbaric oxygen
  - D. Phlebotomy
  - E. Intravenous immunoglobulin

After being hospitalized for a week, R.C. recovered to go home to live with her sister. She went back to her job as a physical therapist, but her co-workers noted that she was increasingly withdrawn and distracted. Intermittently, they would find her in the bathroom crying. She became frustrated when she forgot some of her patients' names.

3. What is her diagnosis?

- A. Anxiety
- B. Depression
- C. Delayed neurologic damage
- D. Limbic encephalitis
- E. Posttraumatic stress disorder

She was seen as an outpatient by a neurologist who obtained this MRI scan:



4. Where is the abnormality on the MRI of the brain?

- A. Basal ganglia
- B. Thalamus
- C. Periventricular white matter
- D. Corpus callosum
- E. Frontal cortex

**1. The answers is E.** This woman has carbon monoxide (CO) poisoning, with progression from nonspecific symptoms of headaches and dizziness to coma. Carbon monoxide, a colorless, odorless gas that binds to hemoglobin many times more strongly than does oxygen, can cause progressive cerebral hypoxia with prolonged exposure to elevated concentrations. Serum levels of carbon monoxide can be determined by measuring carboxyhemoglobin, a stable complex of carbon monoxide and hemoglobin. Carboxyhemoglobin levels may range up to 10% in normal individuals depending on environmental exposure; progressive symptoms of cerebral hypoxia may begin as levels increase above around 20%.



This woman's house had an old furnace that was leaking CO, thus exposing her during the hours she was home from work. Her indoor cat died from chronic CO exposure. Carbon monoxide poisoning can present initially with nonspecific symptoms, including headache, dizziness, and flu-like symptoms, but continued exposure to the dangerous environment can lead to coma, permanent neurologic damage, or death.

**2. The answer is C.** Emergency treatment of CO poisoning begins with inhalation of supplemental oxygen and aggressive supportive care. Hyperbaric oxygen treatment accelerates dissociation of CO from hemoglobin but this treatment in CO poisoning remains controversial. Hyperbaric oxygen may be used in neurologically devastated patients.

**3. The answer is C.** This woman had mood and cognitive dysfunction occurring after recovery from CO poisoning. This delayed neurologic damage can present as depression, dementia, or change in personality that occurs days to weeks after the episode of CO poisoning. This cognitive and mood disorder may develop weeks to months after the CO exposure and is more common in patients who had alteration in consciousness with the initial exposure.

**4. The answer is A.** The MRI in patients with delayed neurologic damage after CO poisoning characteristically shows abnormal signal in the basal ganglia bilaterally. (Kao & Nañagas, *Emerg Med Clin North Am* 2004)

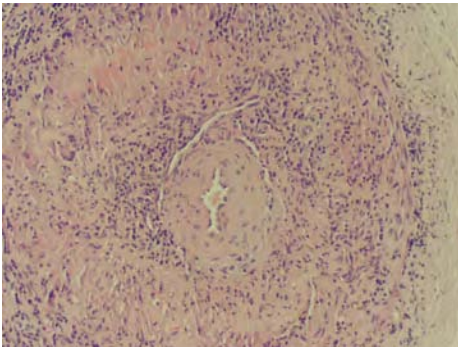
### SCENARIO 3

A 69-year-old woman suffered an ischemic stroke due to a vertebral artery occlusion, with residual dysarthria and ataxia. While in an inpatient rehabilitation facility to undergo intensive physical therapy, she developed right temporal headaches. Despite delicious institutional food, she was losing weight because of decreased appetite and pain in her jaws with eating. Her physical therapist was also concerned that she seemed to have less stamina, with complaints of proximal muscle aching, and that she was not making the expected progress in physical therapy. She had tenderness on palpation of her right temporal area.

1. What diagnosis concerns you when you see her in consultation?
  - A. Rheumatoid arthritis
  - B. Cerebral vasculitis
  - C. Giant cell arteritis (GCA)
  - D. Systemic lupus erythematosus (SLE)
  - E. Polymyositis
  
2. What testing would be most likely to provide her the reason for her headaches?
  - A. Magnetic resonance imaging (MRI) scan of the brain
  - B. Magnetic resonance angiogram (MRA) scan of brain vessels
  - C. Carotid ultrasound
  - D. Complete blood count
  - E. C-reactive protein (CRP)

Treatment was initiated based on testing results.

3. What study would be appropriate to confirm the diagnosis?
  - A. Antinuclear antibody titer
  - B. Pathologic examination of the superficial temporal artery
  - C. Four-vessel catheter angiography
  - D. Computed tomography (CT) venography
  - E. CT angiography
  
4. What does this image show?



- A. Intramural lymphocytic infiltration
- B. Multinucleated giant cells
- C. Fibrinoid necrosis
- D. Disruption of the internal elastic membrane
- E. All of the above

**1. The answer is C.** This elderly woman has a posterior circulation ischemic stroke, proximal muscle weakness suggestive of polymyalgia rheumatic (PMR), and a unilateral temporal headache with unilateral superficial temporal artery (STA) tenderness on examination. Her clinical presentation is concerning for giant cell arteritis (GCA), an immune-mediated chronic vasculitis of large- and medium-sized vessels, found in elderly individuals, especially women. Headache is the most common clinical manifestation and monocular visual loss is the most common complication of GCA. Patients with CGA may also have PMR with proximal muscle pain and weakness. Rarely extracranial cerebrovascular disease causes an ischemic stroke, most commonly in the posterior circulation.

**2. The answer is E.** Most cases of GCA are associated with elevated C-reactive protein (C-RP), which is more sensitive than an erythrocyte sedimentation rate (ESR), which may be increased with anemia. Ultrasound imaging of the superficial temporal artery may show luminal abnormalities; the diagnosis is best made with clinical suspicion, elevated C-RP, and superficial temporal artery biopsy. Imaging of the anterior circulation in the neck by carotid ultrasound, obtained prior to the biopsy, rules out internal carotid artery occlusion with the STA (a distal branch of the external carotid artery) supplying collateral circulation to the brain.

**3. The answer is B.** Pathologic examination of the STA should confirm the diagnosis of GCA prior to subjecting an elderly patient to a prolonged course of treatment with steroids. Multiple sections of a long biopsied specimen may need to be examined pathologically to make the diagnosis. Bilateral STA biopsies are sometimes necessary to make the diagnosis. In this woman who has known occlusive cerebrovascular disease, use of the STA as a collateral vessel should be ruled out prior to its obliteration by biopsy.

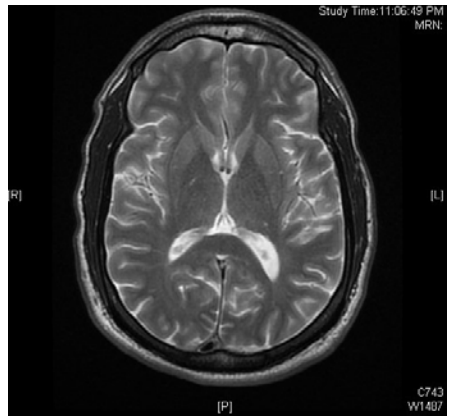
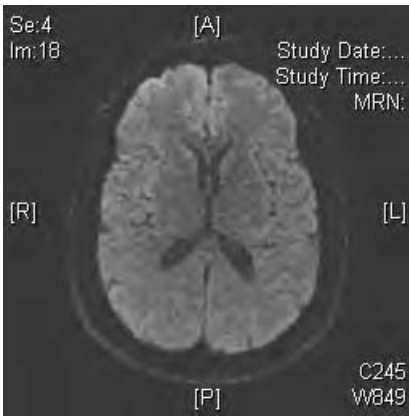
**4. The answer is E.** This image of shows a hematoxylin and eosin stained transverse microscopic section of a STA in a patient with giant cell or temporal arteritis. There are multinucleated giant cells along with intramural lymphocytic infiltration, fibrinoid necrosis, and disruption of the internal elastic membrane. This pathology confirms the diagnosis of GCA and justifies the use of long-term steroids in this elderly woman. (Hall & Balcer, *Curr Treat Opt Neurol* 2004)

#### SCENARIO 4

A 45-year-old executive was brought into the emergency department with aphasia, right-sided sensory loss with mild weakness, agitation, and a headache. He did not have any chronic medical conditions and reported only mild headaches in the

past. His mother had migraines. His wife reported that he had been discharged from another hospital a week ago after he had been admitted for 2 days with a severe headache and transient speech difficulty and right-sided sensory loss. A magnetic resonance image (MRI) of the brain and carotid ultrasonography, done in the outside hospital the week before, were reported by the patient's wife to be normal. The man felt back to normal and was at work, where he again developed a headache and neurologic complaints, which precipitated this emergency department visit. An MRI was ordered in the emergency department.

1. What do these axial DWI and T2 images show?



- A. Leptomeningeal enhancement
- B. Mesial temporal abnormal signal
- C. Acute ischemia
- D. Mass lesion
- E. Normal brain

He was admitted to the hospital for evaluation. An MRA of brain and neck vessels was unrevealing.

2. What test would be diagnostic in this man?

- A. Electroencephalogram (EEG)
- B. Echocardiogram
- C. Electromyography and nerve conduction testing
- D. Lumbar puncture with cerebrospinal fluid (CSF) analysis
- E. Magnetic resonance venogram (MRV)

3. What finding on lumbar puncture would be consistent with his diagnosis?
- A. Elevated spinal fluid protein
  - B. Normal spinal fluid glucose
  - C. Lymphocytic pleocytosis
  - D. Elevated opening pressure
  - E. All of the above
4. What is the diagnosis?
- A. Migraine with aura
  - B. Headache with neurologic deficits and cerebrospinal fluid (CSF) lymphocytosis (HaNDL)
  - C. Echovirus meningitis
  - D. Cryptococcal meningitis
  - E. Transient ischemic attacks
5. What should you tell the patient and his wife about his prognosis?
- A. He may have further episodes of headache with neurologic deficit in the next 2–3 months.
  - B. He will likely accumulate permanent neurologic deficits with further episodes.
  - C. He will most likely not have another episode of headache with neurologic deficits again.
  - D. You cannot offer any prediction of what will happen to him.
  - E. He has an increased risk of developing viral meningitis.

**1. The answer is E.** This man with the sudden onset of headache and focal neurologic deficits does not have any abnormality on brain imaging. These are the images of a normal brain. There are no lesions on diffusion weighted imaging (DWI) to indicate acute ischemia. There is no mass lesion seen on the T2 image. No contrast was given.

**2. The answer is D.** A lumbar puncture to evaluate his opening pressure and spinal fluid is appropriate to reach a diagnosis in this man who may have a CNS infection. A subarachnoid hemorrhage (SAH) or meningitis are unlikely, but should be ruled out by spinal fluid analysis.

**3. The answer is E.** Elevated opening pressure, elevated spinal fluid protein, normal spinal fluid glucose, and lymphocytic pleocytosis are all characteristic of the indicated diagnosis of headache with neurologic deficits and CSF lymphocytosis

(HaNDL). Opening pressure is often elevated. In one study of patients with this disorder, lymphocytic pleocytosis ranged from 10 to 760 lymphocytic cells/mm<sup>3</sup> (mean 199), and protein was increased in 96% of patients. Spinal fluid glucose is normal. This CSF profile is also consistent with a viral infection or a partially treated bacterial meningitis, which should be ruled out prior to making the diagnosis of a noninfectious disorder. Clinical presentation without evidence of systemic infection and rapid improvement are consistent with HaNDL.

**4. The answer is B.** This man has HaNDL, also known as pseudomigraine with lymphocytic pleocytosis. This disorder, which is more frequent in males, consists of one to 20 episodes of transient neurologic deficits accompanied by moderate-to-severe headache. The headaches are migraine-like with unilateral or bilateral throbbing lasting hours. The transient neurologic deficits last for hours, generally less than a day. Sensory symptoms are the most common, followed by aphasia and then motor symptoms. Visual symptoms are relatively unusual. The most frequent combination of symptoms is motor aphasia plus sensory and motor right hemi-body symptoms.

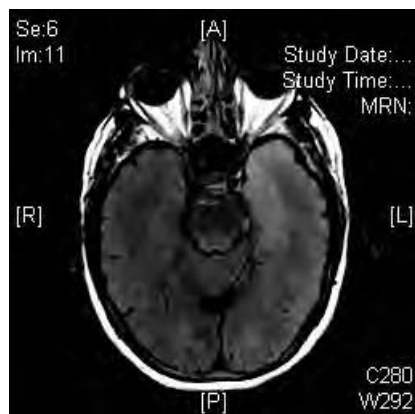
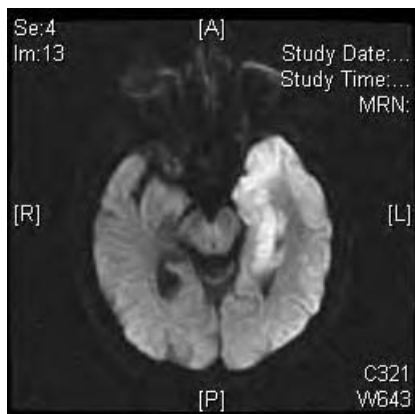
**5. The answer is A.** Patients are asymptomatic between episodes of headache and neurologic deficits and after the symptomatic period, which generally lasts less than 3 months. This man had five more episodes of transient headache and neurologic deficits, but these episodes were not as severe as during the initial two hospitalizations. After the symptomatic period he had no further episodes. (Gómez-Aranda et al., *Brain* 1997)

## SCENARIO 5

A 38-year-old healthy lawyer noted headaches for several days. She attributed them to long hours litigating medical malpractice cases. Her co-workers felt that her recent behavior was odd, as she brought pastries and flowers to the office for 2 days running; however, they enjoyed her improved personality and said nothing. But when she took off her shoes and jacket and sat on a table with her legs splayed open as she made closing arguments at trial, the judge suggested that she call her doctor. When she was seen in the doctor's office, she was pleasant, garrulous, and flirtatious, with periods of inattention. Her temperature was mildly elevated. Her doctor was very concerned.

An MRI scan of the brain was obtained immediately.

1. What do these images suggest?



- A. Frontal lobe mass lesion
  - B. Mesial temporal signal abnormality
  - C. Leptomeningeal enhancement
  - D. Hydrocephalus
  - E. Normal brain
2. What should her doctor do next?
- A. Send her home with antipsychotic medication
  - B. Send her home with antiepilepsy medication
  - C. Refer her for admission to a hospital with neurologic consultation
  - D. Refer her for admission to a psychiatric hospital
  - E. Suggest she take a vacation on a singles cruise
3. Which test is most likely to indicate her diagnosis?
- A. Spinal fluid analysis
  - B. Electroencephalogram (EEG)
  - C. Echocardiogram
  - D. Skin biopsy
  - E. Genetic testing
4. What treatment should be started?
- A. Cyclophosphamide
  - B. Acyclovir
  - C. Prednisone
  - D. Vancomycin
  - E. Phenytoin

**1. The answer is B.** The mesial temporal signal abnormalities, which can be unilateral or bilateral, are suggestive of herpes simplex virus type 1 (HSV-1) encephalitis, although they can be seen in other viral or paraneoplastic encephalitis. When unilateral, these lesions may be mistaken for an ischemic infarct. This sporadic cerebral infection, which is generally due to the reactivation of a latent virus, can cause an aseptic meningitis or a fulminant, rapidly progressive, fatal meningoencephalitis.

**2. The answer is C.** This woman has a subacute change in behavior with headache, fever, and a markedly abnormal MRI scan. She needs an evaluation for encephalitis and should be admitted to a hospital for a neurologic evaluation.

**3. The answer is A.** Detection of HSV-1 DNA in the cerebrospinal fluid (CSF) by polymerase chain reaction (PCR) is the diagnostic test of choice. However, the test may be negative if spinal fluid is obtained very early in the clinical presentation. Temporal spike and slow-wave activity is generally found on EEG, but the EEG findings are not specific. Brain biopsy with tissue diagnosis has been supplanted by PCR testing of the spinal fluid.

**4. The answer is B.** Acyclovir is administered intravenously at 10 mg/kg every 8 hours for up to 21 days, with treatment starting when the diagnosis is felt to be likely, even before PCR results are available. The medication is not benign and may have renal toxicity. Despite early and appropriate treatment, many survivors have significant residual neurologic deficits. This woman was diagnosed with HSV encephalitis, with positive PCR; she received acyclovir early in her clinical course and recovered almost completely. However, after her encephalitis was treated, her personality changed. She donated all her money to support universal pediatric health care and dedicated her life to the administration of health clinics for children in underserved areas. (Whitley, *Antiviral Res* 2006)

## SCENARIO 6

A 73-year-old woman complained that she awoke almost daily in the early morning hours with a headache that lasted about an hour. The pain was a mild to moderate, with pressure sensation over her entire head. Rarely, she notes nausea with the headache, but she denied vomiting or photophobia. She does not note any autonomic symptoms, including nasal congestion, ptosis, or tearing. She has no chronic medical conditions and is taking no medications. In your office, she is pleasant, thin woman who did not appear anxious. Her neurologic examination is normal.



1. What is the most likely cause of her headaches?
  - A. Cluster headaches (CH)
  - B. Early morning headaches due to obstructive sleep apnea
  - C. Hypnic headaches
  - D. Turtle headaches
  - E. Circadian phase-related headaches
  
2. What should be the next step in her evaluation?
  - A. Discuss her diagnosis and suggest treatment.
  - B. Send her for blood work, including a sedimentation rate.
  - C. Order an immediate magnetic resonance imaging (MRI) of the brain.
  - D. Order a carotid ultrasound study.
  - E. Make arrangements for a sleep evaluation including polysomnography.
  
3. Which medication would probably be most effective in preventing her headaches?
  - A. Indomethacin (Indocin<sup>®</sup>)
  - B. Lamotrigine (Lamictal<sup>®</sup>)
  - C. Lithium
  - D. Gabapentin (Neurontin<sup>®</sup>)
  - E. Topiramate (Topamax<sup>®</sup>)

**1. The answer is C.** This elderly woman has hypnic headaches, a rare primary headache disorder found in the elderly who complain of a headache on awakening. Pain is generally holocephalic, although it can be unilateral; pain is of variable severity but commonly moderate. This headache type has a chronobiological origin and appears to be related to rapid eye movement (REM) sleep. The pathophysiology of hypnic headaches is unclear but they may be related to an age-related disorder of the suprachiasmatic nucleus of the hypothalamus. The other headaches listed are also associated with sleep, but this characteristic patient and her clinical history indicate the diagnosis of hypnic headaches.

**2. The answer is A.** While an MRI scan of the brain is appropriate in the investigation of this woman's headache, her history is characteristic and treatment can be initiated prior to obtaining imaging. Mass lesions have been reported rarely in patients who clinically appear to have hypnic headaches, but correlation, as opposed to coincidence, is unclear. A sleep study could indicate the stage of sleep associated with the development of the headache, with both REM and non-REM correlation, but the study is not needed to confirm the diagnosis. The diagnosis

of GCA should be considered in the elderly patient with headaches; however, the diurnal pattern is most consistent with hypnic headaches. A carotid lesion would not cause her headaches.

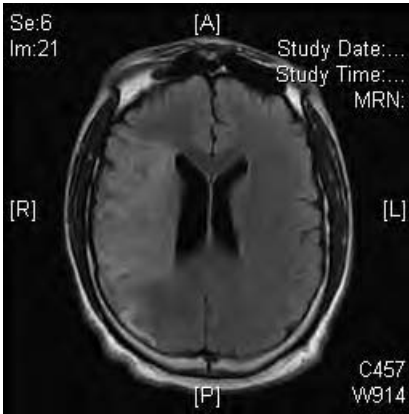
**3. The answer is C.** Treatment of hypnic headaches can be problematic. Lithium is the most effective medication; but, melatonin, indomethacin (Indocin), flunarizine, and caffeine at bedtime may also be of benefit. (Poceta, *Curr Pain Headache Rep* 2003; Evers & Goadsby, *Neurology* 2003)

## SCENARIO 7

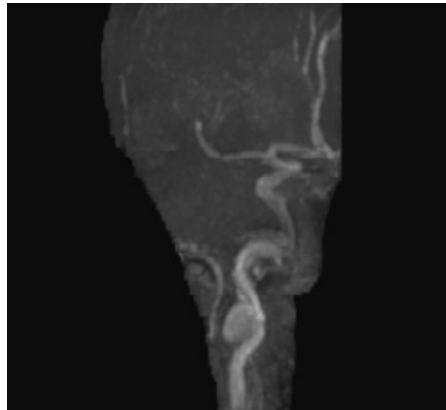
A 40-year-old woman was seen in an emergency room in Florida complaining of a right-sided headache with neck pain for 3 days. Her past medical history was unremarkable, except for occasional headaches associated with her menstrual period. She was visiting amusement parks with her teenage sons, and she attributed her persistent headache to long days at the park in the heat, traipsing from ride to ride. She did not seek medical attention until she experienced a 10-minute episode during which she had confusion about how to get from Morocco to Norway in EPCOT, accompanied by left-hand clumsiness and numbness. On examination, she had a mild right ptosis with a smaller pupil on that side and a left upper extremity drift.

1. What do you think is the most likely cause of her headaches?
  - A. Cluster headaches (CH)
  - B. Right vertebral artery dissection
  - C. Right internal carotid artery dissection
  - D. Right external carotid artery dissection
  - E. Paroxysmal hemicrania (PH)

2. An MRI scan showed a right middle cerebral artery territory infarct (see images below). What is the most important next step in her evaluation?



- A. Computed tomographic (CT) scan of the brain
  - B. Magnetic resonance angiogram (MRA) of the neck and brain
  - C. Carotid ultrasonography
  - D. Transthoracic echocardiogram
  - E. Transesophageal echocardiogram
3. What do her MRA images (left of neck and right of brain) show?



- A. A distal right internal carotid artery dissection
- B. A pseudoaneurysm
- C. A right middle cerebral artery branch occlusion
- D. Normal right carotid bifurcation
- E. All of the above

4. What are options that could be used to treat this woman?
- A. Aspirin and extended release dipyridamole (Aggrenox<sup>®</sup>)
  - B. Aspirin
  - C. Warfarin
  - D. Arterial stenting
  - E. All of the above

**1. The answer is C.** This woman appears to have a right internal carotid artery dissection with a Horner's syndrome (ptosis and miosis), neck pain, headache, and transient right hemispheric symptoms. The arterial dissection that caused her headache and eventual ischemic stroke could have been spontaneous, but it also could be related to neck movements during the amusement park rides.

**2. The answer is B.** This woman has a right middle cerebral artery infarct due to embolization from an internal carotid artery (ICA) dissection. Arterial dissections involve intracranial and extracranial vessels that are stretched and torn, spontaneously or in the setting of trauma ranging from trivial to devastating. Arterial dissections can be imaged by catheter angiography, or less invasively by computed tomography (CT) or MR angiography of brain and neck vessels, or fat-saturated MRI transverse images of the neck. In this woman, an MRA of neck vessels is most likely to diagnose this woman's ICA dissection with no risk to her. Carotid ultrasonography could miss a distal carotid lesion and would not be as useful in delineating the extent of the lesion. An MRA of the brain would show a distal occlusion from an embolus or an intracranial dissection. The dissection would not be seen on a CT scan of the brain parenchyma, as distinct from a CT angiogram of the brain vessels.

**3. The answer is E.** Dissections of extracranial or intracranial cerebral arteries can lead to bleeding within the arterial wall with possible distal embolization, arterial occlusion, or pseudoaneurysm formation. Dissection of intracranial vessels can also result in subarachnoid hemorrhage (SAH). These images show a pseudoaneurysm arising from a focal dissection along the superior cervical right internal carotid artery.

**4. The answer is E.** Long-term treatment with antiplatelet or anticoagulant medications both reduce the risk of initial or recurrent ischemic stroke in acute arterial dissection, but without evidence to favor one treatment over another. Stenting the arterial flap is an experimental option that may be appropriate in some cases. (Caplan, *Nat Clin Pract Neurol* 2008)

## SCENARIO 8

An 18-year-old college freshman developed fever, headache, nausea, lethargy, and a skin rash. She thought that she had a viral infection and did not go to the student health service at her college until the second day of her symptoms. On examination, she had a fever of 103°F, a non-blanching petechial rash, and a stiff neck. She was inattentive and falling asleep when not stimulated.

1. What should be done to evaluate and treat this woman's headache?
  - A. Give her an antipyretic and fluids for a viral infection.
  - B. Arrange for her to be seen by a neurologist within the next few days.
  - C. Call 911 to send her to the nearest hospital emergency department.
  - D. Start her on an oral antibiotic and send her back to her dorm with a friend.
  - E. Give her an oral antibiotic and keep her in the student health service for observation.

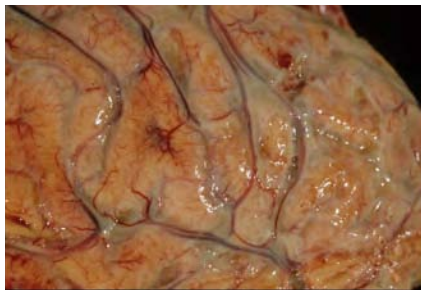
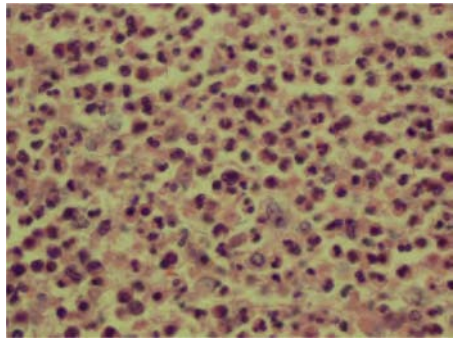
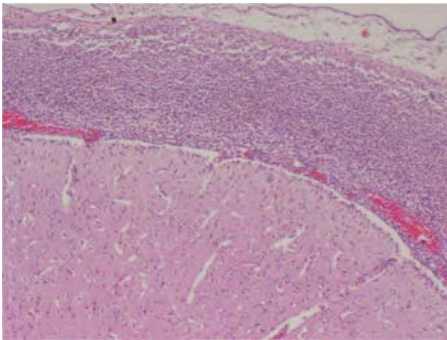
She was admitted to the hospital and started on intravenous (IV) antibiotics (ceftriaxone and vancomycin). A CT scan of the head did not show any mass lesion or hydrocephalus. A lumbar puncture was performed.

2. What would you expect her spinal fluid to show?
  - A. Decreased glucose level
  - B. Elevated protein level
  - C. Neutrophilic pleocytosis
  - D. Gram negative diplococci
  - E. All of the above
3. What is the organism causing her clinical picture?
  - A. *Neisseria meningitidis*
  - B. *Streptococcus pneumoniae*
  - C. *Haemophilus influenzae*
  - D. *Escherichia coli*
  - E. Group B streptococci

4. The infectious disease specialist at the hospital contacted the college's student health service. What did the ID specialist recommend?

- A. Prophylaxis of her roommates with IV vancomycin
- B. Prophylaxis of her roommates with oral trimethoprim and sulfamethoxazole
- C. Prophylaxis of her roommates with oral rifampin
- D. Closure of her dorm floor; sending the students home to their local doctors
- E. Psychological counseling but no medical treatment

5. Despite rapid evaluation and treatment, the woman became unresponsive and needed to be intubated for worsening hypoxia. Pressors and fluids could not maintain her blood pressure as septic shock developed. She suffered a cardiac arrest from which she could not be resuscitated. What do these images from her autopsy show?



- A. Granulomatous infiltration of the pachymeninges
- B. Hemorrhage within the subarachnoid space
- C. Gross necrosis of the brain
- D. Polymorphonuclear cells within the subarachnoid space
- E. Normal brain

**1. The answer is C.** A young person in a closed and crowded environment (e.g., college dorm, military barracks, religious pilgrimage) is at risk for bacterial meningitis. This college student with a possible life-threatening bacterial meningitis causing headache, fever, rash, stiff neck, and lethargy should be evaluated and treated emergently in a hospital setting. She should be started emergently on broad-spectrum antibiotics that penetrate the central nervous system (CNS) on the suspicion that she has bacterial, as opposed to viral, meningitis. She needs a CT scan of the brain and spinal fluid analysis to determine the specific organism and its sensitivities.

**2. The answer is E.** This woman's presentation is consistent with bacterial meningitis, as she appears toxic after just 2 days of symptoms. After she was started on emergent broad-spectrum antibiotics and a CT scan of the head showed that she had no contraindication to a lumbar puncture, spinal fluid was obtained. The elevated protein, decreased glucose, elevated white blood cells (neutrophils), and the gram-negative diplococci are consistent with bacterial meningitis due to *Neisseria meningitidis*.

**3. The answer is A.** Her clinical presentation with a characteristic rash indicates meningitis due to *Neisseria meningitidis*. Her CSF profile is also consistent with *N. meningitidis*, an obligate human bacterial pathogen that is a cause of epidemic meningitis and sepsis. The organism is transmitted through respiratory secretions and saliva, and colonizes up to a quarter of healthy individuals, more in closed populations such as military recruits or college students. Vaccinations against bacterial meningitis, while not protective against all strains, can decrease the risk of acquiring an infection in susceptible populations.

**4. The answer is C.** Oral chemoprophylaxis of close friends or family members who may have come in contact with oral secretions should be initiated with rifampin. Third-generation cephalosporins, azithromycin, and quinolones are used less frequently. Many meningococcal strains are resistant to sulfa drugs, which are not recommended.

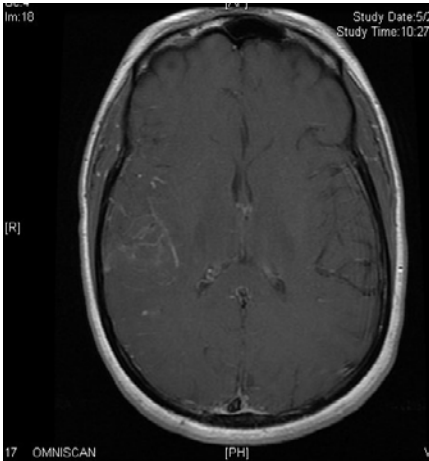
**5. The answer is D.** The gross brain specimen reveals cloudy leptomeninges due to the presence of infectious exudate in the subarachnoid space. Microscopic sections show marked infiltration of polymorphonuclear cells within the subarachnoid space (between the pial surface of the brain and the arachnoid layer), a typical histologic manifestation of acute bacterial meningitis. (Stephens, Greenwood, & Brandtzaeg, *Lancet* 2007)

## SCENARIO 9

A healthy 30-year-old woman with a medical history notable only for occasional migraine with visual aura developed a mild headache along with a sense of clumsiness in her left hand. When she noticed that she was dropping objects and that her left arm was tingling, she came to the emergency department. On examination, her mental status and cranial nerves were normal. She had a mild left upper extremity drift and sensory extinction in her left arm. Her biceps and brachioradialis reflexes were brisker on the right than on the left.

An MRI of the brain was obtained with the images below.

## 1. What does this MRI image show?

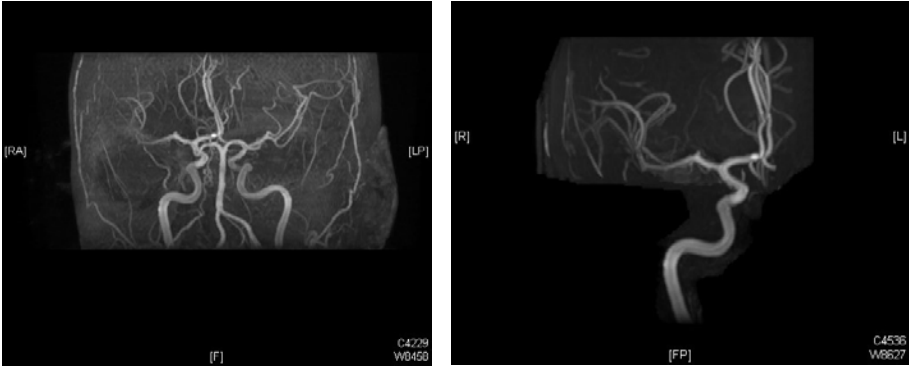


- A. A cerebral abscess
- B. An acute right middle cerebral artery distribution infarct
- C. An area of demyelination in the right parietal white matter
- D. A right venous infarct
- E. A right arteriovenous malformation (AVM)

An MRA of the head and neck vessels was obtained.



2. What do these MRA images show?



- A. Right internal carotid artery dissection
- B. Right middle cerebral artery branch occlusion
- C. An arteriovenous malformation
- D. Diffuse cerebral vasculitis
- E. No vascular abnormality

Her neurologic deficits resolved in 2 days, and she became neurologically normal. Further testing was suggested.

3. Which test listed below is most likely to explain the cause of her neurologic event?

- A. Catheter angiography of the brain
- B. Computed tomography angiography (CTA) of the brain
- C. Magnetic resonance venography (MRV) of the brain
- D. Transesophageal echocardiogram (TEE)
- E. Magnetic resonance imaging (MRI) of the cervical spine

A transesophageal echocardiogram (TEE) showed a right to left shunt with spontaneous passage of a significant number of bubbles through a patent foramen ovale (PFO). She also had an atrial septal aneurysm on TEE. Venous ultrasound imaging of her legs and magnetic imaging evaluation of the pelvic venous structures were normal.

4. What do you recommend?

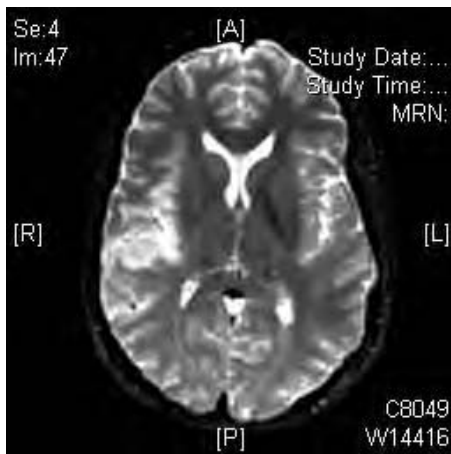
- A. Consideration of device closure of her cardiac defect
- B. Consideration of warfarin anticoagulation prior to closure
- C. Evaluation for thrombophilias
- D. Hydrating well and flying first class on long airplane trips
- E. All of the above

A hematologic evaluation revealed a Factor V Leiden gene mutation.

5. What do you suggest?

- A. Anticoagulation with warfarin
- B. Avoidance of pregnancy on warfarin
- C. Discontinuation of oral contraceptives
- D. Eventual device closure of the patent foramen ovale (PFO)
- E. All of the above

1. **The answer is B.** These MRI scans show an acute right middle cerebral artery territory infarct with restricted diffusion on DWI. Hyperintense vessels are seen on contrasted FLAIR MRI, indicating slow flow and early ischemia with vessel occlusion and poor collateral circulation.



**2. The answer is B.** There is occlusion of a branch of the right middle cerebral artery on MRA correlating with her infarct. In a young woman without vascular risk factors, this finding is suspicious for an embolus that has lodged in a distal arterial vessel.

**3. The answer is D.** Since this woman had an embolic infarct with a history of migraine with aura, she needs to be evaluated for a patent foramen ovale (PFO). Echocardiography (transthoracic or transesophageal) or cardiac MRI can be used to assess for a right-to-left cardiac shunt.

**4. The answer is E.** This woman has a PFO, a common finding in migraineurs with aura. The presence of an atrial septal aneurysm increases her risk for a cardioembolic source of embolization. Although she does not have any clear deep vein thrombosis (DVT), she needs to be evaluated for a hematologic propensity for venous thrombosis. She should avoid situations that would put her at risk for DVT formation. The best long-term prevention of recurrent ischemic strokes in patients with PFO is unknown, with options including antiplatelet and anticoagulant medication, or catheter-inserted device or surgical closure.

**5. The answer is E.** This woman has the most common thrombophilia causing venous thrombosis. She had a presumed paradoxical embolization with a peripheral venous clot traversing her right-to-left cardiac shunt to her brain. A reasonable treatment plan would be to start oral anticoagulation and plan to close the cardiac shunt eventually. She should not take warfarin while pregnant because of its teratogenicity. She should not take exogenous estrogens (e.g., oral contraceptives or hormone replacement therapy) because of her risk of venous thrombosis. (Kurth et al., *JAMA* 2006)

## SCENARIO 10

A 30-year-old woman, in week 25 of an uneventful pregnancy, awoke with a headache that came on as she got out of bed. The headache was relieved with lying down, but returned when she tried to stand up. She came into the neurologist's office, bending down as she walked, to lie on the waiting room floor until she could be seen. She denied photophobia or phonophobia, but she felt that sound was muffled. She had mild nausea, but not to the extent that she suffered earlier in her pregnancy. Other than appearing in distress from a positional headache, her neurologic examination was normal.

1. What is the most likely diagnosis to explain this woman's headaches?
  - A. Cerebral venous thrombosis
  - B. Aqueductal stenosis
  - C. Colloid cyst of the third ventricle
  - D. Spontaneous intracranial hypotension
  - E. Subarachnoid hemorrhage (SAH)
  
2. What is the most appropriate diagnostic test?
  - A. A computed tomography (CT) scan with contrast
  - B. A CT myelogram
  - C. A magnetic resonance imaging (MRI) scan with contrast
  - D. An MRI scan without contrast
  - E. Cisternography
  
3. What is the most appropriate initial treatment for this woman?
  - A. Bed rest, oral hydration, and time
  - B. Epidural blood patch
  - C. Surgical repair of a cerebrospinal fluid (CSF) leak
  - D. Percutaneous placement of fibrin sealant
  - E. Surgical dural graft

You arrange to see her 2 weeks later in your office.

4. What is her most likely presentation?
  - A. She has a continuing headache with complaints of left-sided weakness with a mild left hemiparesis on examination.
  - B. There is no improvement in her headaches.
  - C. The headaches have persisted but are improved.
  - D. Her headaches have resolved, and she is going to name the child after you.
  - E. She does not show up for her appointment and is lost to follow-up.

**1. The answer is D.** This woman has a positional headache due to a spontaneous spinal fluid leak with intracranial hypotension. This diffuse headache worsens with sitting or standing and is accompanied by neck stiffness, tinnitus, hypacusis, photophobia, or nausea. Cerebral venous thrombosis and SAH may present with a sudden-onset headache, but would not be as clearly positional. Hydrocephalus due to aqueductal stenosis or a colloid cyst would be associated with chronic headaches and would not be of sudden onset. Positional headaches due to dural puncture are usually worse on standing and better supine, but rarely patients report the reverse symptoms after lumbar puncture or spinal anesthesia.

**2. The answer is D.** The clinical suspicion of spontaneous intracranial hypotension is confirmed the MRI findings of enhancement of pachymeninges, engorgement of venous structures, pituitary hyperemia, sagging of the brain, and subdural fluid collections. These MRI findings are the most specific for the diagnosis, and the other tests involve contrast dye or radionuclide tracers that would not be appropriate in this pregnant woman. In this woman, use of contrast with an MRI scan to look for pachymeningeal enhancement would not be appropriate, but an MRI without contrast could rule out conditions causing hydrocephalus.

**3. The answer is A.** Conservative treatment with bed rest, oral hydration, and caffeine (in moderation) is appropriate initial treatment in this pregnant woman, because this headache may resolve in time. If this therapy is unsuccessful, epidural blood patch is the next step. Surgical repair of the CSF leak or percutaneous placement of fibrin sealant are used to treat intractable spontaneous intracranial hypotension.

**4. The answer is C.** All of the listed scenarios at 3 weeks are possible. Some patients with spontaneous spinal fluid leak may develop subdural hematomas and present in follow-up with focal neurologic findings on examination. The most likely scenario, however, is that the headaches resolve with treatment, or spontaneously. The likelihood of the baby being a neurologist's namesake is small. (Schievink, *JAMA* 2006)

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# ABBREVIATIONS

<b>5-HIAA</b>	5-hydroxyindolacetic acid
<b>5-HT</b>	5-Hydroxytryptamine
<b>ADC</b>	Apparent diffusion coefficient
<b>AMPA</b>	$\alpha$ -Amino-3-hydroxy-5-methyl-4-isoxazopropionic acid
<b>AMS</b>	Acute mountain sickness
<b>AVM</b>	Arteriovenous malformations
<b>BMI</b>	Body mass index
<b>BPPV</b>	Benign paroxysmal positional vertigo
<b>CADASIL</b>	Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
<b>cAMP</b>	Cyclic adenosine monophosphate
<b>CDH</b>	Chronic daily headache
<b>CGRP</b>	Calcitonin gene-related peptide
<b>CH</b>	Cluster headache
<b>CJD</b>	Creutzfeldt-Jakob disease
<b>CNS</b>	Central nervous system
<b>CO</b>	Carbon monoxide
<b>CP</b>	Cerebellopontine (angle)
<b>CPAP</b>	Continuous positive pressure airway pressure
<b>CRP</b>	C-reactive protein
<b>CSD</b>	Cortical spreading depression
<b>CSF</b>	Cerebrospinal fluid
<b>CT</b>	Computed tomography



<b>CTTH</b>	Chronic tension-type headache
<b>CTV</b>	Computed tomography venography
<b>CVD</b>	Cardiovascular disease
<b>CVT</b>	Cerebral venous thrombosis
<b>DIND</b>	Delayed ischemic neurologic deficit
<b>DWI</b>	Diffusion-weighted imaging
<b>EDH</b>	Epidural hematoma
<b>EEG</b>	Electroencephalogram
<b>EM</b>	Endometriosis
<b>EPC</b>	Endothelial progenitor cell
<b>ESR</b>	Erythrocyte sedimentation rate
<b>ETTH</b>	Episodic tension-type headache
<b>FHM</b>	Familial hemiplegic migraine
<b>FLAIR</b>	Fluid-attenuated inversion recovery
<b>FrHE</b>	Frequent Headache Epidemiology study
<b>GABA</b>	$\gamma$ -Aminobutyric acid
<b>GAD</b>	Generalized Anxiety Disorder
<b>GCA</b>	Giant cell arteritis
<b>GFAP</b>	Positive glial fibrillary acidic protein
<b>GOM</b>	Granular osmiophilic material
<b>GRE</b>	Gradient recalled echo
<b>HAH</b>	High-altitude headache
<b>HaNDL</b>	Headache with neurologic deficits and lymphocytosis
<b>HDH</b>	Hemodialysis headache
<b>IBS</b>	Irritable bowel syndrome
<b>ICA</b>	Internal carotid artery
<b>ICHD</b>	International Classification of Headache Disorders
<b>IHS</b>	International Headache Society
<b>IIH</b>	Idiopathic intracranial hypertension
<b>IL</b>	Interleukin
<b>INO</b>	Internuclear ophthalmoplegia

<b>LMZ</b>	Lamotrigine
<b>MDCTA</b>	Multidetector-row CT angiography
<b>MI</b>	Myocardial infarction
<b>MLF</b>	Medial longitudinal fasciculus
<b>MOH</b>	Medication-overuse headache
<b>MRA</b>	Magnetic resonance angiogram
<b>MRI</b>	Magnetic resonance imaging
<b>MRM</b>	Magnetic resonance myelography
<b>MRV</b>	Magnetic resonance venogram
<b>MS</b>	Multiple sclerosis
<b>MV</b>	Migrainous vertigo
<b>NDPH</b>	New daily persistent headache
<b>NFD/NFS</b>	Nephrogenic fibrosing dermopathy/nephrogenic systemic fibrosis
<b>NMDA</b>	N-methy-D-aspartate
<b>NSAID</b>	Nonsteroidal anti-inflammatory drugs
<b>OPG</b>	Oculoplethysmography
<b>OSA</b>	Obstructive sleep apnea
<b>PACNS</b>	Primary angiitis of the central nervous system
<b>PAG</b>	Periaqueductal gray
<b>PDPH</b>	Post-dural puncture headache
<b>PFO</b>	Patent foramen ovale
<b>PH</b>	Paroxysmal hemicranias
<b>PLPH</b>	Post lumbar puncture headache
<b>PRES</b>	Posterior reversible encephalopathy syndrome
<b>PWI</b>	Perfusion-weighted imaging
<b>RA</b>	Rheumatoid arthritis
<b>RIC</b>	Radioisotope cisternography
<b>RLS</b>	Restless legs syndrome
<b>RPLS</b>	Reversible posterior leukoencephalopathy syndrome
<b>RVCL</b>	Retinal vasculopathy with cerebral leukodystrophy
<b>SAH</b>	Subarachnoid hemorrhage

<b>SAMS</b>	Sinus, Allergy and Migraine Study
<b>SCN</b>	Suprachiasmatic nucleus
<b>SDE</b>	Subdural empyema
<b>SLE</b>	Systemic lupus erythematosus
<b>SMART</b>	Stroke-like migraine attacks after radiation therapy
<b>SSC</b>	Somatosensory cortex
<b>SUNA</b>	Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms
<b>SUNCT</b>	Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing
<b>TAC</b>	Trigeminal autonomic cephalalgias
<b>TCH</b>	Thunderclap headache
<b>TGA</b>	Transient global amnesia
<b>THS</b>	Tolosa-Hunt syndrome
<b>TNF</b>	Tumor necrosis factor
<b>TPH</b>	Tryptophan hydroxylase
<b>TTH</b>	Tension-type headache
<b>VPA</b>	Valproic acid
<b>VZV</b>	Varicella zoster virus
<b>WHS</b>	Women's Health Study
<b>WMH</b>	White matter hyperintensities
<b>WML</b>	White matter lesions