

IN THE NAME OF GOD

Headache

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Headache

- ❖ Is a remarkably common problem in neurology and general medicine
- ❖ Most primary headaches causes face pain
- **Facial neuralgias and facial pain syndromes are discussed later**

General principles

Common causes of headache:

- ✓ Primary
- ✓ Secondary

Primary headache :

Headache and associated features are seen in the absence of any exogenous cause

Primary headache and prevalence :

- ✓ Migraine : 16%
 - ✓ Tension- type: 69%
 - ✓ Cluster headache: 0.1%
 - ✓ Idiopathic stabbing: 2%
 - ✓ Exertional: 1%
- ❖ The most disabling primary headaches :
Migraine, cluster headache

Secondary headache and prevalence :

- ✓ Systemic infection: 63%
- ✓ Head injury: 4%
- ✓ Subarachnoid hemorrhage: <1%
- ✓ Vascular disorders: 1%
- ✓ Brain tumor: 0.1%

Warning signs in head pain

- Sudden-onset pain
- Fever
- Marked change in pain character or timing of attack
- Neck stiffness
- Pain associated with higher center complaints
- Pain associated with neurologic disturbance, such as clumsiness or weakness
- Pain associated with local tenderness, such as of the temporal artery

Anatomy and physiology

The key structures involved in head pain are:

1. The large intracranial vessels and dura matter
2. The peripheral terminals of trigeminal nerve that innervate these structures
3. The central terminals and second-order neurons of the caudal trigeminal nucleus and dorsal horns of C1 and C2 (trigeminocervical complex)

4. Higher center processing in the thalamus, ventroposteromedial and posterior thalamus and cortex.

5. Modulatory centers in diencephalon and brainstem, such as periaquiductal gray matter, locus coeruleus and parts of the hypothalamus

- ❖ The innervation of the **large intracranial vessels** and **dura** matter by the **trigeminal nerve** is known as the **trigeminovascular system**
- ❖ The **cranial parasympathetic** autonomic innervation provides the basis for symptoms such as **lacrimation** and nasal **stiffness**, which are prominent in trigeminal autonomic cephalgias (**TACs**) , although they **may** be seen in **migraine**

Note:

- Imaging → migraine and cluster headache → neuronal vasodilator system → neurovascular headache , **HOWEVER** ;
- The term **vascular headache** has **no place** in modern medical practice when referring to primary headache because :
 - ✓ It neither explain the pathogenesis of what are complex CNS disorders,
 - ✓ nor does it necessarily predict treatment outcomes.

Mechanism

- Channelopathies or ionopathathies, disorders involving dysfunction of ion channel fluxes (now)
- Functional neuroimaging has suggested :
 - Brainstem region in migraine
 - Posterior hypothalamic region in cluster headache

Secondary headache

- Patients with a short history require prompt attention and may require prompt investigation and management.
- Longer history → require time and practice
- MRI & CT

NOTE:

- ❖ Patients with a history of recurrent headache over a period of 1 year or more, fulfilling criteria for migraine and with a normal physical examination, have **positive brain imaging findings in only about 1/1000 images**

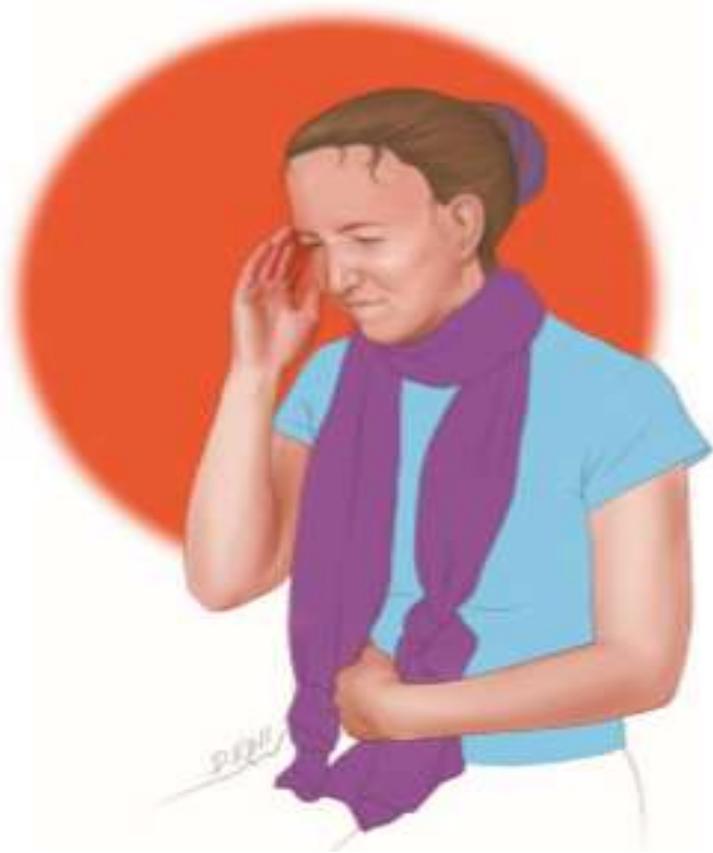
NOTE: Brain tumor and headache

- Brain tumor is a rare cause of headache
 - Is rarely a cause of isolated long-term histories of headache
 - **A notable exception:**
 - ✓ Pituitary tumor
- (can trigger underlying primary headache, especially in the differential diagnosis of TACs)

The management of secondary headache

- Treatment of the underlying condition
- ✓ One notable exception is:
 - Persistent posttraumatic headache (after CNS infection, trauma, blunt or surgical, intracranial bleeds and ...)
 - It can often be both prolonged and disabling

Migraine

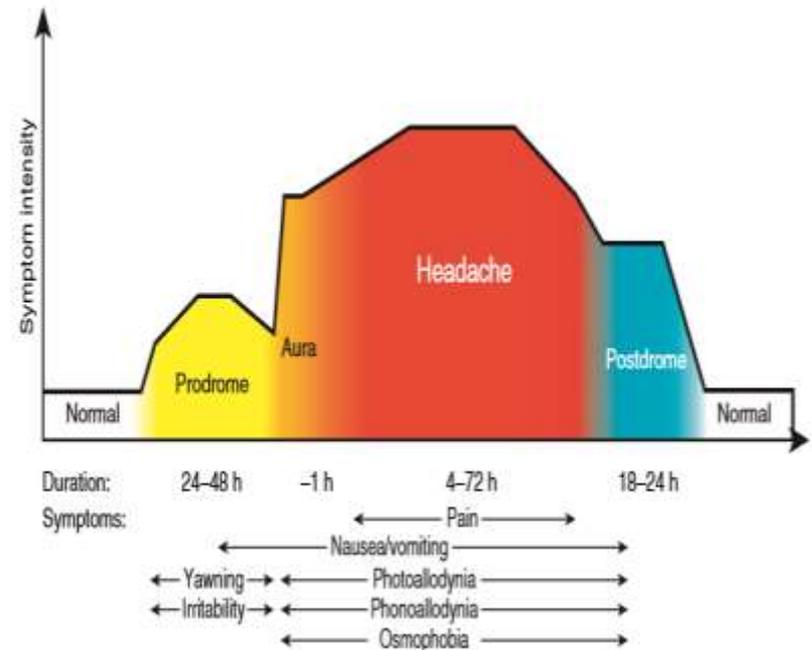


Clinical features of migraine

- An episodic brain disorder
- Prevalence: 12% - 15%
- Can be highly disabling
- May begin in **childhood**, but **almost always develops before age 30 years.**
- **Female > Male**
- Headache generally accompanied by features, such as sensitivity to light, sounds, or movement and often with nausea, or less often vomiting

The typical migraine headache is characterized by four phases (waldman/common pain syndrome'4th ed.)

1. The prodrome
2. The aura
3. The headache
4. The postdrome



- **Prodrome**: a premonition or warning that a migraine may be on the horizon(mood changes, food cravings, frequent yawning, changes in libido, and constipation)
- **Aura**: neurologic event before the onset of pain(visual disturbance, olfactory and auditory auras)
- **Postdrome**: confusion, dizziness, weakness, or elation

Diagnostic criteria according to IHS

TABLE 61.3 Simplified Diagnostic Criteria for Migraine

Repeated attacks of headache lasting 4–72 h that have these features, normal physical examination and no other reasonable cause for the headache

At Least Two of

- Unilateral pain
- Throbbing pain
- Aggravation by movement
- Moderate or severe intensity

At Least One of

- Nausea/vomiting
- Photophobia and phonophobia

Adapted from Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd Edition. *Cephalalgia* 2018;38:1–211.

NOTE:

- ✓ **Non of the features is compulsory and indeed**
- ✓ The headache is **never bilateral at its onset**
- ✓ The time from **onset to peak** of migraine pain is short, ranging from **20 minutes to 1 hour**
- ✓ A high index of suspicion is required to diagnose migraine

Migraine aura

- Visual disturbances with flashing lights or zigzag lines moving across the fields or other neurologic symptoms
- **Is reported in only about 25% of patients**
- The aura is thought to be the result of ischemia of specific regions of the cerebral cortex.
- A visual aura often occurs 30 to 60 minutes before the onset of headache pain

Aura

- ✓ **Olfactory auras**: strong odors of substances that are not actually present or extreme hypersensitivity to otherwise normal odors, such as coffee or copy machine toner
- ✓ **Migraine with prolonged aura**:
 - Rarely
 - neurologic dysfunction may last for **more than 24 hours**
 - These patients are at risk for the development of: **permanent neurologic deficit**
 - **Risk factors** such as HTN, smoking, and OCP, must be addressed

Aura

☐ Migraine with complex aura:

- Even less common than migraine with prolonged aura
- Significant neurologic dysfunction that may include aphasia or hemiplegia.
- May develop **permanent** neurologic deficits (similar prolonged aura)

Patients suffering from all forms of migraine headache appear:

- Systemically ill
 - Pallor
 - Tremulousness
 - Diaphoresis
 - Light sensitivity
 - The temporal artery and the surrounding area may be tender
- **Neurologic examination:**
- **With Aura:** Abnormal
 - **Without Aura:** normal (before, during, and after)

Frequent migraine

- The word migraine can both describe:
Attack (using standard criteria) + describe **disorder** itself
 - ✓ Amplified at various times by triggers
 - ✓ The brain of the migraineur is more sensitive to sensory stimuli and to change
 - ✓ Amplified during menstrual cycle

Other triggers

- Oversleep or changes in sleep patterns
- Tried
- Skip meals
- Stress
- Relax from a stressor
- Overexertion
- Diet (tyramine-containing foods, monosodium glutamate, nitrates, chocolate, wine, or citrus fruits)
- Changes in endogenous and exogenous hormones (OCP)
- Nitroglycerine for angina

NOTE!

- Migraine → less tolerance to change → a part of successful management : advice them to maintain regularity in their lives
- **Recent onset of migraine**: Brain MRI
- **Migraine with neurologic Dysfunction**:
 - Brain MRI with and without gadolinium
- **Inexplicable change in symptoms**: MRI (MRA)
- **If the diagnosis of migraine is in question**:
 - CBC, ESR, Blood chemistry
- **Significant ocular symptoms**: Ophthalmologic evaluation

Chronic Migraine

- Is the **largest part** of the group of headaches known collectively as “**chronic daily headache**”, a term best not often employed because almost invariably, a more specific diagnosis can be made

Chronic Migraine

- **Some 15 days a month** of headache which:
 - ❑ **8** are clearly **migrainous** and
 - ❑ With a **predating history of migraine**

Migraine Disability Assessment Scale (MIDAS)

INSTRUCTIONS: Please answer the following questions about ALL your headaches you have had over the last 3 months. Write your answer in the box next to each question. Write zero if you did not do the activity in the last 3 months (Please refer to the calendar below, if necessary)

1. On how many days in the last 3 months did you miss work or school because of your headaches? days
2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches (*Do not include days you counted in question 1 where you missed work or school*)? days
3. On how many days in the last 3 months did you **not** do household work because of your headaches? days
4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches (*Do not include days you counted in question 3 where you did not do household work*)? days
5. On how many days in the last 3 months did you miss family, social, or leisure activities because of your headaches? days

- A. On how many days in the last 3 months did you have a headache? (If a headache lasted more than one day, count each day) days
- B. On a scale of 0 - 10, on average how painful were these headaches?
(*where 0 = no pain at all, and 10 = pain as bad as it can be*)

Principles of Management of migraine

1. **Inherited tendency** → it can not be cured, **but**
2. It can be modified and controlled by lifestyle adjustment and use of medications
3. Migraine **is not life-threatening nor associated with serious illness** the **exception** of females who smoke and use estrogenic OCP but migraine can make life a misery
4. Migraine management takes time and cooperation

Differential diagnosis of migraine

- TTH (**Featureless**)
- Diseases of eyes, ear, nose and sinuses
- Glaucoma
- Temporal arteritis
- Glaucoma
- Intracranial disease: chronic subdural hematoma, tumor, pseudotumor cerebri
- Inflammatory conditions: sarcoidosis

Nonpharmacologic Management of migraine

- Identify things making the problem worse
- Know that the brain sensitivity to triggers
- Regulate their lives, healthy diet, regular exercise, regular sleep patterns, avoiding excess caffeine and alcohol, modifying or minimizing changes in stress
- The balanced life with less light

Preventive treatments of migraine

- **Which patient needs preventive treatment?**
 - ✓ Sufficient disability
 - ✓ Attack unresponsive to abortive medications
 - ✓ Increasing frequency of attacks

Note: Patients with simply treated attacks may be less obvious candidates.

Rule for frequency and preventive treatment (headache / month)

- 1-2 : No need
- 3-4 : May be needed but not necessarily
- 5 or more : Should definitely be considered

NOTE:

- Preventive treatment → modify the brain sensitivity
- Each drug should be started at a low dose and gradually increased to a reasonable maximum if there is going to be a clinical effect.

TABLE 61.4 Preventive Treatments in Migraine*

Drug	Dose	Selected Side Effects
Pizotifen	0.5-2 mg daily	Weight gain Drowsiness
β -Blocker Propranolol	40-120 mg bid	Reduced energy Tiredness Postural symptoms Contraindicated in asthma
Tricyclics • Amitriptyline • Doxepin (dothiepin) • Nortriptyline	25-75 mg every night	Drowsiness <i>Note: Some patients are very sensitive and may only need a total dose of 10 mg, although generally 1-1.5 mg/kg body weight is required.</i>
Anticonvulsants • Valproate • Topiramate	400-600 mg twice daily 50-200 mg/d	Drowsiness Weight gain Tremor Hair loss Fetal abnormalities Hematologic or liver abnormalities Paraesthesia Cognitive dysfunction Weight loss Care with a family history of glaucoma Nephrolithiasis Dizziness Sedation
Candesartan	4-24 mg daily	Postural dizziness
Flunarizine	5-15 mg daily	Drowsiness Weight gain Depression Parkinsonism
Chronic migraine only • Onabotulinum toxin type A	155 units	Injection site pain
Single studies ^b • Lisinopril • Single-pulse transcranial magnetic stimulation	20 mg daily 2-24 pulses daily	Cough Neck discomfort (5%)
Nutraceuticals ^c • Riboflavin • Coenzyme Q10 • Butterbur • Feverfew	400 mg daily 100 mg three times daily 75 mg twice daily 6.25 mg three times daily	GI upset
No convincing controlled evidence • Verapamil		
Controlled trials to demonstrate no effect • Nimodipine • Clonidine • SSRIs: fluoxetine		

Pizotifen

- Dose: 0.5-2 mg daily

- Side effect:

Weight gain, drowsiness

Beta blocker: propranolol

- Dose: 40-120 mg bid

- Side effect:

Reduced energy, tiredness, postural symptoms,
contraindicated in asthma

TCA(amitriptyline, nortriptyline, dosulepin)

- Dose: 25-75 mg every night
- Side effect: drowsiness
- Note:

Some patients are very sensitive and may only need a total dose of 10 mg, although generally 1-1.5 mg/kg body weight is required

Anticonvulsants

- Valproate : 400-600 mg twice daily
- Topiramate : 50-200 mg/d

➤ Side effects:

Drowsiness, weight gain and loss, tremor, hair loss, fetal abnormalities, hematologic or liver abnormalities, paraesthesia, cognitive dysfunction, nephrolithiasis, dizziness, sedation, care with family history of glaucoma

- Candesartan: 4-24 mg daily
- Flunarizine: 5-15 mg daily

➤ Side effects:

Postural dizziness, drowsiness, weight gain, depression, parkinsonism

❖ **No convincing evidence: Verapamil**

➤ **Controlled trial to demonstrate no effect:**

- Nimodipine
- Clonidine
- SSRIs: fluoxetine

Chronic migraine only:

- ✓ **Onabotulinum toxin type A**
 - 155 units
 - Side effects: injection site pain
- ✓ **Single-pulse transcranial magnet stimulation**
 - 2-4 pulses daily
 - Side effects: neck discomfort (5%)
- ✓ **Lisinopril**
 - 20 mg daily
 - Side effects: cough

Chronic migraine only:

✓ **Nutraceuticals:**

- Riboflavin
- Coenzyme Q10
- Butterbur
- Feverfew

New advances in preventive treatments of migraine

- ❖ **Monoclonal antibodies to the calcitonin gene – related peptid (CGRP)**
 - To **CGRP**: Eptinezumab, fremanezumab, galcanezumab
 - To the **receptor**: Erenumab
 - Effective in both episodic and chronic migraine
- ❖ **Neuromodulation or neurostimulation**
 - sTMS (single-pulse TMS)

Acute attack therapies of migraine

1. Disease-nonspecific treatments

- Analgesics
- NSAIDs

2. Disease-specific treatments

- Ergot-related compounds

(Not be used in patients with peripheral vascular diseases, CAD or HTN)

- Triptans
- Neuromodulation (sTMS, nVNS)

Important note:

Most acute attack medications seem to have a propensity to **aggravate headache frequency** and can induce a state of **refractory daily, near daily, or medication overuse headache**

Note:

- Codeine-containing analgesics are particularly troublesome when available in over-the counter (OTC) preparations

Waldman/ common pain syndrome/ 4th Ed. :

- Inhalation of 100% oxygen
- Intravenous lidocaine + antiemetic
- SPG block
- **Note:**. Caffeine-containing preparations, barbiturates, ergotamines, triptans, and opioids have a propensity to cause analgesic rebound headache (may ultimately be more difficult to treat than the original migraine)

Advise patients with migraine to:

- ❑ Avoid taking acute attack medicines on more than 2 days a week

Nonspecific acute migraine attack treatment

Nonspecific Treatments

Often used with antiemetic/prokinetics, such as domperidone (10 mg) or metoclopramide (10 mg)

Aspirin (900 mg)

Paracetamol (acetaminophen—
1,000 mg)

NSAIDs

- Naproxen (500–1,000 mg)
- Ibuprofen (400–800 mg)
- Tolfenamic acid (200 mg)

Nonspecific acute migraine attack treatment

- Nonspecific + antiemetic:

- ✓ Domperidone 10 mg
- ✓ Metoclopramide 10 mg
- ✓ Ondansetron 4 mg
- ✓ Aprepitant 80 mg

Note: Their success is often limited by inappropriate dosing

Specific acute migraine attack treatment

Ergot derivatives

- Ergotamine (1–2 mg)

Triptans

- Sumatriptan (50 or 100 mg)
- Naratriptan (2.5 mg)
- Rizatriptan (10 mg)
- Zolmitriptan (2.5 or 5 mg)
- Eletriptan (40 or 80 mg)
- Almotriptan (12.5 mg)
- Frovatriptan (2.5 mg)

Neuromodulation

- Single-pulse transcranial magnetic stimulation (sTMS)
- Noninvasive vagus nerve stimulation (nVNS)

Specific acute migraine attack treatment

- Ergotamine: 1-2 mg
 - Although ergotamine remains a useful treatment, it can **no** longer be considered the **treatment of choice** in acute migraine
 - Ergotamine overuse:
 - Produces dreadful headache
 - Vascular problem

Specific acute migraine attack treatment

➤ Triptans

- Serotonin 5-HT 1B/1D receptor agonist
- **Most powerful option** available to stop a migraine headache
- Recent data suggests that **combining a triptan** with an **NSAID** can improve **efficacy** and **reduce headache recurrence**

Stratification of acute specific migraine treatment

Clinical Situation	Treatment Options
Failed analgesics/ NSAIDs	<p>First tier</p> <ul style="list-style-type: none"> Sumatriptan 50 mg or 100 mg po Almotriptan 12.5 mg po Rizatriptan 10 mg po Eletriptan 40 mg po Zolmitriptan 2.5 mg po <p>Slower effect/better tolerability</p> <ul style="list-style-type: none"> Naratriptan 2.5 mg po Frovatriptan 2.5 mg po <p>Infrequent headache</p> <ul style="list-style-type: none"> Ergotamine 1–2 mg po Dihydroergotamine nasal spray 2 mg
Early nausea or difficulties taking tablets	<ul style="list-style-type: none"> Zolmitriptan 5 mg nasal spray Sumatriptan 20 mg nasal spray Rizatriptan 10 mg MLT wafer
Headache recurrence	<ul style="list-style-type: none"> Ergotamine 2 mg (most effective pr/usually with caffeine) Naratriptan 2.5 mg po Almotriptan 12.5 mg po Eletriptan 40 mg

Clinical Situation

Treatment Options

Tolerating acute treatments poorly

Naratriptan 2.5 mg
Almotriptan 12.5 mg
Single-pulse transcranial magnetic stimulation (sTMS)
Noninvasive vagus nerve stimulation (nVNS)

Early vomiting

Zolmitriptan 5 mg nasal spray
Sumatriptan 25 mg pr
Sumatriptan 6 mg sc

Menstrually related headache

Prevention
Ergotamine po every night
Oestrogen patches
Treatment
Triptans
Dihydroergotamine nasal spray

Very rapidly developing symptoms

Zolmitriptan 5 mg nasal spray
Sumatriptan 6 mg sc
Dihydroergotamine 1 mg IMI

New advances in acute migraine treatment

➤ **Neuromodulation:**

1. Supraorbital stimulation
2. Single-pulse TMS (sTMS)
3. Noninvasive vagus nerve stimulation (nVNS)

➤ Lasmiditan (ditan)

- Serotonin 5-HT_{1F} receptor agonist , that is **without vasoconstrictor effects (in Study phase)**

Medication overuse headache

- Also known as Analgesic rebound headache

Definition:

Acute attack therapy ≥ 10 days/month

Pathophysiology: has not been fully elucidated (probably: dysfunction of the trigeminal modulating system and central sensitization)

Drugs: Acetaminophen, sinus medications, aspirin, caffeine, butalbital (Fiorinal), NSAIDs, opioid, ergotamines, triptans

Medication overuse

❖ Advise:

1. Reduce their use 10% every week or 2 weeks
or
2. If there is no contraindication: **immediate cessation**

Small dose of NSAIDs, such as naproxen 500 mg BD or TDS, if tolerated

If greater doses needed → GON injection

- When the patient has reduced their analgesic use substantially, a preventive should be introduced
- **Note:** Medication overuse is a common cause of intractability to preventive treatment
- Some patients with medication overuse will require admission for treatment

Admission for medical overuse:

2 groups:

1. Those who fail outpatient withdrawal.
 2. Those who have a significant complicating medical indications or medicine such as brittle DM or opioid user
- **acute medications are **withdrawn completely on the first day**, unless there is some contraindication.**

Admission for medical overuse:

- Antiemetic (domperidone, ondansetron, aprepitant)
- fluid
- clonidine for opioid withdrawal symptoms.
- for acute intolerable pain:
 - During the waking hours: Aspirin 1 g IV
 - At night: chlorpromazine (inj.), after ensuring adequate hydration.

Admission for medical overuse:

- If the patient dose not settle over 3 to 5 days:
Intravenous Dihydroergotamine (DHE)

Tension-Type Headache (TTH)

- Most prevalent primary headache
 - 2 forms (according to IHS):
 - 1. Episodic TTH:** attack < 15 days/month
 - 2. Chronic TTH:** attack \geq 15 days/month
- **Chronic** form are a part of clinical syndrome of **chronic daily headache**, but chronic TTH and chronic daily headache **are not equal concept**

TTH criteria

✓ **The headache is completely featureless**

- No nausea
- No vomiting
- No photophobia
- No phonophobia
- No osmophobia
- No throbbing
- No aggravation with movement

TTH

- Bandlike
- Bilateral, but can be unilateral
- Sleep disturbance
- Most frequently occur between 4 and 8 am and 4 and 8 pm
- F > m
- No hereditary
- Cervical DJD can also trigger it



Pathophysiology of TTH

- ❑ Is poorly understood
- Nervous tension? No clear evidence
- Muscle contraction (similar migraine)? No
- ✓ Seems be due to a primary disorder of CNS pain modulation alone (in contrast with migraine, which is a more generalized disturbance of sensory modulation)
- ✓ MMPI test: Somatization

Management of TTH

- TTH → less disabling, more often described by patients as irritating
- ❖ **Episodic form**: simple analgesics, paracetamol, aspirin, or other NSAIDs
- ❖ **TTH alone**: Triptans are not helpful
- ❖ **TTH + migraine**: Triptans are effective
- ❖ **Chronic TTH**: **Only treatment with clear evidence** → Amitriptyline

Management of TTH

❖ **NO effect:**

- ✓ Other TCA
- ✓ SNRI
- ✓ Benzodiazepines
- ✓ Electromyography (EMG) biofeedback
- ✓ Relaxation therapy
- ✓ Acupuncture
- ✓ Botulinum toxin
- ✓ opioid

❖ **Effective:**

- **Stress management (in a clinical trial): Effective**
- **Multiple studies: Cervical epidural nerve block with steroid** → Providing long-term relief
 - **When:**
 - ✓ Other treatment modalities have failed
 - ✓ While waiting for antidepressant compounds to become effective

Short-lasting headache

1. With prominent cranial autonomic syndrome
(Trigeminal Autonomic Cephalgias or **TACs**)

Cluster headache, paroxysmal hemicrania,
SUNCT/SUNA syndrome

2. Without prominent cranial autonomic
syndrome

Short-lasting headache **Without** prominent cranial autonomic syndrome

1. Primary stabbing headache
2. Trigeminal neuralgia
3. Primary cough headache
4. Primary exertional headache
5. Primary sex headache
6. Hypnic headache

Cluster headache (CH)

- **Rare** form of primary headache
- **No hereditary** (opposite to migraine)
- No aura
- Frequency: approximately **0.1%**
- late 3th or early 4Th decade of life (migraine: almost always : early second decade)
- Perhaps the most painful condition of human (~ childbirth, multiple FX of the limbs or renal stone)
- **Male** > female 3:1
- Seasonal (chronobiologic pattern) (changes in the length of the day): increased frequency in the spring and fall

Features of CH

- **Core Feature**: periodicity or circadian (active and inactive bouts over weeks and months)
- **Male** > female 3:1 (**Waldman: 5:1**)
- Relatively short duration
- Unilateral pain
- Every day for 8 to 10 weeks a year
- They are generally perfectly well between times

Features of CH

- Patients tend to move about during attacks, pacing, rocking, or even rubbing their head for relief
- The pain: usually retroorbital, boring, and very severe (may be suicide in prolonged cases)
- Associated with ipsilateral symptoms of cranial (parasympathetic) autonomic activation
- Horner syndrome
- **Peau d'orange skin** over the **malar** region, **deeply furrowed glabellar folds**, and **telangiectasia**
- Provoked by: Alcohol, nitrates, histamines, vasoactive substances, high altitude

Features of CH

Cranial (parasympathetic) autonomic activation:

- Red or watering eye
- The nose running or blocking
- Cranial sympathetic dysfunction (eyelid droop)

Pathology: Posterior hypothalamus

Summary of CH

Gender	M > F 3:1
Pain	
Type	Boring/throbbing
Severity	Very severe
Cranial location	Any
Duration	15–180 min
Frequency	1–8/d
Autonomic	+
Alcohol	+
Cutaneous trigger to attacks	–
Indomethacin	–

Diagnostic Criteria for Cluster Headache

- A. At least five attacks fulfilling B–D
 - B. Severe or very severe unilateral orbital, supraorbital, and/or temporal pain lasting 15–180 min if untreated
 - C. Headache is accompanied by at least one of the following:
 1. Ipsilateral conjunctival injection and/or lacrimation
 2. Ipsilateral nasal congestion and/or rhinorrhea
 3. Forehead and facial sweating
 4. Ipsilateral eyelid edema
 5. Ipsilateral forehead and facial sweating
 6. Ipsilateral miosis and/or ptosis
 7. A sense of restlessness or agitation
 - D. Attacks have a frequency from one every other day to eight per day.
 - E. Not attributed to another disorder
-

Episodic CH

Description: occurs in periods lasting 7 d to 1 y separated by pain-free periods lasting 3 mo or more

Diagnostic criteria:

- A. All fulfilling criteria A–E of 3.1
- B. At least two cluster periods lasting from 7 to 365 d and separated by pain-free remissions of ≥ 3 mo.

Chronic CH

Description: Attacks occur for more than 1 y without remission or with remissions lasting less than 3 mo.

Diagnostic criteria:

- A. All alphabetical headings of 3.1
- B. Attacks recur over >1 y without remission periods or with remission periods <3 mo

CH

➤ **Episodic:**

Pain-free remission \geq 3 months

➤ **Chronic:**

Without remission

or

remission period $<$ 3 months

Managing CH

1. Acute attack treatment
2. Preventive agents
 - ✓ For CH
 - ✓ Shorten the active periods of episodic form

Preventive treatment of CH

Short-term Prevention

Episodic cluster headache

- Prednisolone
- Verapamil
- Greater occipital nerve injection
- (Daily nocturnal ergotamine)

Long-term Prevention

Episodic cluster headache and prolonged chronic cluster headache

- Verapamil
- Lithium
- Melatonin
- ?Topiramate
- ?Noninvasive vagus nerve stimulation
- Sphenopalatine ganglion stimulation

?, unproven but promising.

Preventive treatment of CH

➤ Oral corticosteroids

- When the bout is relatively short
- Starting dose of prednisone: 80 mg given in divided doses and tapered by 10 mg/dose per day

➤ Verapamil

- First-line treatment
- When the bout is prolonged or in chronic CH

❖ Dose:

Start: 40-80 mg twice daily

Up to 960 mg daily (higher doses than those used in cardiologic indications)

Preventive treatment of CH

☐ Verapamil side effects:

Gingival hyperplasia, constipation, leg swelling, cardiac dysrhythmias, AVN block

- ✓ **The effects on the AVN take up to 10 days to manifest**, 2-week intervals are recommended between dose change on the first exposure, with ECGs prior the next escalation, and routine 6 monthly ECGs after the dose is established

Preventive treatment of CH

➤ nVNS:

When patients have contraindications or intolerability to standard therapies

Acute attack treatment of CH

Note: Attack often peak rapidly → treatment with quick onset

1. Oxygen inhalation

100%, 10-12 L/min (high flow, high concentration)

2. Injectable sumatriptan: 6 mg

(effective, rapid onset, no tachyphylaxis)

Acute attack treatment of CH

3. Nasal spray:

Sumatriptan 20 mg

Zolmitriptan 5 mg

Note:

Oral sumatriptan is not effective when given preemptively

4. nVNS:

Unproven but promising

5. Octreotide (synthetic form of somatostatin)[[waldman](#)]

Surgical treatment of CH

- For chronic CH and refractory form
- ✓ **Sphenopalatinectomy**: without clear effects
- ✓ **Trigeminal ganglion CRF**: helpful but often at significant costs (ocular complications or anesthesia dolorosa)
- ✓ **Trigeminal rhizotomy** : all of complications of TG CRF + occasional death
- ✓ **DBS**: posterior hypothalamic region
- ✓ **Occipital nerve stimulation**
- ✓ **Sphenopalatine ganglion stimulation**

Paroxysmal Hemicrania (PH)

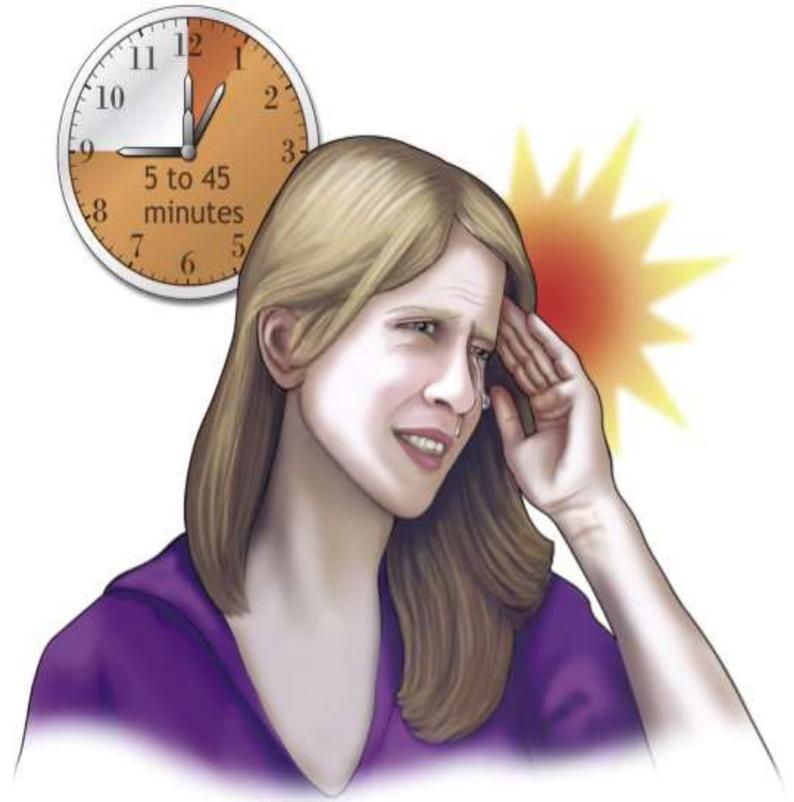
- **Gender**: F=M (**Waldman: F>M**) (CH: M>F)
- **Pain type**: boring/throbbing (Similar CH)
- **Pain severity**: very severe (similar CH)
- **Cranial location of pain**: Any (similar CH)
- **Duration**: 1-45 min (CH: 15-180 min)
- **Frequency**: 1-40/d (CH: 1-8/d)
- **Autonomic**: + (CH: +)
- **Alcohol**: one-third (CH: +)
- **Cutaneous trigger to attack**: - (CH: -)
- **Indomethacin response**: + (CH: -)

PH

- Unilateral very severe pain
- Short-lasting attacks typically 20 minutes in length
- Very frequent attacks (usually $> 5/d$)
- Robust, quick (less than 72 hour)
- Horner syndrome
- **Excellent response to indomethacin**

Pathophysiology of PH

- **PH:**
 - ✓ Contralateral hypothalamus
 - ✓ Contralateral ventral midbrain
- **Posterior hypothalamic:**
 - CH
 - SUNCT
 - Hemicrania continua



Treatment of PH

- Indomethacin (25 mg TDS, max dose: 150mg/d)
- Topiramate
- nVNS
- **If sleep disturbance:** TCA (nortriptyline 25 mg bedtime)
- ❖ If Indomethacin need > 200 mg/day or bilateral PH → secondary PH (such as raised ICP)
- **Note: Indomethacin reduces CSF pressure** by unknown mechanism
- When a diagnosis of PH is being considered → MRI

SUNCT/SUNA

SUNCT: Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing or cranial autonomic activation

SUNA: SUNCT - Conjunctival injection and Tearing or cranial autonomic activation

- Gender: M > F (peak incidence: 5th decade)
- Rapid onset to peak
- **Duration: 15-60 seconds (5-300 sec.)**
- **Frequency: 1/d-30/hr (20-200/d)**



SUNCT/SUNA

- Frequency: 5-30/hour
- Could be precipitated by chewing or eating certain foods, such as citrus fruits
- **Alcohol: -**
- **Significant eye inflammation (CH:-)**
- No response to indomethacin
- Pathology: posterior hypothalamic (→ brain imaging)
- **Cutaneous trigger to attack** [washing the face, brushing the teeth] (similar trigeminal neuralgia) with no refractory period to triggering (opposite to trigeminal neuralgia)

SUNCT/SUNA

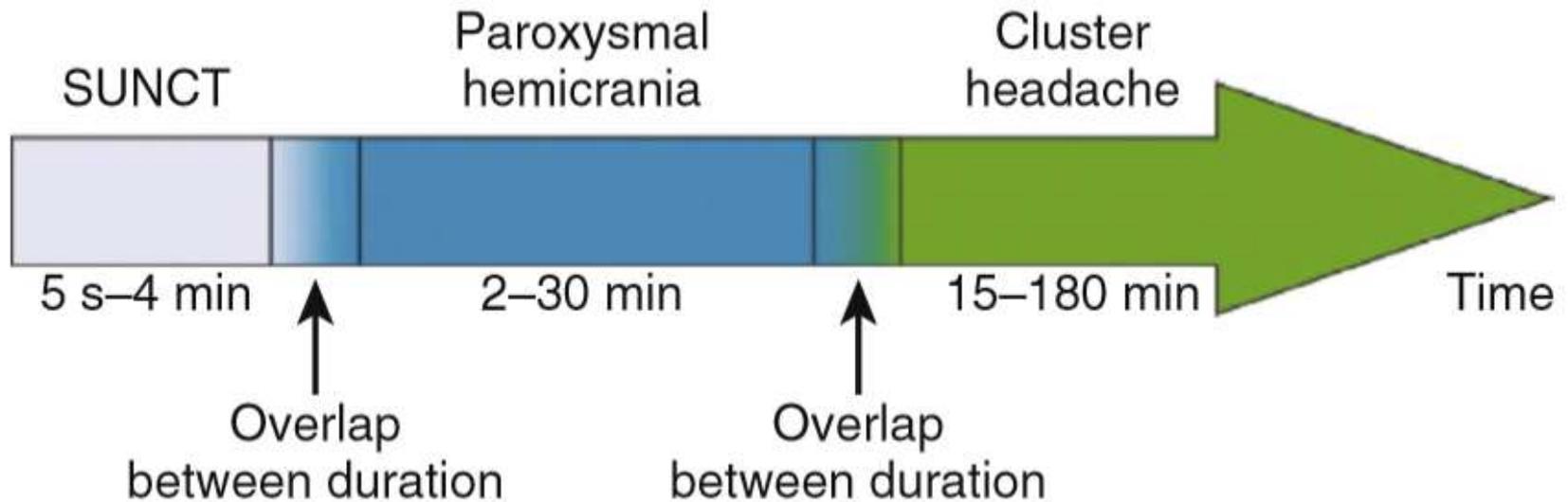
- The 2 key clinical features:
 1. The attacks being triggerable
 2. With **no refractory period to triggering**
 - **No.2** is a very useful **distinction** between SUNCT/SUNA and trigeminal neuralgia
 - **Refractory period** to triggering is a **very common feature of trigeminal neuralgia**

Treatment of SUNCT/SUNA

- Lamotrigine
- Topiramate
- Gabapentin
- Carbamazepine: is useful but incomplete effect
- High dose of steroid (tapered over 10 days)
- **SPG block: little value**
- **Trigeminal G. block (daily):**
+
- SUNCT/SUNA: MRI with pituitary and posterior fossa views



Overlap Between Attack Duration in TACs



Other primary headaches

Primary stabbing headache

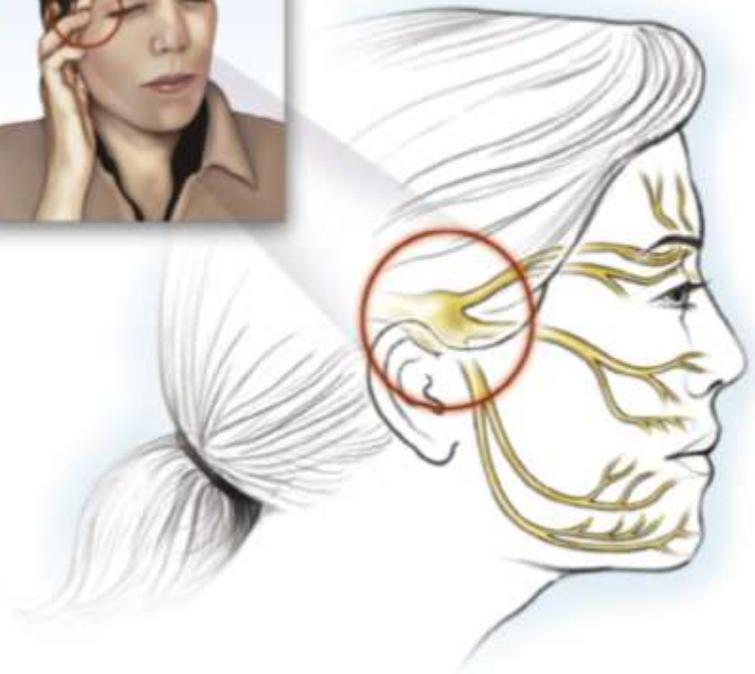
Primary stabbing headache = **Ice pick headache**

The **essential clinical features** are:

1. Pain confined to the **head**, although rarely is it facial
2. Stabbing pain **lasting from 1 to many seconds** and occurring as a single stab or a series of stabs
3. Recurring at **irregular intervals** (hours to days)

Primary stabbing headache

- Gender: **F** > M (4th decade)
- Pain severity: **severe**
- Cranial location: Any
- Duration: Seconds to 3 min
- Frequency: **Any**
- Cranial autonomic activation: -
- Alcohol: -
- Cutaneous trigger to attack: -
- Indomethacin Response: +



Primary stabbing headache

- Short-lived jabs pain
- In **association** with most types of primary headache (TACs, hemicrania continua)
- The symptoms tend to wax and wane
- Respond to indomethacin: 25-50 mg, BD or TDS (max dose: 150 mg/d)
- Failure to respond to indomethacin puts the diagnosis of ice pick headache in question
- Most of patients will not want treatment when the nature of problem is explained, and they are reassured that the attacks are not sinister in any way

Primary cough headache

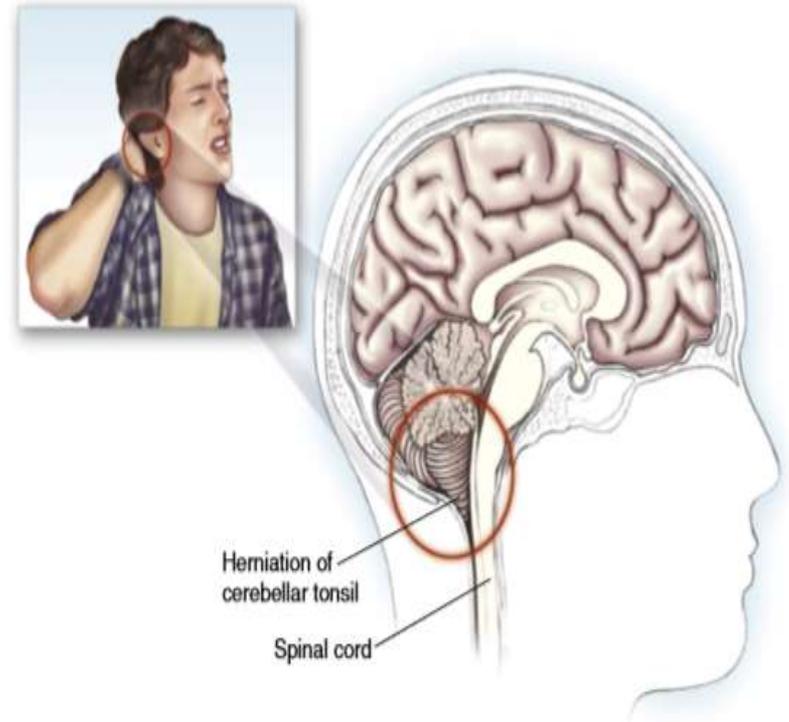
- Sharp pain in the head
- Coughing, sneezing, straining, laughing, stooping
- **Benign form: M>F** (symptomatic: M=F)
- **Age:** benign: 3th decade (symptomatic: any age)
- **R/O** organic intracranial disease, commonly with obstruction of the CSF pathway such as Arnold-Chiari malformation, cerebral aneurysm, carotid stenosis, vertebrobasilar disease (in Primary cough headache and Primary exertional headache)

Essential clinical features of Primary cough headache

- Bilateral headache
- Sudden onset
- Lasting minutes
- Precipitated by coughing
- May be prevented by avoiding coughing
- Diagnosed only after structural lesions, such as posterior fossa tumor, have been excluded by neuroimaging

Treatment of Primary cough headache

- **Choice**: indomethacin, 25 mg BD to TDS, max dose: 150 mg/d
- **Lumbar puncture** (Raskin NH.)
 - Mechanism: Unclear
- **In Symptomatic cough headache** (herniation of cerebellar tonsil, difficulty swallowing, faintness, and numbness in the face and upper extremities): **surgical decompression** of the foramen magnum



Primary exertional headache

- The clinical features are:
 1. Pain specifically brought on by **physical exercise**
 2. Bilateral and throbbing in nature at onset and may develop migrainous features in those patients susceptible to migraine.
 3. **Duration: 5 minutes to 24 hours**
 4. Prevented by avoiding excessive exertion, particularly in hot weather or at high altitude

Primary exertional headache

- The relationship with cough headache and migraine: ? (Unclear)
- **Mechanism:** Acute venous distension
- Acute onset
- With straining and breath holding (**weightlifter's headache**)
- **Cardiac cephalgia**: Anginal pain may referred to the head: (probably by central connections of **vagal afferents**, and may be misdiagnosed with exertional headache)

Primary exertional headache

- **The important clinical clue:** The link to exercise
- Pheochromocytoma may occasionally be responsible for exertional headache
- Similar to benign cough headache intracranial lesions or carotid stenosis may have to be excluded
- Pulsatile quality similar to migraine

Treatment of Primary exertional headache

- Take exercise gradually and progressively whenever possible
 - **Indomethacin**: 25-150 mg/day
- **Short-term prevention:**
- ✓ Indomethacin: 50 mg PO
 - ✓ Frovatriptan: 2.5 mg PO

Primary Sex Headache

- The essential clinical features are:
 1. Precipitation by sexual excitement
 - 2. Bilateral at onset**
 3. Prevented or eased by ceasing sexual activity before orgasm

Primary Sex Headache

- May be precipitated by masturbation or coitus
- Usually starts as a dull bilateral ache while sexual excitement increases
- Suddenly becoming intense at orgasm
- Note: the term “orgasmic cephalgia” is not accurate because not all sex headache require orgasm

2 types of Primary Sex Headache

1. A dull ache in the head and neck that intensifies as sexual excitement increases (occipital)
 2. A sudden severe (explosive) headache occurring at orgasm (usually occipital)
- ✓ **Low CSF volume headache** may also be precipitated by **sexual activity** (a form of New Daily Persistent Headache or NDPH)

Primary Sex Headache

- Headache at the time of orgasm are not always benign and consideration of a diagnosis of SAH headache is essential
- Male > Female
- May occur at any time during the years of sexual activity
- Associated with the use of: cannabis, pseudoephedrine, OCP and amiodarone
- It may develop on several occasions in succession and then not trouble the patient again, despite no obvious change in sexual technique
- [waldman: postural sexual headache: before or during orgasm/ explosive/ headache symptom recur when the patient stand up/ similar to PDPH/ due to minute tears in the dura during intense sexual activity]

Primary Sex Headache

- **Stop** sexual activity → **subside** within **5 minutes to 2 hours**
- One-third of the patients with sex headache have a history of exertional headache
- There is no excess of cough headache in patients with sex headache
- Sex headache → **50%** → will **settle** in **6 months**
- **Migraine** in sex headache patients: **25%**

Treatment of Primary Sex Headache

- **Occurrence:** Irregular and infrequent
 - ✓ Reassurance
 - ✓ Ceasing sexual activity
 - **Preventive therapy:** If sex headache recurs regularly or frequently
 - ✓ **Propranolol:** 40-200 mg daily
 - ✓ **Diltiazem:** 60 mg TDS
 - ✓ **Indomethacin:** 25-50 mg, 30 to 45 minutes prior to sexual activity
 - ✓ **Frovatriptan:** 2.5 mg, 30 to 45 minutes prior to sexual activity

Hypnic Headache = alarm clock headache

Wake the person up at the same time each night.

- **Gender:** F > M
- **Pain type:** Throbbing
- **Pain severity:** moderate
- **Cranial location of pain:** Generalized
- **Duration:** 15-30 min
- **Frequency:** 1-3 per night (15/month)
- **Alcohol, cutaneous trigger to attacks, indomethacin:** -



First night: 2:34 AM



Second night: 2:34 AM



Third night: 2:34 AM

Hypnic Headache

- **Typically** came on **a few hours after going sleep**
- **Generalized**, although may be unilateral
- No photophobia, no phonophobia
- No nausea, no vomiting
- **Age: mostly > 60 years**
- An **important secondary cause** of hypnic headache is HTN
- **Most commonly** during **REM**
- Pathologic mechanism: hypothalamic dysregulation

Treatment of Hypnic Headache

- ✓ Blood pressure treatment
- ✓ **Lithium carbonate**: 200-600 mg at bedtime
- ✓ **Verapamil**
- ✓ One to two cups of **coffee** or **Caffeine** 60 mg orally at bedtime (is effective in one-third of patients)
- ✓ **Indomethacin response**: - (**Bonica**) [Waldman: +]
- ✓ **Gabapentin, pregabalin** : Effective (waldman)
- ✓ **Oxygen inhalation: No effect**

Primary Thunderclap headache

- Sudden-onset
- Severe
- **Very rapid onset to peak of less than 1 minute**
- May last from 1 to 10 days
- **Without obvious inciting factors** (e.g., sexual activity, coughing, straining at stool)
- Often appears **frightened** and **anxious**
- **Cranial location:** anywhere in the head or neck
- **Nausea & vomiting:** approximately **75%**
- **Nuchal rigidity, focal neurological signs:** absent

Primary Thunderclap headache

➤ **Differential diagnosis:**

1. Sentinel bleed of an intracranial aneurysm
2. Cervicocephalic arterial dissection
3. Cerebral venous thrombosis
4. Sympathomimetic drugs
5. Tyramine-containing food and MAOI interaction
6. Pheochromocytoma
7. HTN crisis
8. Infection of CNS
9. Neoplasm
10. Collagen vascular diseases such as lupus cerebritis

Comparison of Primary Thunderclap Headache and SAH

Comparison Factors	Primary Thunderclap Headache	Subarachnoid Hemorrhage
Severe headache	Yes	Yes
Nausea and vomiting	Yes	Yes
Focal neurological signs	No	Yes
Nuchal rigidity	No	Yes
Photophobia	No	Yes
Vertigo	No	Yes
Neck and back pain	No	Yes

Primary Thunderclap headache

- Whether thunderclap headache can be presentation of unruptured cerebral aneurysm is **unclear**
- **Imaging:** (any sudden-onset severe headache)
 1. CT scan
 2. CSF analysis (SAH)
 3. MRI
 4. MRA, MRV
 5. Cerebral Angiography

Primary Thunderclap headache

- Reversible Cerebral Vasospasm:
 - ✓ Sometimes causes this type of headache
 - ✓ Response to Nimodipine (IV)
- **Vasoconstrictor drugs (e.g., ergots, triptans) should be avoided**
- Gabapentin

Hemicrania Continua

➤ Essential features:

1. Unilateral [is side locked (it does not change sides like migraine headache occasionally does)]
2. Continuous but with exacerbation that may be severe
3. Complete resolution of pain with indomethacin (diagnostic “indotest”)
4. **Exacerbations** may be associated with **autonomic features**

Hemicrania Continua

- Classified as a TACs
- Gender predominance: **F**
- **Absolute response to indomethacin: +**
- Chronobiological pattern: - (**CH: +**, Migraine: -)
- Alcohol trigger: -
- Length of attacks: Continuous, with exacerbations
- Autonomic symptoms: +
- Photophobia: +
- Phonophobia: +
- Nausea & vomiting: +
- Continuous pain with exacerbations: +

Hemicrania Continua

□ Pathology:

- Contralateral posterior hypothalamus
- Ipsilateral dorsal rostral pons

□ Indotest:

**Indomethacin 50 mg →
IM → a diagnostic and
Therapeutic tool**



Treatment of Hemicrania Continua

- **Indomethacin**: 25 mg TDS to 75 mg TDS
- **Topiramate**
- **GON injection**
- **nVNS**
- **COX-2 antagonist**: seem effective, although undesirable
- **Sumatriptan**: no benefit in acute treatment

New Daily Persistent Headache (NDPH)

DDx of NDPH:

✓ **Primary**

- Migrainous-type
- Featureless (Tension-type)

✓ **Secondary**

- SAH
- Low CSF volume headache
- Raised CSF pressure headache
- Posttraumatic headache (include postinfective)
- Chronic meningitis

New Daily Persistent Headache (NDPH)

- History of headache on most if not all days
- Began from one day to the next
- The onset of headache is abrupt, often moment-to-moment

Typical history:

Recall the exact day and circumstances, so from one moment to the next, a headache develops that **never leaves them.**

Primary NDPH

- F = M
- Migrainous features are common.
- A number of these patients have a history of previous migraine (not more than prevalence of migraine).
- Primary NDPH is perhaps the most intractable and least therapeutically rewarding form of headache.

Low CSF volume headache

- Commonly after lumbar puncture
- Usually settles rapidly with bed rest
- In chronic situation: typically presents with a history of headache from one day to the next.
- Is generally not present on waking
- Worsen during the day
- Is relieved by lying down.

Low CSF volume headache

- **Recumbency** usually **improves** the headache in minutes.
- It takes only **minutes to an hour** for the pain to **return** when the patient is again **upright**.

➤ **Causes (index events):**

L.P, epidural injection, vigorous valsalva (such as lifting, straining, coughing, clearing the Eustachian tubes in an aeroplane, multiple orgasm)

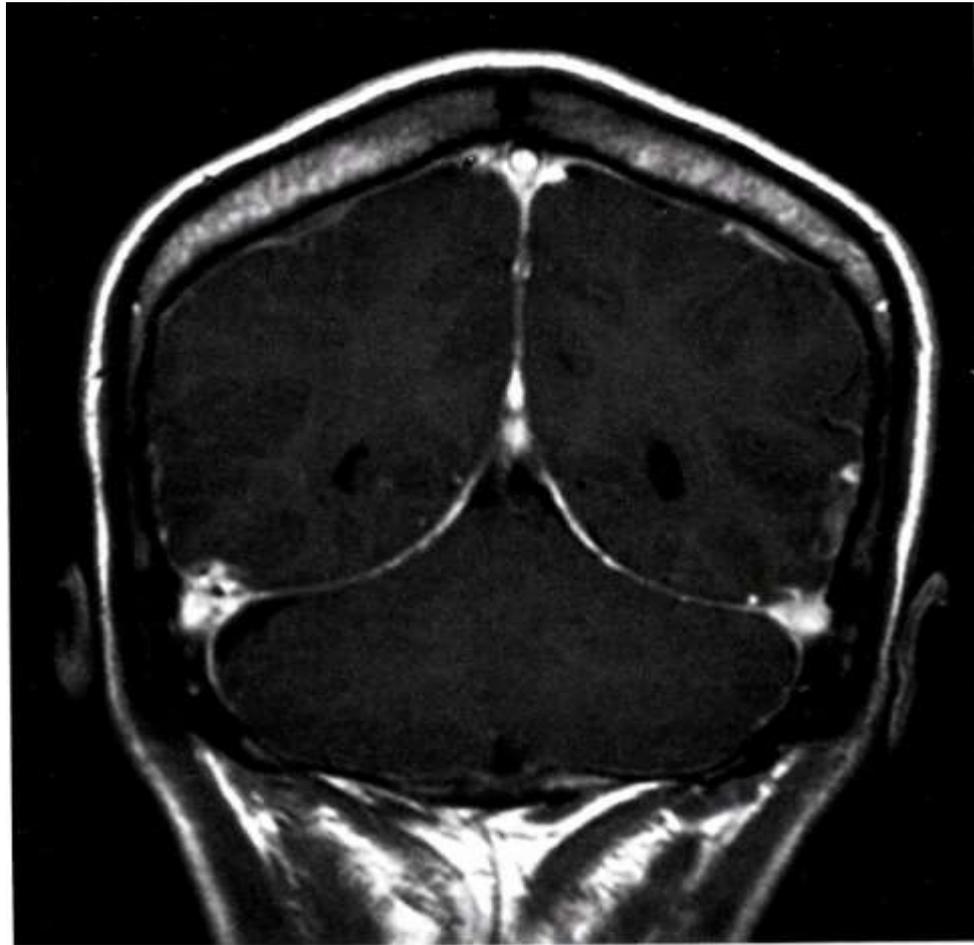
Low CSF volume headache

- Soft drinks with **caffeine** provide temporary **respite**.
- **As time passes** from the index event, the **postural nature may be less obvious**; certainly ,cases whose index events was several years prior to diagnosis.
- The term “**low volume**” rather than “low pressure” is used because there is no clear evidence at which point the pressure can be called low.

Low CSF volume headache

- Possibility of the development of subdural collection in these patients (imaging is important)
- **Imaging: Choice** → MRI with gadolinium
- **Pattern:** diffuse patchy meningeal enhancement (**typical/ immediate treatment is appropriate**).
- Although in about 10% of cases a leak can be documented without enhancement.

MRI with gadolinium showing diffuse meningeal enhancement in a patient with low CSF volume headache



- Chiari malformation in MRI with some degree of descent of cerebellar tonsil:

→ Surgery worsen the headache problem

Note: any patient being considered for such surgery for a headache indication should be reviewed by a neurologist first

- **CSF pressure/leak/leak site determination:**
IN-DPTA CSF study (radioisotope study), MR-myelography, CT myelogram

Treatment of Low CSF volume headache

- ✓ Bed rest
- ✓ Intravenous **caffeine**: 500 mg in 500 ml saline over 2 hours
- **ECG** should be checked prior to administration.
- At least 2 infusion separated by 4 weeks
- Mechanism: unknown
- ✓ Abdominal binder

Treatment of Low CSF volume headache

- ✓ Autologous blood patch (**EBP**)
- ✓ Theophylline: **in more intractable situation**
- Onset of action: rather slow

Raised CSF pressure headache

- Is well recognized by neurologists.
- Brain imaging (R/o SOL and ...): **Is Mandatory**
- The Intractable chronic migraine can be triggered by persistently raised ICP.

Clinical features of Raised CSF pressure headache

- Generalized headache
- Present on waking
- Gets better as the day goes on
- Worse with recumbency
- Often report a curious whooshing sensation in the occipital region.
- Visual obscurations are frequently reported.

Raised CSF pressure headache

- Fundal changes would make the diagnosis relatively straightforward, it is in those without such changes the history must drive investigation (Normal or fundal change)
- Brain imaging If raised ICP suspected: Is Mandatory
- MRI, MRV, CSF pressure measuring

Treatment of Raised CSF pressure headache

- ✓ **Acetazolamide**: Initial treatment
 - 250-500 mg BD
 - Response: in weeks
- ✓ **Topiramate**
 - Carbonic anhydrase inhibition, weight loss, neuronal membrane stabilization
- ✓ **L.P (20-30 cc)**: when the patient is symptomatic (determine pressure and response to removal of CSF) → Diagnostic and therapeutic
- ✓ **ICP monitoring and shunting**

Posttraumatic headache

- After a blow to head
- After an infective episode: **more commonly, typically meningitis**
- A recent series identified **one-third** of all patients with NDPH reported the headache **starting after a flu-like illness.**
- The patient may note a period in which they had a significant infection: fever, neck stiffness, photophobia, and marked malaise.

Posttraumatic headache

- The headache starts during the period and never stops.
- A complicating factor will often be that the patient had a LP during that illness, so a persistent low CSF volume headache needs to be considered first.
- Other causes of posttraumatic headache:
 - After carotid artery dissection
 - SAH
 - intracranial surgery for a benign mass

Posttraumatic headache

- A **traumatic** event involving the **dura mater** can **trigger** a headache process that lasts for **many years after that event**.
- **Treatment: Empirical**
 - **TCA**, notably amitriptyline
 - **Anticonvulsant**: valproate, topiramate, gabapentin

Other important forms of secondary headache

- ❑ **Giant cell arteritis = temporal arteritis = cranial arteritis**
 - Delayed in steroid treatment may result in blindness due to retinal artery ischemia
 - **Focal tenderness** on the scalp which may be provoked markedly by resting the head on the pillow
 - **Jaw claudication** provoked by **chewing** is a characteristic but **relatively uncommon feature**.

Giant cell arteritis

- **Constitutional symptoms are common**, particularly weight loss, malaise or polymyalgia rheumatica.
- **Strong pointer to the diagnosis: ↑ESR**
- The temporal artery may be **tenderly inflamed, swollen, or pulseless**
- Steroid treatment should be started pending the result of temporal artery biopsy
- Treatment is very often long term and requires careful monitoring for reactivation and the side effects of corticosteroids

Cervicogenic headache

- The Neck is responsible for much headache
- There is a **rich overlap between innervation** of intracranial pain-producing structures by ophthalmic division of the trigeminal nerve, and the posterior fossa and high cervical innervation by branches especially of the C2 dorsal root
- Most of these patient have migraine

Cervicogenic headache

- Neck stiffness or discomfort
- May respond to local therapies, such as GON injection

Sinus Headaches

- Although commonly used, it is **inaccurate term**.
- It refers to headache or facial pain associated sinus disease.
- **Rhinogenic headache** is a **more accurate term**.

The HIS diagnostic criteria for headache attributed to rhinosinusitis:

Frontal headache associated with pain in one or more regions of the face and fulfilling **criteria 2 and 3**.

1. Presence of clinical, nasal endoscopic, CT and/or MRI, and/or laboratory evidence of acute or acute on top of chronic rhinosinusitis.
2. Headache and facial pain that develops simultaneously with onset of rhinosinusitis.
3. Headache and/or facial pain that resolves within 7 days after remission or treatment of acute rhinosinusitis.

Treatment of sinus headache

- Treatment of sinusitis
- Migraine-directed therapy
- Nasal surgery for mucosal contact point.

THANKS FOR YOUR ATTENTION