Chapter 1
Headache

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1.1 Introduction

Headache is the fourth most common reason for patient presentation to an emergency department (ED), with approximately 14 % per year of adults experiencing migraine or other severe headache in the previous 3 months [1]. Given the wide differential and potential morbidity and mortality of this nonspecific complaint, clinicians may find the workup and treatment of headache intimidating. Fortunately, the vast majority of presentations do not portend a more serious etiology.

Lacking intrinsic pain receptors, the brain itself is typically not the source of pain of headache. Rather, headache is usually caused by inflammation or pressure changes at vasculature or the meninges surrounding the central nervous system (CNS), whether this is caused by benign or serious causes (e.g., dehydration or intracranial neoplasm, respectively). Headache may also be a manifestation of other nearby structures (e.g., sinusitis, tension at cervical or frontotemporalis muscles, or inflammation of peripheral nerves).

The workup and treatment of the headache are generally directed by the history and physical exam. These will in turn direct delineate whether outpatient treatment, imaging, or immediate transport to the emergency department for emergent imaging (e.g., CT or MRI) and/or invasive testing (e.g. lumbar puncture) is indicated.

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1.2 Risk Factors

Risk factors vary depending on the specific etiology

- Prior headache
- Family history of migraine or other headache
- Analgesic use, overuse, or dependence
- Increased life stress
- URI for sinusitis, ear infection for mastoiditis
- Immunosuppression
- Uncontrolled hypertension
- Neoplasm and metastasis
- Coagulopathy
- Benign intracranial HTN
- Vascular risk factors for CVA

1.3 Differential Diagnosis

1.3.1 Common Complaints and Red Flags of Headache

Headache is divided into primary and secondary causes [1]. Headaches are considered primary when the headache is itself the main pathologic condition, whereas secondary headaches are thought to be a symptom of another pathology. For specific diagnostic criteria, practitioners are encouraged to refer to current International Headache Society guidelines.

The most common types of primary headache are migraine (with or without aura), tension-type headache, cluster headache, and hemicrania continua.

- Migraine:
  - Headaches are typically unilateral, pulsating, of moderate to severe intensity, and worsened by physical activity.
  - Symptoms may include nausea, vomiting, and photophobia.
  - Auras may include visual disturbances, paresthesias, numbness, and dysphonia (among others).
- Tension-type headache:
  - Headaches are typically bilateral, non-pulsating, of mild to moderate intensity, and not worsened by physical activity.
- Cluster headache:
  - During headache clusters, patients experience brief, excruciating unilateral pain.
  - Pain is periorbital and associated with ocular disturbances such as conjunctival injection, tearing, ptosis, or meiosis.
  - Pain is very responsive to high-concentration inhaled oxygen.

- Hemicrania continua:
  - Continuous daily unilateral pain is associated with conjunctival injection, rhinorrhea, ptosis, or miosis.
  - Pain is completely relieved by indomethacin.

Multiple other less common primary causes of headache exist, such as primary cough headache, primary headache associated with sexual activity, hypnic (sleep) headache, and benign thunderclap headache. These headaches must fulfill specific criteria, are not due to another disorder, and are generally diagnoses of exclusion.

The differential list for secondary causes of headache is extensive.

- Vascular and hematological:
  - Ischemic cerebrovascular accident (CVA) or transient ischemic attack (TIA)
  - Hemorrhagic CVA, including hypertensive
  - Aneurysmal subarachnoid hemorrhage (SAH):
    - Low-grade SAH (Hunt and Hess Grade 1) may have only mild headache.
  - Non-ruptured aneurysm (non-ruptured)
  - Arteritis (including temporal arteritis)
  - Cerebral venous thrombosis
  - Subdural hemorrhage (SDH)
  - Cervical artery dissection
- Nonvascular intracranial:
  - Neoplasm, either CNS primary or as site of metastasis
  - Benign intracranial hypertension/pseudotumor cerebri:
    - Impaired cerebrospinal fluid (CSF) absorption leads to increased intracranial pressure.
  - Inflammatory disease, e.g., systemic lupus erythematosus (SLE), Behçet's syndrome
  - Chiari malformation (Type 1):
    - Cerebellar tonsillar intrusion into foramen magnum leads to impaired CSF circulation and absorption.
    - Patients typically present with cervical pain and suboccipital headache provoked by exertion or cough.
  - CSF leak – Headache typically worse with standing
  - Seizure
- Posttraumatic:
  - Acute or chronic, for example, after concussion or whiplash
  - Epidural, subdural, subarachnoid hemorrhage
- Infectious:
  - Intracranial, e.g., bacterial meningitis, herpes encephalitis

  - Mastoiditis, osteomyelitis, sinusitis
  - As a symptom of system infection, e.g., influenza, HIV/AIDS
- Medications:
  - Many medications, most commonly phosphodiesterase inhibitors, nitroglycerin, nifedipine, nimodipine, digitalis, disulfiram, hydralazine, imipramine
- Medication overuse:
  - Defined by the presence of headache for 2–4 weeks after analgesic usage 10–15 days per month for 3 months
  - May be provoked by overuse of nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, opioids, triptans, ergotamine, or combination analgesics
  - May be associated with nausea, vomiting, tachycardia, anxiety (Ref. Evers et al [2].)
- Substance or withdrawal:
  - Caffeine, nicotine, alcohol, cocaine, cannabis, carbon monoxide, or other toxic exposure
- Headache due to or worsened by psychiatric disorder:
  - For example, depression, generalized anxiety disorder, somatization disorder
- Disorder of homeostasis:
  - Hypertension (typically SBP >160 or DBP >120 mmHg; with or without encephalopathy)
  - Hypercapnia or hypoxia (including sleep apnea)
  - Post-dialysis
  - Eclampsia/preeclampsia
- Eye pain and headache:
  - Acute glaucoma or other ocular inflammatory disorders
- Facial pain and headache due to rhinosinusitis
- Cranial pain due to bony destruction:
  - Multiple myeloma, Paget's disease
- Temporomandibular disorder:
  - Associated with painful jaw clicking, locking, tenderness at muscles of mastication, or temporomandibular joint (HA primary care guidelines)
- Cervicogenic headache:
  - Occipital pain associated with cervical paraspinous musculature tenderness
  - Exacerbated by neck movement

1.4 History

The single most important historical feature to elicit is whether the patient has had similar headaches in the past. However, even with benign headache presentations, if asked "is the worst headache of your life?," many patients will say "yes" regardless of prior identical presentations or diagnoses. The label "worst headache of one's life" may pigeonhole the emergency physician into unnecessary testing and should be used sparingly. A useful way to initiate this discussion is to ask "when was the last time you had a headache like this?" Patients with benign headaches will generally affirm prior similar headaches, patients with new-onset headaches will say never, and occasionally the patient will provide the diagnosis (e.g., an HIV-positive patient stating "the last time I had cryptococcal meningitis").

Headache Red Flags [3]

- A new or different headache
- Sudden onset and maximum severity at onset ("thunderclap")
- Precipitated by a Valsalva maneuver, exertion, or sex
- Fever and neck stiffness
- Progressive worsening over weeks to months
- The presence of neurological signs or seizure
- Worsened by recumbent position
- Uncontrolled hypertension
- New-onset headache after age 50
- Unexplained weight loss
- Scalp tenderness

Important historical features to elicit include:

- The presence of similar prior headaches or significant change from prior headaches
- Timing:
  - Time of onset
  - Time to peak intensity:
    - Maximal intensity at onset suggests SAH.
  - Discrete time of onset vs. gradual onset
- If chronic:
  - Frequency of recurrence.
  - Progressive worsening may suggest neoplasm, SDH, or hydrocephalus
- Provoking or palliating factors:
  - Worsened with exertion:
    - Suggestive of migraine (if recurrent) or SAH (if new-onset thunderclap)

  - Association with menstrual cycle:
    - Migraine often worsened in late luteal phase [US guideline Beithon]
  - Association with chewing (jaw claudication) associated with temporal arteritis
  - Worse in the morning:
    - Increased intracranial pressure, e.g., pseudotumor cerebri or due to space-occupying malignancy
    - Sleep apnea causing hypercapnia or hypoxia
  - HA from space-occupying lesion and cerebral venous thrombosis, worse with lying down
  - Sudden headache associated with decrease in environmental light (e.g., entrance into a darkened room) associated with acute angle closure glaucoma
  - Worse with cough or Valsalva may suggest Chiari 1 malformation
- Location – e.g., facial, bitemporal, unilateral, occipital, and radiation from the neck
- Quality:
  - Sharp vs. dull
  - "Throbbing" associated with migraine
  - "Band-like" associated with tension
- Severity:
  - Mild: able to continue daily activities with minimal alteration
  - Moderate: inhibits daily activities but is not incapacitating
  - Severe: incapacitating:
    - Low-grade SAH (Hunt and Hess Grade 1) may have mild or no headache, so this is not a predictive factor for differentiating this from other etiologies.
- Infectious symptoms:
  - Association with fever and meningismus should prompt immediate evaluation for meningitis:
    - Differentiate meningismus (neck stiffness) vs. diffuse myalgias
- Neurologic symptoms:
  - Visual disturbances or nausea may indicate migraine.
  - Altered level of consciousness with papilledema suggests space-occupying lesion, e.g., malignancy.
  - Loss of consciousness may suggest SAH.
- Ocular and nasal symptoms:
  - Rhinorrhea, tearing, eyelid ptosis, and edema may suggest cluster headache.

- Head or neck trauma:
  - Relatively minor head trauma may result in SDH, especially in older patients, alcoholics, or patients taking anticoagulants.
  - Neck trauma or manipulation (e.g., whiplash, yoga, chiropractic manipulation) may cause vascular injury (e.g., vertebral artery dissection).
- Medications:
  - Medications tried for relief
  - Medications used daily which may predispose to MOH
  - Anticoagulants or antiplatelet agents which may predispose to or worsen ICH
  - Exogenous estrogens may contribute to coagulopathy (e.g., dural venous thrombosis)
- Travel history
  - Possible exposure endemic viral or zoonotic diseases
- Sleep adequacy
- Significant life stressors
- Other medical conditions which may be contributory:
  - Hypertension.
  - Hypoxia due to COPD or obstructive sleep apnea (OSA).
  - Malignancy.
  - Dialysis.
  - Diabetes.
  - Immunosuppression, e.g., HIV/AIDS and transplant.
  - Recent upper respiratory tract infection or allergen exposure may predispose to sinus headache.

1.5 Physical Exam

The physical examination should focus on potential emergency conditions related to the headache. Numerous other etiologies may be identified during workup.

- Vital sign assessment:
  - The presence of fever, hypothermia, tachypnea, or unexplained tachycardia (indicative of an occult fever) should alert the physician to a possible infectious cause.
  - Hypertension with systolic blood pressure > 160 mmHg or diastolic blood pressure >120 mmHg may indicate hypertension as cause of headache:
    - Severely elevated blood pressure (e.g., SBP >200 mmHg or DBP >110) should prompt consideration of intracranial hemorrhage.
  - Tachycardia may indicate stimulants or dehydration.

- Neurologic examination:
  - Assess general alertness and orientation.
  - Evaluate cranial nerve function.
  - Assess for signs of cerebellar dysfunction.
  - Romberg test.
  - Assess reflexes.
  - Evaluate gait.
- Head, eyes, ears, nose, and throat examination:
  - Evaluate for signs of trauma which may have caused intracranial hemorrhage or concussion:
    - Battle sign
    - Raccoon eyes
  - Evaluate for signs of infection:
    - Mastoid tenderness suggestive of mastoiditis (temporal bone infection)
    - Pain reproduced or worsened with manual pressure to maxillary or frontal sinuses
    - Evaluate ears for evidence of:
      - Otitis media
      - Otitis externa
    - Evaluate sinuses for evidence of sinusitis.
    - Evaluate pharynx for evidence of:
      - Pharyngitis
      - Abscesses:
        - Peritonsillar
        - Retropharyngeal:
          - Typically will have odynophagia and voice changes
    - Evaluate dentition for evidence of abscesses.
  - Palpate for tenderness at the area of the temporal artery (tenderness may indicate temporal arteritis).
  - Evaluate pupillary size, symmetry, and reactivity:
    - Fundoscopic exam if possible to evaluate for papilledema as sign of increased intracranial pressure
    - Mid-range and minimally or nonreactive pupil concerning for acute angle closure glaucoma
- Neck examination:
  - Assess flexion, extension, and rotation.

  - Meningismus (neck stiffness suggesting meningitis or SAH) should be differentiated from diffuse myalgias (e.g.. due to influenza).
  - Tenderness of cervical paraspinous muscles may suggest cervicogenic headache.
- Skin:
  - Bruising, pallor, or other changes which might indicate coagulopathy
- Psychiatric evaluation:
  - Brief screen for depression and increased life stress

1.6 Additional Testing

Headache is generally diagnosed by history and physical exam. Imaging and/or laboratory tests are typically not needed [3].

Indications for imaging in the workup of headache include [4]:

- Headache that is new onset, worse than prior, or abrupt onset
- Progressive headache associated with neurological signs
- Headache in association with trauma, cough, exertion, or sexual activity
- Persistent and positional headache or headache associated with papilledema
- Headache associated with pregnancy, malignancy, or hypercoagulable disorders
- Headache with temporal location in older individuals
- Headache radiating to the neck
- New headache associated with HIV/AIDS

Head CT is generally indicated in investigation of possible hemorrhage, trauma, or gross anatomical disturbance such as normal pressure hydrocephalus or Chiari malformation. It may also provide evidence of sinusitis, mastoiditis, or other infection. CT angiography may demonstrate aneurysm. CT venography is an indication in the workup of possible cerebral venous thrombosis. If lumbar puncture is to be performed, CT is often performed first to evaluate for space-occupying lesions. Magnetic resonance imaging (MRI) is more sensitive for evaluation for soft tissues (e.g., malignancy) and, lacking ionizing radiation, is safe in pregnancy.

Similar to imaging, blood labs are generally not indicated in the workup of headache unless investigating specific diagnoses. For example, in an older individual, a normal ESR excludes the diagnosis of temporal arteritis (if abnormal this should be followed by referral to the appropriate specialist for temporal artery biopsy). Lumbar puncture and cerebrospinal fluid analysis should be performed if subarachnoid hemorrhage (sudden-onset, severe headache with a negative noncontrast head CT) or meningitis/encephalitis is suspected. Analyses should include cell count, gram stain, protein and glucose measurement, and fluid culture. In combination with negative head CT, absence of RBCs and xanthochromia on LP rules out SAH. If pseudotumor cerebri or cryptococcal meningitis is suspected, opening pressure should be measured.

1.7 Introduction to Treatment

If a specific underlying cause of the headache (e.g., caffeine withdrawal, dehydration) can be identified, treatment can be directed accordingly. In the emergency setting, however, the precise etiology of the headache may not be immediately identifiable. Fortunately, most headache sufferers get relief from a "headache cocktail" that simultaneously addresses multiple pharmacologic and physiologic targets, regardless of the specific headache etiology. It is important to reiterate that response to analgesia does not predict etiology and should not be used in diagnostic decision-making.

First-line headache cocktail:

- Metoclopramide (Reglan; 10–20 mg IV; 20 mg PO; dopamine antagonism and acetylcholine sensitization) or prochlorperazine (Compazine (brand name discontinued in the United States); 10 mg IV or 10 mg PO; dopamine and CNS adrenergic antagonism)
  - These medications have multiple side effects and contraindications, notably extrapyramidal side effects (EPS) including but not limited to dystonias, akathisia, neuroleptic malignant syndrome, etc.
- Diphenhydramine (Benadryl; nonselective antihistamine; 25 mg IV or 25–50 mg PO) to prevent EPS
- Ketorolac (Toradol; NSAID; 30 mg IV) or ibuprofen (Motrin; NSAID; 800 mg PO)
- Fluid bolus (e.g., normal saline 1–2 L IV)

In the ED setting, most headaches will respond to aforementioned "headache cocktail" with or without additional acetaminophen. For migraine headaches, second-line therapy consists of triptans (e.g., sumatriptan or zolmitriptan), but only if the patient has not used ergotamines (e.g., dihydroergotamine (DHE)) within prior 24 h as their additive mechanisms of action may cause vasospasm. Some patients may also benefit from additional IV or PO steroids, though the clinical literature has shown mixed results. Similarly, clinicians can also consider adding combination drugs that include butalbital (an intermediate-acting barbiturate), such as butalbital, acetaminophen, and caffeine combination therapy. Barbiturate-containing formulations should be used sparingly because they can lead to dependence and overuse. Likewise, opioids (e.g., hydrocodone, oxycodone, or hydromorphone) may be efficacious in treating headache, though most guidelines and consensus statement discourage their use. If barbiturates and opioids are the only substances from which the patient obtains relief, clinicians should consider investigation of dependence or medication overuse as the headache etiology. Long-term therapy for migraine prevention may include amitriptyline (a tricyclic antidepressant), beta-blockers, calcium channel blockers, antidepressants (e.g., venlafaxine, a serotonin-norepinephrine reuptake inhibitor), antiepileptic drugs (e.g., topiramate and divalproex), as well as multiple alternative and non-pharmacologic therapies (HA primary care guidelines). In practice these long-term therapies are rarely initiated in

the emergency setting. Treatment of tension-type headache is similar to that of migraine, though triptans and ergotamines are rarely used. Benzodiazepines, barbiturates, and opioids are also discouraged for tension headache treatment. A unique feature of treatment for cluster headache is response to high-flow oxygen. If the patient has a history suggestive of cluster headaches, a trial of high-concentration inhaled oxygen is indicated (100 % O_2 12 lpm for 15 via non-rebreather mask). Triptans can also be considered for cluster. If medication-overuse headache is suspected, guidelines recommend abrupt withdrawal for analgesic-, ergotamine-, or triptan-related headache. If overuse of opioids, benzodiazepines, or barbiturates is suspected, a more gradual taper is recommended (Evers et al.). If specific secondary headache can be diagnosed, varying therapies directed at the cause may be helpful (e.g., lumbar puncture for pseudotumor cerebri or CPAP for OSA).

1.8 Pharmacologic Treatment

- NSAIDS, acetaminophen, aspirin:
  - Block the inflammatory arachidonic acid cascade at COX-1 and COX-2 to inhibit prostaglandin synthesis.
  - Ibuprofen 200–400 mg PO.
  - Naproxen 275–550 mg PO.
  - Acetaminophen 500–1,000 mg PO or IV.
  - Aspirin 500–1,000 mg PO.
  - Ketorolac 30 mg IV or 60 mg IM or IV.
  - Indomethacin 25–75 mg PO or IV.
  - Pitfalls. These agents may cause many adverse reactions, notably gastric irritation, GI bleeding, and renal dysfunction. Aspirin causes permanent dysfunction of currently circulating platelets. Acetaminophen should be avoided in conjunction with ethanol and/or liver disease and should be limited to no more than 4 g daily. Ibuprofen has a black box association with cardiovascular disease.
- Neuroleptics, antiemetics, and antihistamines:
  - Multiple pharmacologic targets, including dopaminergic blockade and acetylcholine sensitization.
  - Metoclopramide 10 mg IV.
  - Prochlorperazine 10 mg IV.
  - Droperidol 2.5 mg IV or haloperidol 5 mg IV may have efficacy in headaches resistant to other drug classes.
  - Pitfalls: These agents also have many possible adverse reactions, notably dystonic reactions, sedation, and QTc prolongations. Clinicians are advised to familiarize oneself with preferred agents. Side effects may be decreased or eliminated by pretreatment with diphenhydramine which also provides ancillary benefit of drowsiness

- Triptans and DHE:
  - Causes vasoconstriction via selective serotonergic agonism (5HT-1 for triptans, 5HT-1D for DHE).
  - Triptan dose can be repeated once.
  - Sumatriptan 100 mg PO, 6 mg SC, 20 mg IN.
  - Zolmitriptan 5 mg IN.
  - Dihydroergotamine (DHE) 1 mg SC, IM, or IV.
  - Pitfalls: These classes may contribute to serotonin syndrome, chest pain, and possible coronary vasoconstriction. Avoid if there is history of Prinzmetal's angina, cardiovascular disease, uncontrolled hypertension or concurrent SSRI, MAOI, or other vasoconstrictive medications. Do not give triptans within 24 h of dihydroergotamine. DHE carries a black box warning for peripheral ischemia and cerebral vasospasm when given with 3A4 inhibitors (including macrolide antibiotics and protease inhibitors) and should not be used in hemiplegic or basilar migraine.
- Steroids:
  - Multiple anti-inflammatory, glucocorticoid, and mineralocorticoid effects.
  - Prednisone 60 mg PO.
  - Methylprednisolone 125 mg IV.
  - Daily steroid therapy should be initiated immediately if temporal arteritis is suspected.
  - Pitfalls: Usually well tolerated as short-term therapy, but efficacy data are mixed. Some research has shown benefit of steroids as monotherapy or in addition to other therapies in treatment of migraine, especially in those for whom migraines are recurrent, frequent, and refractory to other treatments [5].
- Opioids:
  - Analgesia through opioid receptor antagonism
  - Numerous preparations, routes, and combination therapies available
  - Hydrocodone 5 mg or oxycodone 5 mg
  - Hydromorphone 0.5–1 mg IV
  - Administered in 35 % of ED visits despite usage discouragement by guidelines and consensus statements [6]
  - Pitfalls: Opiates are pro-inflammatory and increase vasodilation, which is counterproductive to current understanding of migraine pathophysiology. If opioids are the only medications by which the patient obtains relief, the physician should consider MOH or dependence as cause.

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