

# Neurology II

Headaches



# Pathophysiology of Headache & Facial Pain

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Headache is caused by traction, displacement, inflammation, or distention of the pain-sensitive structures in the head or neck.

## A. Pain-Sensitive Structures Within the Cranial Vault

## B. Extracranial Pain-Sensitive Structures

### Radiation or Projection of Pain

- trigeminal (V) nerve

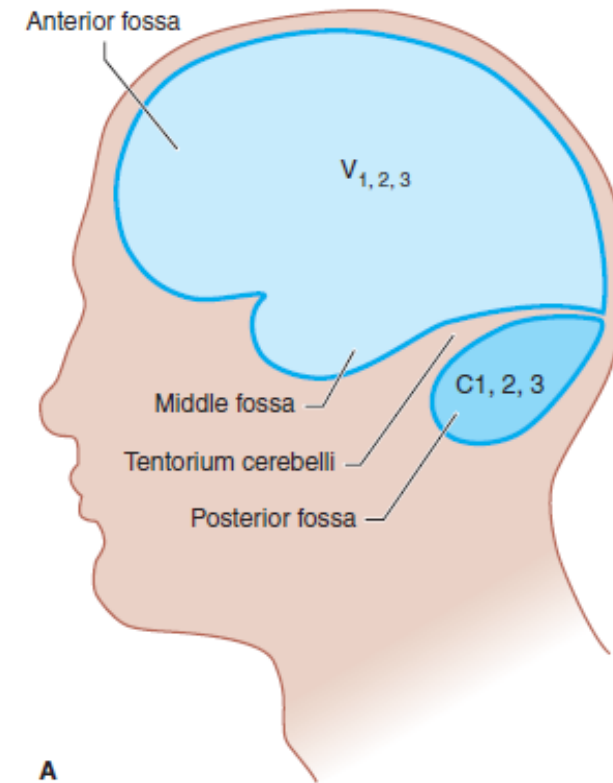
- glossopharyngeal (IX) and vagus (X) nerves

- upper cervical (C2-C3) nerves

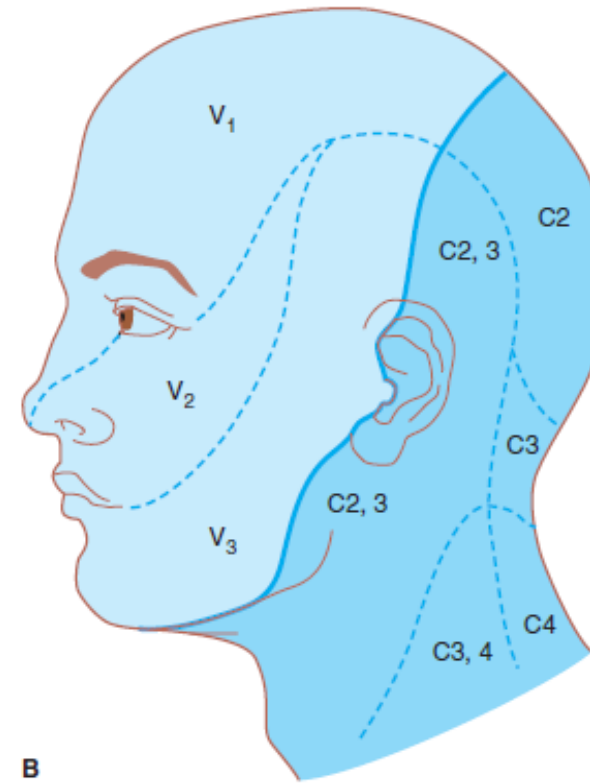
## Causes of Headache and Facial Pain.

| Acute onset                                                                                                                                                                                                                                                                                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Common causes</i><br>Subarachnoid hemorrhage<br>Other cerebrovascular diseases<br>Meningitis or encephalitis<br>Ophthalmic disorders (glaucoma, acute iritis)                                                                                                                             |
| <i>Less common causes</i><br>Seizures<br>Lumbar puncture<br>Hypertensive encephalopathy<br>Coitus                                                                                                                                                                                            |
| Subacute onset                                                                                                                                                                                                                                                                               |
| Giant cell (temporal) arteritis<br>Intracranial mass (tumor, subdural hematoma, abscess)<br>Pseudotumor cerebri (idiopathic intracranial hypertension)<br>Trigeminal neuralgia (tic douloureux)<br>Glossopharyngeal neuralgia<br>Postherpetic neuralgia<br>Persistent idiopathic facial pain |
| Chronic                                                                                                                                                                                                                                                                                      |
| Migraine<br>Medication overuse headache<br>Cluster headache<br>Tension-type headache<br>Icepick-like pain<br>Cervical spine disease<br>Sinusitis<br>Dental disease                                                                                                                           |

Innervation of pain-sensitive intracranial compartments (A) and corresponding extracranial sites of pain radiation



(B). The trigeminal (V) nerve, especially its ophthalmic (V<sub>1</sub>) division, innervates the anterior and middle cranial fossae; lesions in these areas can produce frontal headache. The upper cervical nerve roots (especially C<sub>2</sub>) innervate the posterior fossa; lesions here can cause occipital headache.



B

# History

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Acute Headache & Facial Pain

Subacute Headache & Facial Pain

Chronic Headache & Facial Pain

**Precipitating Factors**

**Prodromal Symptoms (Auras )**

**Characteristics of Pain**

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### **Location of Pain**

Unilateral, Ocular, Paranasal, Local, Bandlike, Trigeminal (V1), (V2), (V3), Pharynx, Ext meatus

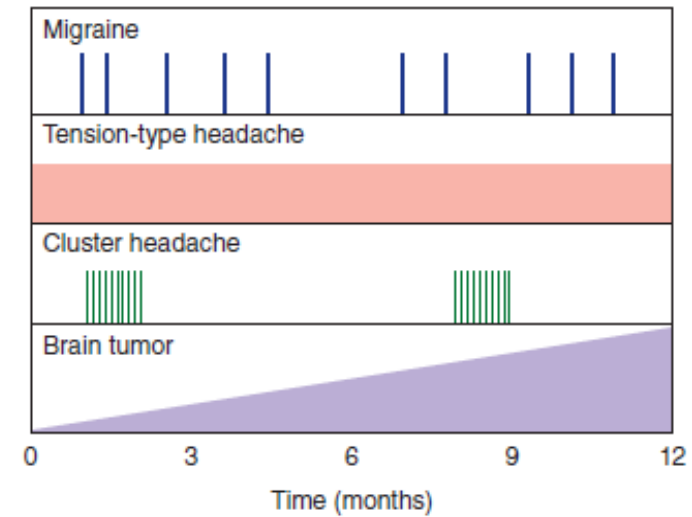
### **Associated Symptoms**

Weight loss, fever, dyspnea, visual findings, nausea, photophobia, myalgia, TIA, rhinorrhea

### **Other Features of Headache**

Temporal pattern of headache, relieving, exacerbating conditions

Temporal patterns of headache.  
Migraine headache is episodic and may occur at varying intervals. Tension-type headache may be present every day. Cluster headache occurs in bouts separated by symptom-free periods. Headache caused by brain tumor often increases in severity with time.



# Physical Examination

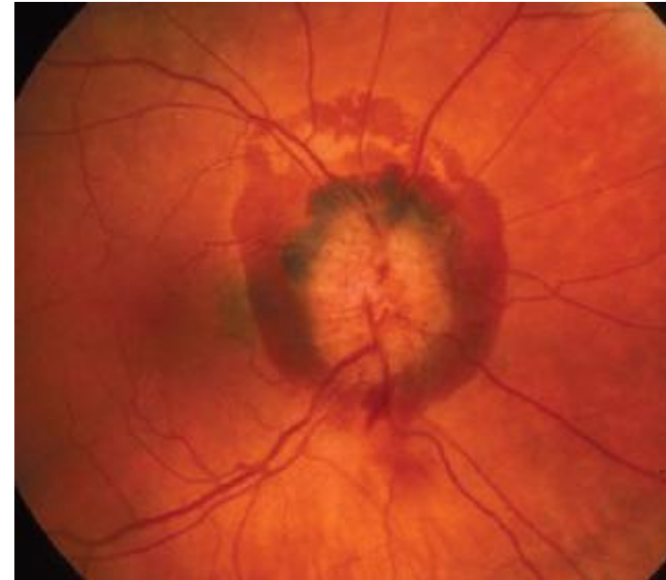
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Vital signs

General physical examination: weight, skin, face & head, neck, heart & lungs

Neurologic examination: mental status, cranial nerves, motor, sensory,

Disc edema and a large peripapillary subhyaloid hemorrhage in the right eye of a patient with aneurysmal rupture and subarachnoid hemorrhage.



# Acute Headache

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## Subarachnoid Hemorrhage

Pathology

Pathophysiology

Clinical findings

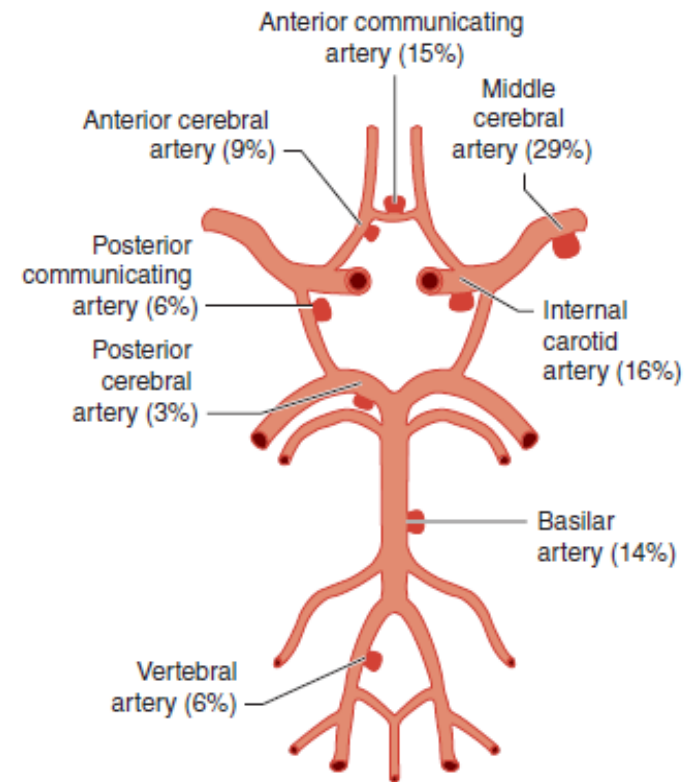
Differential diagnosis

Complication

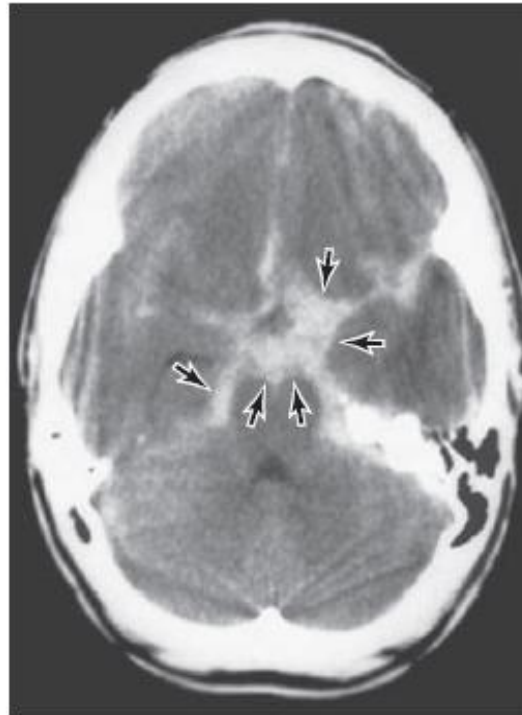
Treatment

Prognosis

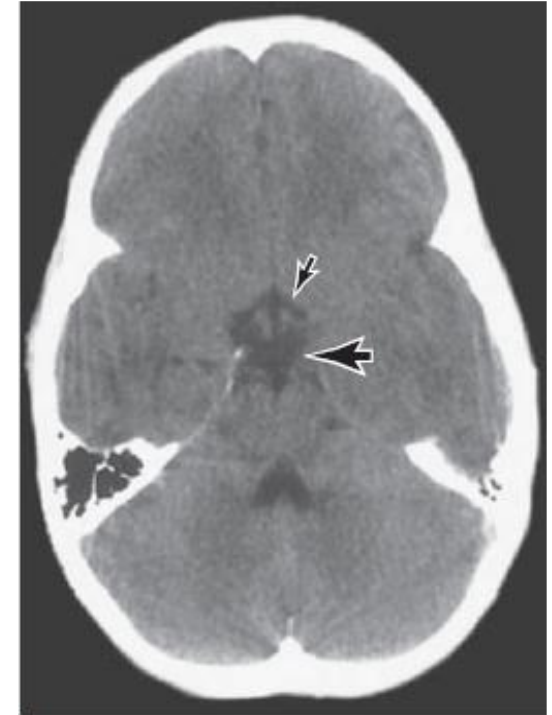
Frequency distribution of intracranial aneurysms.



(A) Nonenhanced brain CT scan from a patient with an acute aneurysmal subarachnoid hemorrhage. Areas of high density (arrows) represent blood in the subarachnoid space at the base of the brain (most aneurysms occur in this region about the circle of Willis). (B) A normal nonenhanced brain CT scan of the same region. Interpeduncular cistern, large arrow; suprasellar cistern, small arrow.



A



B

Clinical Grading of Patients With  
Aneurysmal Subarachnoid  
Hemorrhage.

| Grade | Level of Consciousness | Associated Clinical Features                                                                         | Surgical Candidate |
|-------|------------------------|------------------------------------------------------------------------------------------------------|--------------------|
| I     | Normal                 | None or mild headache and stiff neck                                                                 | Yes                |
| II    | Normal                 | Moderate headache and stiff neck; minimal neurologic deficit (eg, cranial nerve palsy) in some cases | Yes                |
| III   | Confusional state      | Focal neurologic deficits in some cases                                                              | Yes                |
| IV    | Stupor                 | Focal neurologic deficits in some cases                                                              | No                 |
| V     | Coma                   | Decerebrate posturing in some cases                                                                  | No                 |

# Other Cerebrovascular Disorders

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## Intracerebral Hemorrhage

## Cerebral Ischemia

Headache occurs at onset of stroke or TIA in one-third of patients and may persist for hours to several days.

Headaches associated with **ischemic stroke** are typically mild to moderate in intensity, and non throbbing in character.

Headache associated with cerebral infarction may require analgesics for symptomatic relief.

# Meningitis or Encephalitis

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Headache is a prominent feature of inflammation of the brain (encephalitis) or its meningeal coverings (meningitis) caused by bacterial, viral, or other infections.

The headache is commonly throbbing in character, bilateral, and occipital or nuchal in location.

Mental status abnormalities accompany most cases of bacterial but few cases of aseptic meningitis.

The diagnosis of bacterial meningitis is suggested by a CSF examination.

# Brain Abscess

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Headache is the most frequent presentation but the classic triad of headache with fever and focal neurologic signs occurs in less than 20%.

MRI and CT scanning differentiate abscess from primary or metastatic cancers.

# Other Causes of Acute Headache

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Seizures

Lumbar Puncture

Hypertensive Encephalopathy

Coitus

Ophthalmic Disorders

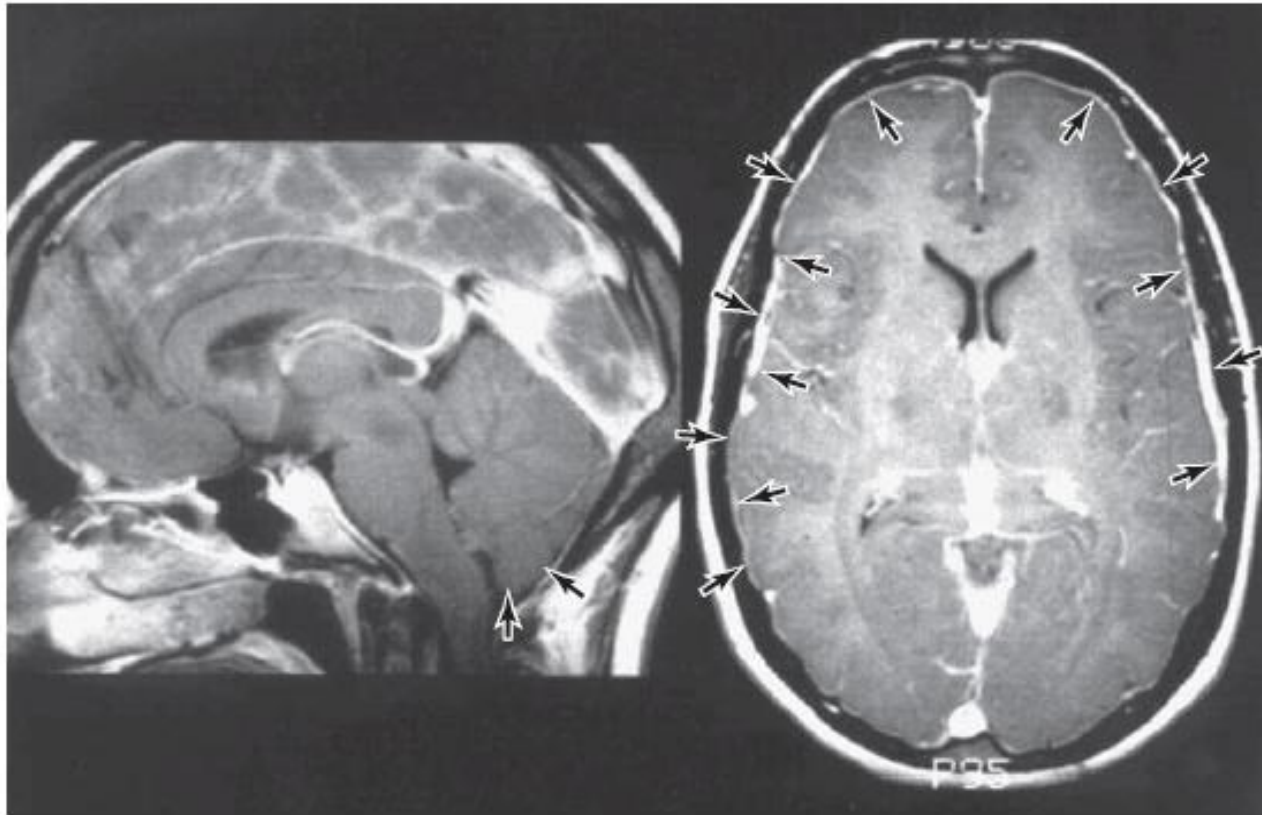
# Subacute Headache

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Giant cell arteritis

Intracranial mass

Idiopathic intracranial hypertension



▲ **Figure 6-6.** Spontaneous intracranial hypotension in a 27-year-old woman presenting with severe postural headaches. Sagittal and axial T1-weighted images obtained after gadolinium injections show features of “sagging brain”: downward displacement of the cerebellar tonsils into the foramen magnum (arrows, left image), effacement of the brainstem cisterns (left image; compare with normal sagittal MRI in Figure 2-3), and diffuse dural enhancement (arrows, right image). MRI abnormalities and symptoms reversed following an epidural blood patch. (Used with

| Tumor Type                | Incidence (%) |
|---------------------------|---------------|
| Meningioma                | 34.4          |
| Glioblastoma              | 16.7          |
| Pituitary                 | 13.1          |
| Nerve sheath <sup>1</sup> | 8.6           |
| Astrocytoma               | 7.0           |
| Other neuroepithelial     | 5.1           |
| Lymphoma                  | 2.4           |
| Oligodendroglioma         | 2.0           |
| Ependymoma                | 1.8           |
| Embryonal <sup>2</sup>    | 1.0           |
| Craniopharyngioma         | 0.7           |
| Germ cell tumor           | 0.5           |
| Other                     | 6.6           |

**Table 6-4.** Symptoms of Brain Tumors.

| Symptom               | Percent With Symptom |                  |                     |
|-----------------------|----------------------|------------------|---------------------|
|                       | Low-Grade Glioma     | Malignant Glioma | Meningioma (Benign) |
| Headache              | 40                   | 50               | 36                  |
| Seizure               | 65-95                | 15-25            | 40                  |
| Hemiparesis           | 5-15                 | 30-50            | 22                  |
| Altered mental status | 10                   | 40-60            | 21                  |

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**Table 6-5.** Disorders Associated With Intracranial Hypertension.

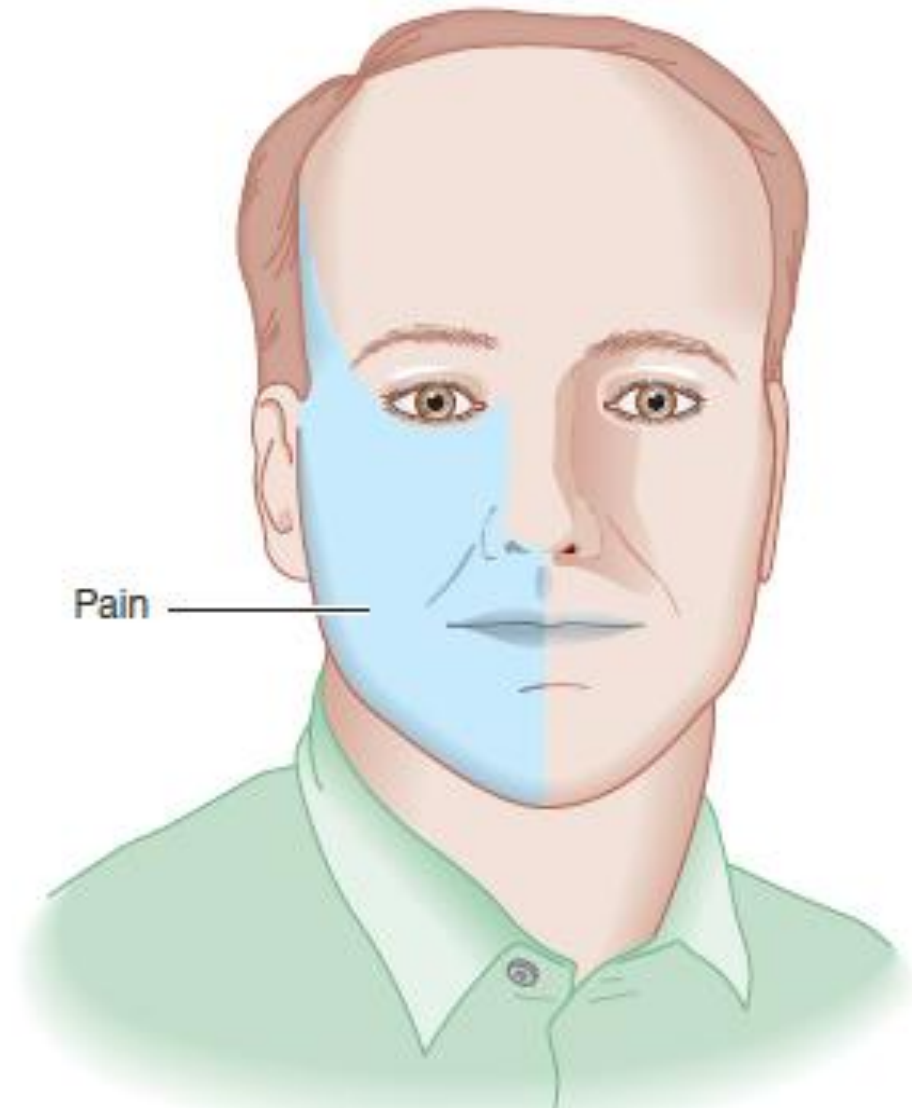
|                                                                                                                                                           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Intracranial venous drainage obstruction (eg, venous sinus thrombosis, head trauma, polycythemia, thrombocytosis)                                         |
| Endocrine dysfunction (eg, obesity, withdrawal from steroid therapy, Addison disease, hypoparathyroidism)                                                 |
| Vitamin and drug therapy (eg, hypervitaminosis A and 13 <i>cis</i> -retinoic acid in children and adolescents, tetracycline, minocycline, nalidixic acid) |
| Other (eg, chronic hypercapnia, severe right heart failure, chronic meningitis, hypertensive encephalopathy, severe iron deficiency anemia)               |
| Idiopathic                                                                                                                                                |

# Trigeminal Neuralgia

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Trigeminal neuralgia (**tic douloureux**) is a facial pain syndrome that develops in middle to late life and is more common in women than men. In many instances, the trigeminal (V) nerve roots are close to a vascular structure, and microvascular compression followed by demyelination of the nerve is believed to cause the disorder.

Distribution of symptoms in  
trigeminal neuralgia.

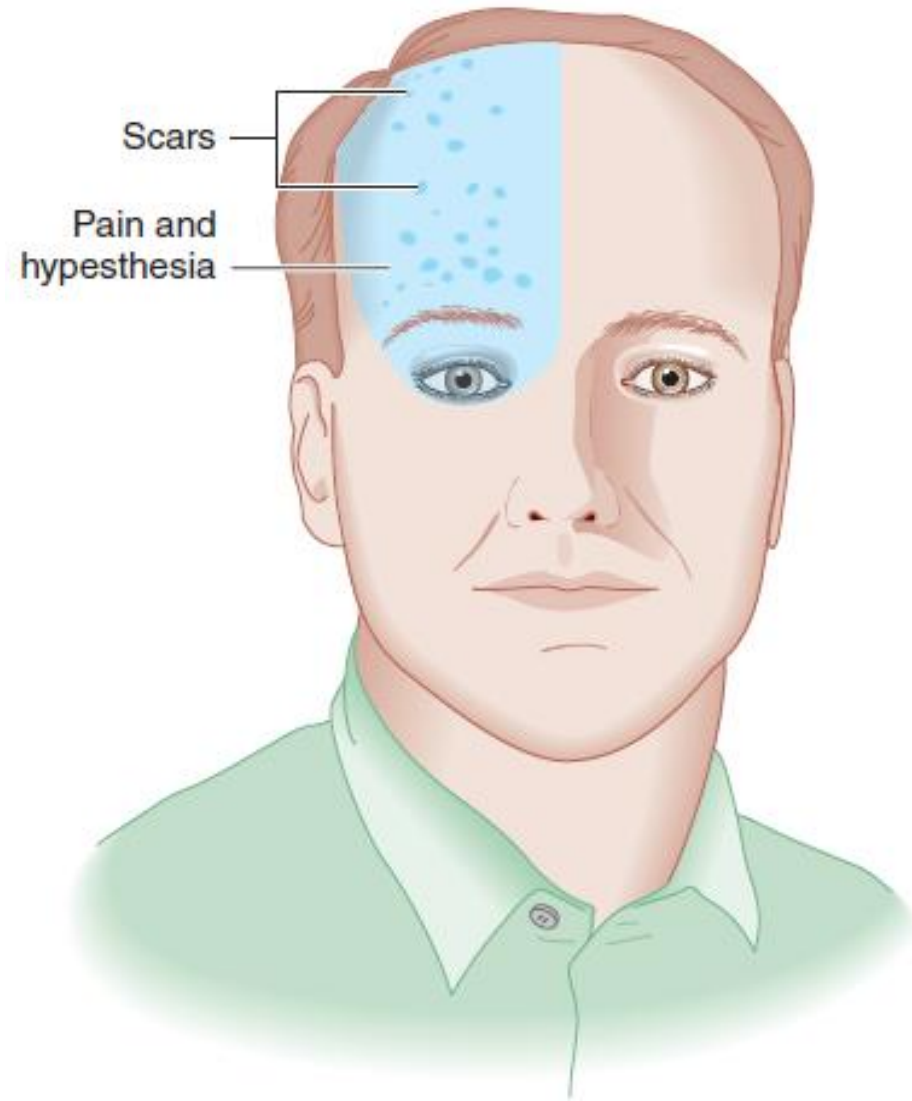


# Postherpetic Neuralgia

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Reactivation of varicella-zoster virus in the trigeminal, or ganglion causes **herpes zoster (shingles)**, a vesicular skin eruption in the distribution of the trigeminal (V) nerve accompanied by pain and tenderness.

Distribution of symptoms and signs in postherpetic neuralgia.



# Chronic Headache

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## Migraine

Genetics

Structural features

Pathogenesis

Clinical findings

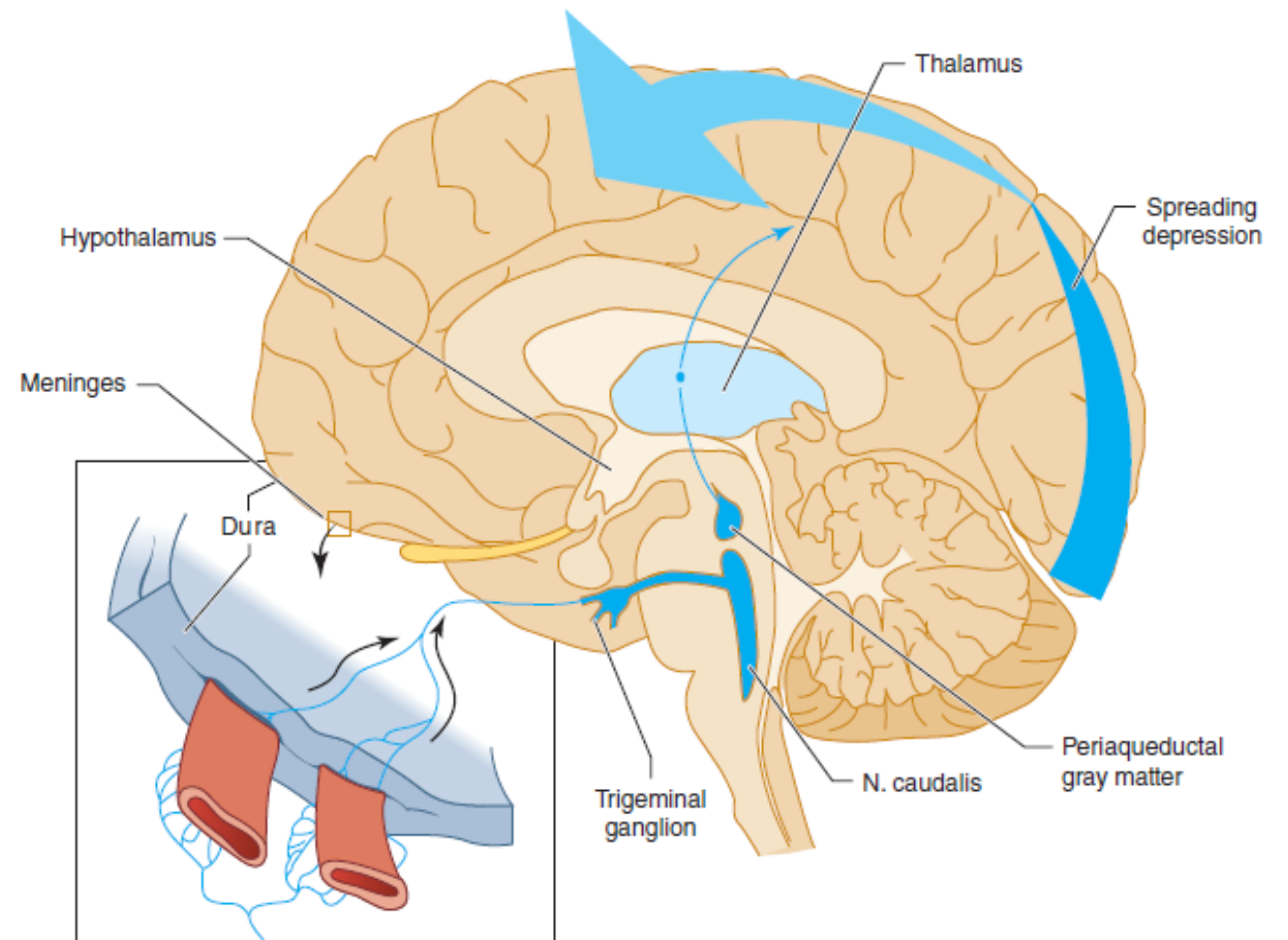
- Classic migraine

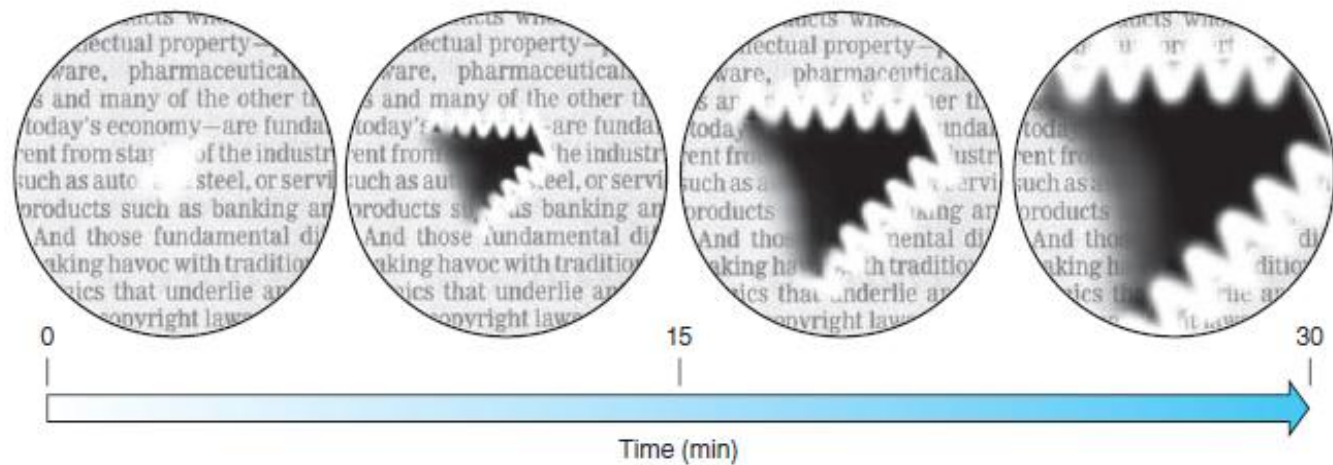
- Common migraine

- Chronic migraine and medication overuse

**Table 6-6.** Autosomal Dominant and Hereditary Disorders Associated With Migraine.

| Gene           | Protein                                                                                  | Disease                                                                                         | Features                                                                                |
|----------------|------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| <i>CACNA1A</i> | $\alpha_1$ subunit of neuronal $\text{Ca}_v2.1$ (P/Q-type) voltage-gated calcium channel | Familial hemiplegic migraine (FHM1); (50% of identified families have <i>CACNA1A</i> mutations) | Hemiplegic migraine, cerebellar ataxia, seizures                                        |
| <i>ATP1A2</i>  | $\alpha_2$ subunit of sodium-potassium pump                                              | Familial hemiplegic migraine (FHM2); (20% of identified families have <i>ATP1A2</i> mutations)  | Hemiplegic migraine, seizures                                                           |
| <i>SCN1A</i>   | $\alpha$ subunit of $\text{Na}_v1.1$ voltage-gated sodium channel                        | Familial hemiplegic migraine (FHM3)                                                             | Hemiplegic migraine, seizures                                                           |
| <i>MTTL1</i>   | mtDNA A-to-G transition at nucleotide 3243                                               | Mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS)              | Migraine, seizures, hemiparesis, hemianopsia, cortical blindness, and episodic vomiting |
| <i>NOTCH3</i>  | Notch3 (transmembrane receptor)                                                          | Cerebral autosomal dominant arteriopathy with subcortical infarcts (CADASIL)                    | Migraine with aura, stroke, dementia                                                    |
| <i>TREX1</i>   | 3' repair exonuclease 1 (DNA repair enzyme)                                              | Retinal vasculopathy with cerebral leukodystrophy (RVCL)                                        | Migraine, blindness, stroke, dementia, Raynaud phenomenon, nephropathy, cirrhosis       |





▲ **Figure 6-10.** Successive maps of scintillating scotoma (blind spot) to show the evolution of fortification figures (jagged edges) and associated scotoma in a patient with classic migraine. As the fortification moves laterally, a region of transient blindness remains.

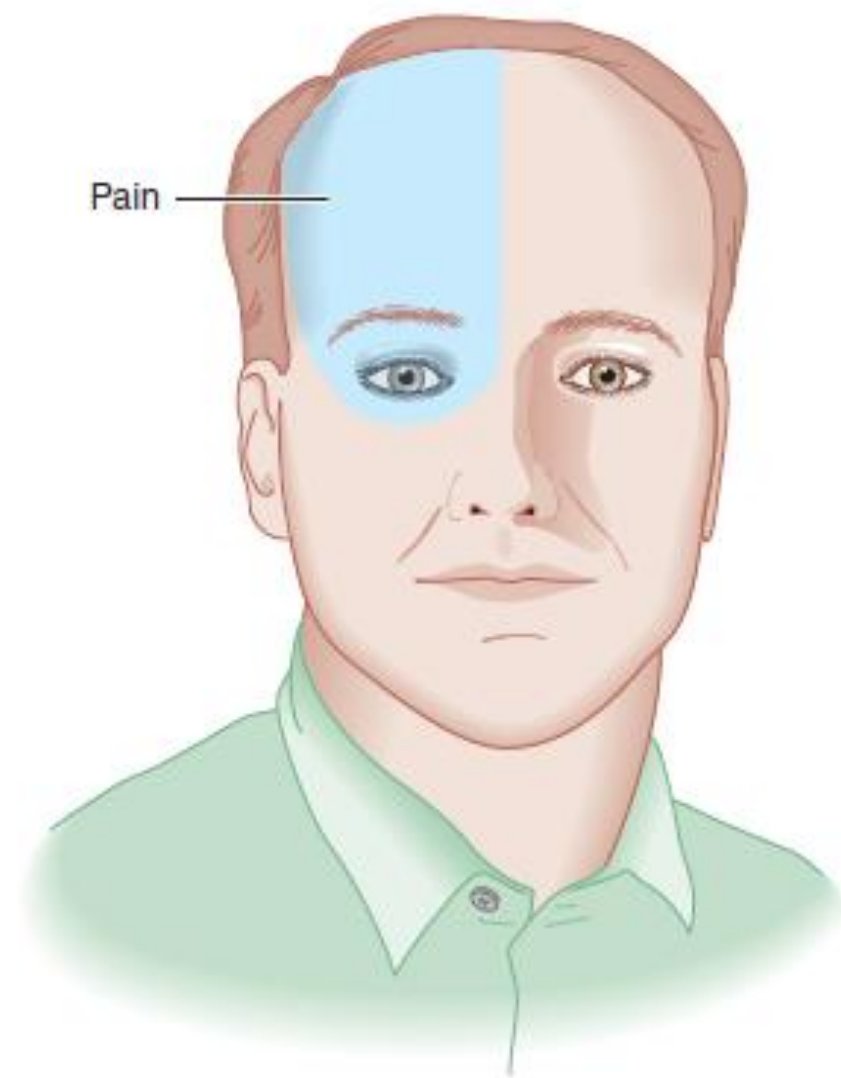


**Table 6-8.** Prophylactic Treatment of Migraine Headache

| Drug                      | Route <sup>1</sup> | Strength                    | Recommended Dose        | Comments                                                                                                                                                                                                                                           |
|---------------------------|--------------------|-----------------------------|-------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Anti-inflammatory agents  |                    |                             |                         |                                                                                                                                                                                                                                                    |
| Aspirin                   | PO                 | 325 mg                      | 325 mg qod              | May cause gastric pain or bleeding                                                                                                                                                                                                                 |
| Naproxen sodium           | PO                 | 275, 550 mg                 | 550-825 mg bid          |                                                                                                                                                                                                                                                    |
| Tricyclic antidepressants |                    |                             |                         |                                                                                                                                                                                                                                                    |
| Amitriptyline             | PO                 | 10, 25, 50, 75, 100, 150 mg | 10-300 mg hs            | May cause dry mouth or urinary retention. Begin with lowest dose and increase slowly. Adding an anticonvulsant may increase efficacy.                                                                                                              |
| Nortriptyline             | PO                 | 10, 25, 50, 75 mg           | 10-150 mg hs            |                                                                                                                                                                                                                                                    |
| Desipramine               | PO                 | 10, 25, 50, 75, 100 mg      | 25-300 mg qhs           |                                                                                                                                                                                                                                                    |
| Protriptyline             | PO                 | 5, 10 mg                    | 15-40 mg/d in 3-4 doses | Protriptyline is less sedating than other tricyclics but dry mouth and constipation may be problematic                                                                                                                                             |
| β-Receptor antagonists    |                    |                             |                         |                                                                                                                                                                                                                                                    |
| Propranolol*              | PO                 | 10, 20, 40, 60, 80, 90 mg   | 20-120 mg bid           | Listed in descending order of efficacy. Symptomatic bradycardia may occur at high doses. Contraindicated in asthma and congestive heart failure and in patients on calcium channel blockers. To discontinue, taper over 1-2 weeks.* most effective |
|                           | PO (long acting)   | 60, 80, 120, 160 mg         | 60-320 mg qd            |                                                                                                                                                                                                                                                    |
| Timolol*                  | PO                 | 10, 20 mg                   | 10-30 mg qd             |                                                                                                                                                                                                                                                    |
| Metoprolol*               | PO                 | 50, 100 mg                  | 100-200 mg qd           |                                                                                                                                                                                                                                                    |
| Nadolol                   | PO                 | 40, 80, 120, 160 mg         | 40-240 mg qd            |                                                                                                                                                                                                                                                    |
| Atenolol                  | PO                 | 50, 100 mg                  | 50-200 mg qd            |                                                                                                                                                                                                                                                    |

|                                    |                        |                                                 |                                                                              |                                                                                                                                                                                                                                                                                                                                                               |
|------------------------------------|------------------------|-------------------------------------------------|------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Anticonvulsants</i>             |                        |                                                 |                                                                              |                                                                                                                                                                                                                                                                                                                                                               |
| Valproic acid                      | PO                     | 125, 250, 500 mg;<br>500 mg extended<br>release | 250-500 mg bid or<br>1,000 mg qhs as<br>single dose with<br>extended release | Begin with lowest dose. Contraindicated in women of<br>childbearing age.<br><br>Start 25 mg hs and increase by 25 mg/d every 7 days as<br>tolerated. Optimal dose 100 mg/d. Paresthesias in<br>50%. Altered mental state may require lowering<br>dose. Rare: nephrolithiasis, angle-closure glaucoma.<br>Less effective than other anticonvulsants. Sedating. |
| Topiramate                         | PO                     | 25, 50, 100, 200 mg                             | 25-200 mg qd                                                                 |                                                                                                                                                                                                                                                                                                                                                               |
| Gabapentin                         | PO                     | 100, 300, 400,<br>600, 800 mg                   | 1800-2,400 mg qd                                                             |                                                                                                                                                                                                                                                                                                                                                               |
| <i>Calcium channel antagonists</i> |                        |                                                 |                                                                              |                                                                                                                                                                                                                                                                                                                                                               |
| Verapamil                          | PO                     | 40, 80, 120 mg                                  | 80-160 mg tid                                                                | Contraindicated by severe left ventricular dysfunction,<br>hypotension, sick sinus syndrome without artificial<br>pacemaker, second- or third-degree AV nodal block,<br>and in patients on $\beta$ -blockers. Constipation is most<br>common side effect. Verapamil ineffective in<br>migraine without aura.                                                  |
| Flunarizine                        | PO<br>(long<br>acting) | 240 mg                                          | 240 mg qd-bid                                                                |                                                                                                                                                                                                                                                                                                                                                               |
|                                    | PO                     | 5, 10 mg                                        | 5-15 mg/day                                                                  |                                                                                                                                                                                                                                                                                                                                                               |
| <i>Other agents<sup>2</sup></i>    |                        |                                                 |                                                                              |                                                                                                                                                                                                                                                                                                                                                               |
| Riboflavin<br>(vitamin B2)         | PO                     | Various                                         | 400 mg/d                                                                     | May require 4-8 weeks for onset and increased effect<br>over 3-6 months. Urine turns dark.                                                                                                                                                                                                                                                                    |
| Onabotulinum<br>toxin A            | IM                     | 100 units/vial                                  | 100-250 units                                                                | Not effective in episodic but very effective in chronic<br>migraine. Injected into head and neck muscles.                                                                                                                                                                                                                                                     |

**Table 6-7.** Acute (Abortive) Treatment of Migraine Headache. (*Continued*)

| Drug               | Route <sup>1</sup> | Strength        | Recommended Dose                   | Comments                                                                                                                         |
|--------------------|--------------------|-----------------|------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| <i>Antiemetics</i> |                    |                 |                                    |                                                                                                                                  |
| Prochlorperazine   | PO                 | 5, 10, 15 mg    | 25 mg q6h                          | Adjunctive treatment to reduce nausea and improve enteric absorption of antimigraine drugs. Extrapyrimal side effects may occur. |
|                    | PR                 | 2.5, 5, 25 mg   | 25 mg q12h                         |                                                                                                                                  |
|                    | IM, IV             | 5 mg/mL         | 10 mg (with 10 mg diphenhydramine) |                                                                                                                                  |
| Chlorpromazine     | IM                 | 25 mg/mL        | 50 mg                              |                                                                                                                                  |
|                    | IV                 | 25 mg/mL        | 0.1 mg/kg drip over 20 minutes     |                                                                                                                                  |
| Promethazine       | PO, PR             | 12.5, 25, 50 mg | 25-50 mg q6h                       |                                                                                                                                  |
| Metoclopramide     | PO                 | 5, 10 mg        | 5-20 mg tid                        |                                                                                                                                  |

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## Migraine

Precipitating factors

Treatment

**Table 6-7.** Acute (Abortive) Treatment of Migraine Headache.

| Drug                                                               | Route <sup>1</sup> | Strength                              | Recommended Dose                                     | Comments                                                                                                                                                                                                                                                                                                                    |
|--------------------------------------------------------------------|--------------------|---------------------------------------|------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Simple analgesics                                                  |                    |                                       |                                                      |                                                                                                                                                                                                                                                                                                                             |
| Aspirin                                                            | PO                 | 325 mg                                | 650 mg q4h                                           | May cause gastric pain or bleeding and rebound headache if used frequently.                                                                                                                                                                                                                                                 |
| Naproxen sodium                                                    | PO                 | 250, 375, 500 mg                      | 500–1,000 mg at onset, then 250–500 prn after 1 hour |                                                                                                                                                                                                                                                                                                                             |
| Ibuprofen                                                          | PO                 | 200, 400, 600, 800 mg                 | 800-1,200 mg at onset, then 600-800 mg q4–8h         |                                                                                                                                                                                                                                                                                                                             |
| Ketoprofen                                                         | PO                 | 25, 50, 75, 100, 150, 200 mg          | 75-150 mg q6h                                        | Acetaminophen/isometheptene/dichloralphenazone is marketed as Midrin.                                                                                                                                                                                                                                                       |
| Acetaminophen                                                      | PO<br>PR           | 325, 500 mg                           | 650-1,000 mg at onset, then q4h                      |                                                                                                                                                                                                                                                                                                                             |
| (If analgesics ineffective, switch to triptans for next headache.) |                    |                                       |                                                      |                                                                                                                                                                                                                                                                                                                             |
| Triptans                                                           |                    |                                       |                                                      |                                                                                                                                                                                                                                                                                                                             |
| Sumatriptan**                                                      | NS<br>PO<br>SC     | 20 mg/spray<br>25, 50, 100 mg<br>6 mg | 20 mg<br>50-100 mg<br>6 mg                           | May repeat once after 2 hours for partial response. May cause nausea and vomiting; contraindicated by pregnancy, coronary or peripheral vascular disease, concurrent treatment with monoamine oxidase inhibitors, and possibly hemiplegic or basilar migraine. Common side effects: chest tightness, extremity parasthesias |
| Rizatriptan*                                                       | PO                 | 5, 10 mg                              | 10 mg                                                |                                                                                                                                                                                                                                                                                                                             |
| Zolmitriptan**                                                     | PO<br>NS           | 2.5, 5 mg<br>5 mg/spray               | 2.5-5 mg<br>5 mg                                     |                                                                                                                                                                                                                                                                                                                             |
| Almotriptan**                                                      | PO                 | 6.25, 12.5 mg                         | 6.25-12.5 mg                                         |                                                                                                                                                                                                                                                                                                                             |
| Eletriptan*                                                        | PO                 | 20, 40 mg                             | 40 mg                                                | *Onset of effect 30 minutes<br>**Onset of effect 45-60 minutes                                                                                                                                                                                                                                                              |
| Frovatriptan***                                                    | PO                 | 2.5 mg                                | 2.5 mg                                               | *** Require 4 hrs for effect but are long acting                                                                                                                                                                                                                                                                            |
| Naratriptan***                                                     | PO                 | 1, 2.5 mg                             | 2.5 mg                                               | Triptan response rate 60-80%. Faster-acting triptans have more frequent headache recurrence which can be attenuated by NSAID co-administration.                                                                                                                                                                             |

|                                                    |    |                       |                                                       |                                                                                                                                         |
|----------------------------------------------------|----|-----------------------|-------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| Ergot alkaloids (not to be combined with triptans) |    |                       |                                                       |                                                                                                                                         |
| Ergotamine/<br>caffeine<br>(Cafergot)              | PR | 2 mg/100 mg           | 1/4-2 suppositories, up<br>to 5 per week              | May cause nausea and vomiting; contraindicated<br>in pregnancy and coronary or peripheral vas-<br>cular disease.                        |
| Dihydroergotamine<br>(DHE)                         | NS | 0.5 mg/spray          | 1 spray to each nostril,<br>up to 5 times per<br>week | Repeat after 15 minutes. May cause nausea and<br>vomiting; contraindicated in pregnancy and<br>coronary or peripheral vascular disease. |
|                                                    | SC | 1 mg/mL               | 1-2 mg                                                | Repeat 1 mg q12h, up to 6 mg                                                                                                            |
|                                                    | IV |                       | 0.75-1.25 mg IV                                       |                                                                                                                                         |
| Narcotic analgesics                                |    |                       |                                                       |                                                                                                                                         |
| Codeine/aspirin                                    | PO | 15, 30, 60/325 mg     | 30-120 mg codeine                                     |                                                                                                                                         |
| Meperidine                                         | PO | 50, 100 mg            | 50-200 mg                                             |                                                                                                                                         |
|                                                    | IM |                       |                                                       |                                                                                                                                         |
| Butorphanol                                        | NS | 10 mg/mL (1 mg/spray) | 1 spray every 3-4 hours<br>as needed                  |                                                                                                                                         |

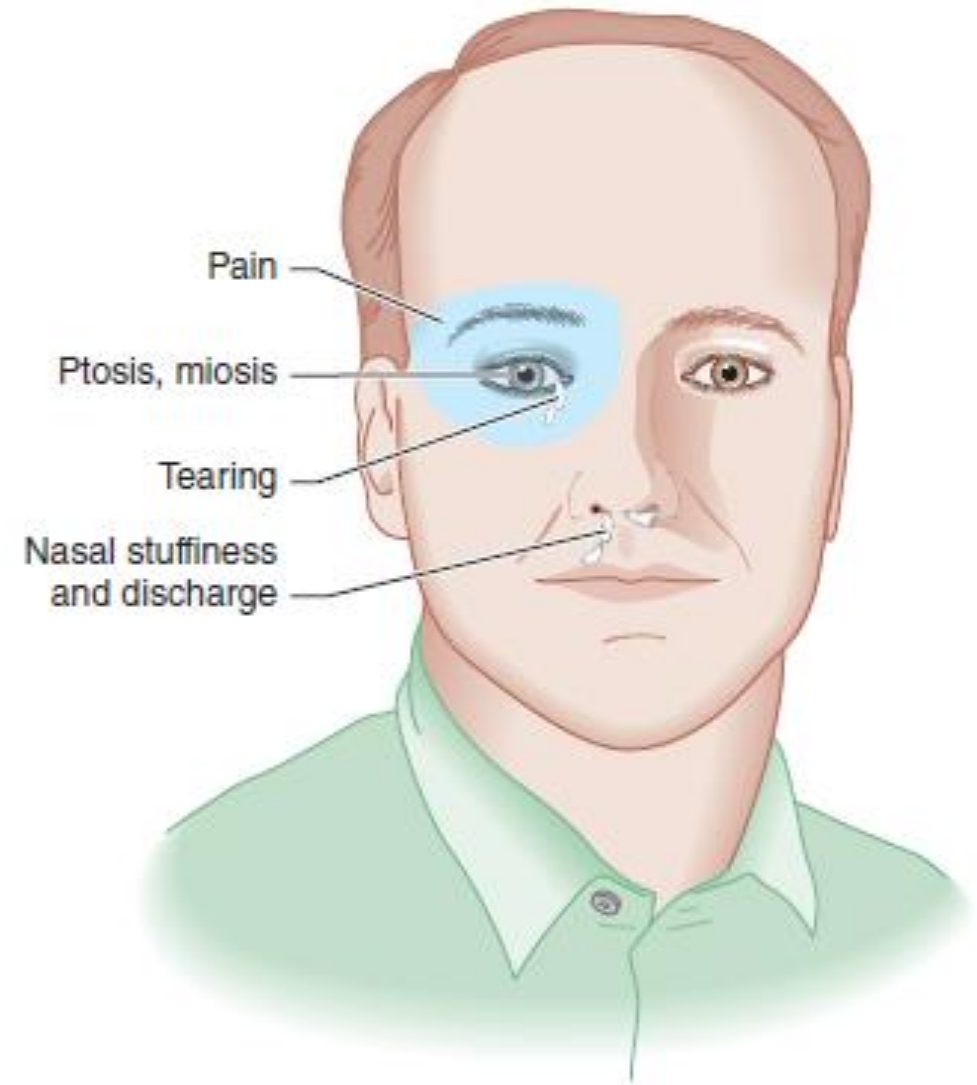
# Cluster Headache

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Cluster headache presents as clusters of brief, very severe, unilateral, constant, nonthrobbing headaches that last from 15 minutes to 3 hours.

Clinical findings

Treatment





# Tension-Type Headache

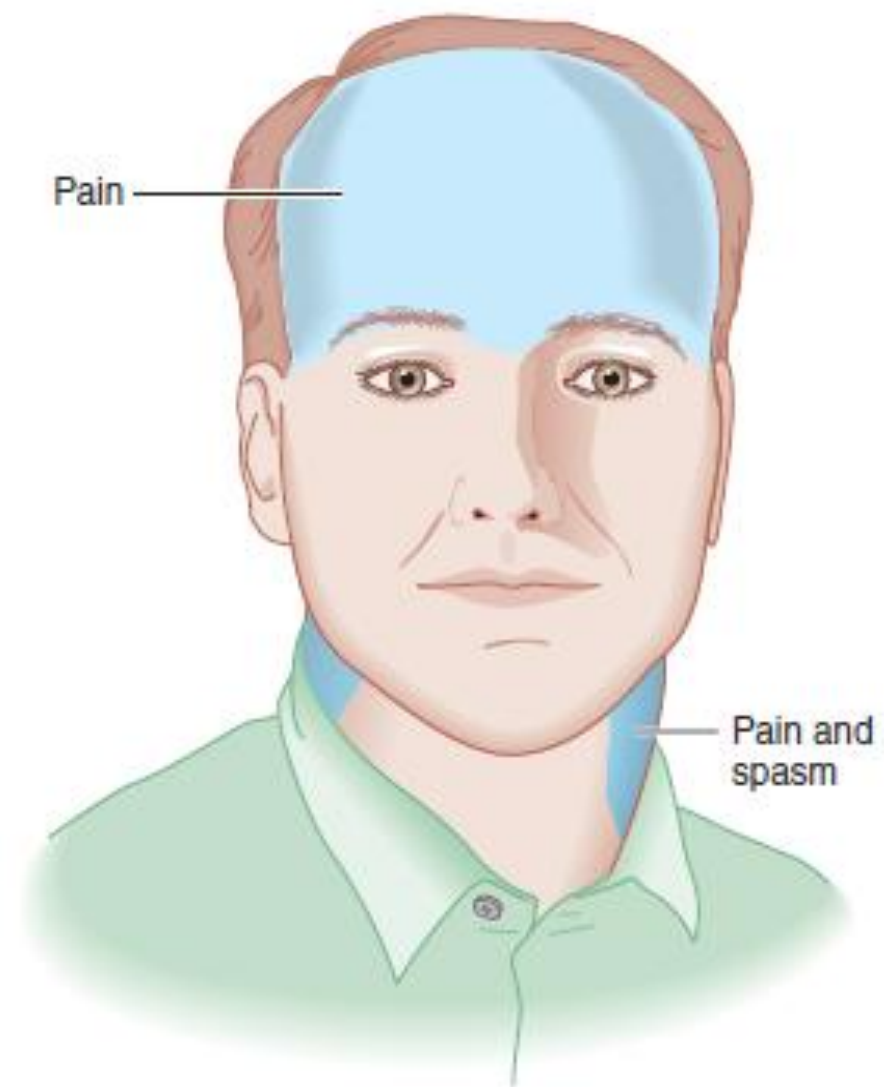
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Tension-type headache is the term used to describe chronic or recurrent headache of inapparent cause that lack features of migraine or other headache syndromes.

In its classic form, tension-type headache is a chronic disorder that begins after age 20 years.

Women are more commonly affected than men.

Drugs used in the treatment of tension-type headache include many of the same agents used for migraine.



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Icepick-Like Pain

Cervical spine disease

Sinusitis

Dental disease