

# Secondary Headache Disorders



**SECONDARY TO A SUBSTANCE OR ITS WITHDRAWAL**

**SECONDARY TO ALTERATION OF HOMEOSTASIS**

# Secondary to a Substance or Its Withdrawal

## Secondary to Alteration of Homeostasis



- 1. CLASSIFICATIONS**
- 2. DIAGNOSTIC CRITERIA**
- 3. PATHOMECHANICS**
- 4. EVALUATION/MANAGEMENT**

# IHS Classification ICDH-II



- International Headache Society
  - [ihs-headache.org/](http://ihs-headache.org/)
- International Headache Classification- 2<sup>nd</sup> ed
  - [ihs-classification.org/en/](http://ihs-classification.org/en/)
- Web based edition
  - Open access detailing of diagnostic criteria
- Lists corresponding ICD-10

# IHS Classification ICDH-II



- Hierarchical classification
- 1<sup>st</sup> or 2<sup>nd</sup> digit classification in clinical practice
  - 2. Tension-type headache, 2.3 Chronic tension-type headache
- 3<sup>rd</sup> or 4<sup>th</sup> digit classification in research/specialist practice
  - 2.3.2 Chronic tension-type headache not associated with pericranial tenderness
- More than one classification may apply
  - 1.1 Migraine without aura, 2.2 Frequent episodic tension-type headache, and 8.2 Medication-overuse headache.
  - should be listed in the order of importance to the patient

# Primary, Secondary, or Both?



- *If* new headache occurs in close temporal relation to another disorder that is a known cause of headache, *then* coded as a secondary headache.
  - even when the headache has the characteristics of migraine, tension-type headache, cluster headache or one of the trigeminal autonomic cephalalgias.
- *If* a pre-existing primary headache is made worse in close temporal relation to another disorder that is a known cause of headache, *then*:
  - diagnosis of the pre-existing primary headache or
  - both the primary diagnosis *and* a secondary diagnosis *if*
    - ✦ temporal relation to associated changes

## 8. HEADACHE ATTRIBUTED TO A SUBSTANCE OR ITS WITHDRAWAL



**A PROBABLE DIAGNOSIS THAT IS  
CONFIRMED RETROSPECTIVELY**

## 8.1 Headache induced by acute substance use or exposure



- an unwanted effect of a toxic substance,
- an unwanted effect of a substance in normal therapeutic use
- unwanted effect of a substance in experimental studies.

## 8.1.1. NO donor-induced headache



- A. Headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A. bilateral
  - B. frontotemporal location
  - C. pulsating quality
  - D. aggravated by physical activity
- B. Absorption of a NO donor
- C. Headache develops within 10 minutes after absorption of NO donor
- D. Headache resolves within 1 hour after release of NO has ended



## 8.1.1. NO donor-induced headache



- Headache is well known as a side effect of therapeutic use of nitroglycerine and other NO donors.
- Sodium nitrate is added to hotdogs and cured meats.



## 8.1.2. Phosphodiesterase (PDE) inhibitor-induced



- A. Headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A. bilateral
  - B. frontotemporal location
  - C. pulsating quality
  - D. aggravated by physical activity
- B. A single dose of a PDE inhibitor has been given
- C. Headache develops within 5 hours of PDE inhibitor intake
- D. Headache resolves within 72 hours

## 8.1.2. Phosphodiesterase (PDE) inhibitor-induced

### Examples:

- Viagra
- Cialis
- Levitra
- Revatio



### Indications:

- Erectile dysfunction
- Sexual dysfunction
  - Both sexes
- Pulmonary hypertension
- Altitude sickness

### 8.1.3. Carbon monoxide-induced headache



- Warehouse workers' headache
- mild headache without gastrointestinal or neurological symptoms with carboxyhemoglobin levels in the range 10-20%
- moderate pulsating headache and irritability with levels of 20-30%;
- severe headache with nausea, vomiting and blurred vision with levels of 30-40%.

### 8.1.4.1. Immediate alcohol-induced headache



- A.** Headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A.** bilateral
  - B.** frontotemporal location
  - C.** pulsating quality
  - D.** aggravated by physical activity
- B.** A single dose of a PDE inhibitor has been given
- C.** Headache develops within 5 hours of PDE inhibitor intake
- D.** Headache resolves within 72 hours

## 8.1.4.2. Delayed alcohol-induced headache



- A.** Headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A.** bilateral
  - B.** frontotemporal location
  - C.** pulsating quality
  - D.** aggravated by physical activity
- B.** Ingestion of a modest amount of alcoholic beverage by a migraine sufferer or an intoxicating amount by a non-migraine sufferer
- C.** Headache develops after blood alcohol level declines or reduces to zero
- D.** Headache resolves within 72 hours

### 8.1.5.1. Monosodium glutamate-induced headache



- A.** Headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A.** bilateral
  - B.** frontotemporal location
  - C.** aggravated by physical activity
- B.** Ingestion of monosodium glutamate (MSG)
- C.** Headache develops within 1 hour after MSG ingestion
- D.** Headache resolves within 72 hours after single intake

## 8.1.5.1. Monosodium glutamate-induced headache

### MSG- Induced Symptoms

- dull or burning and non-pulsating
- but may be pulsating in migraine sufferers.
- pressure in the chest and/or the face
- burning sensations in the chest, neck or shoulders
- dizziness and abdominal discomfort





### 8.1.8.1. Immediate histamine-induced headache

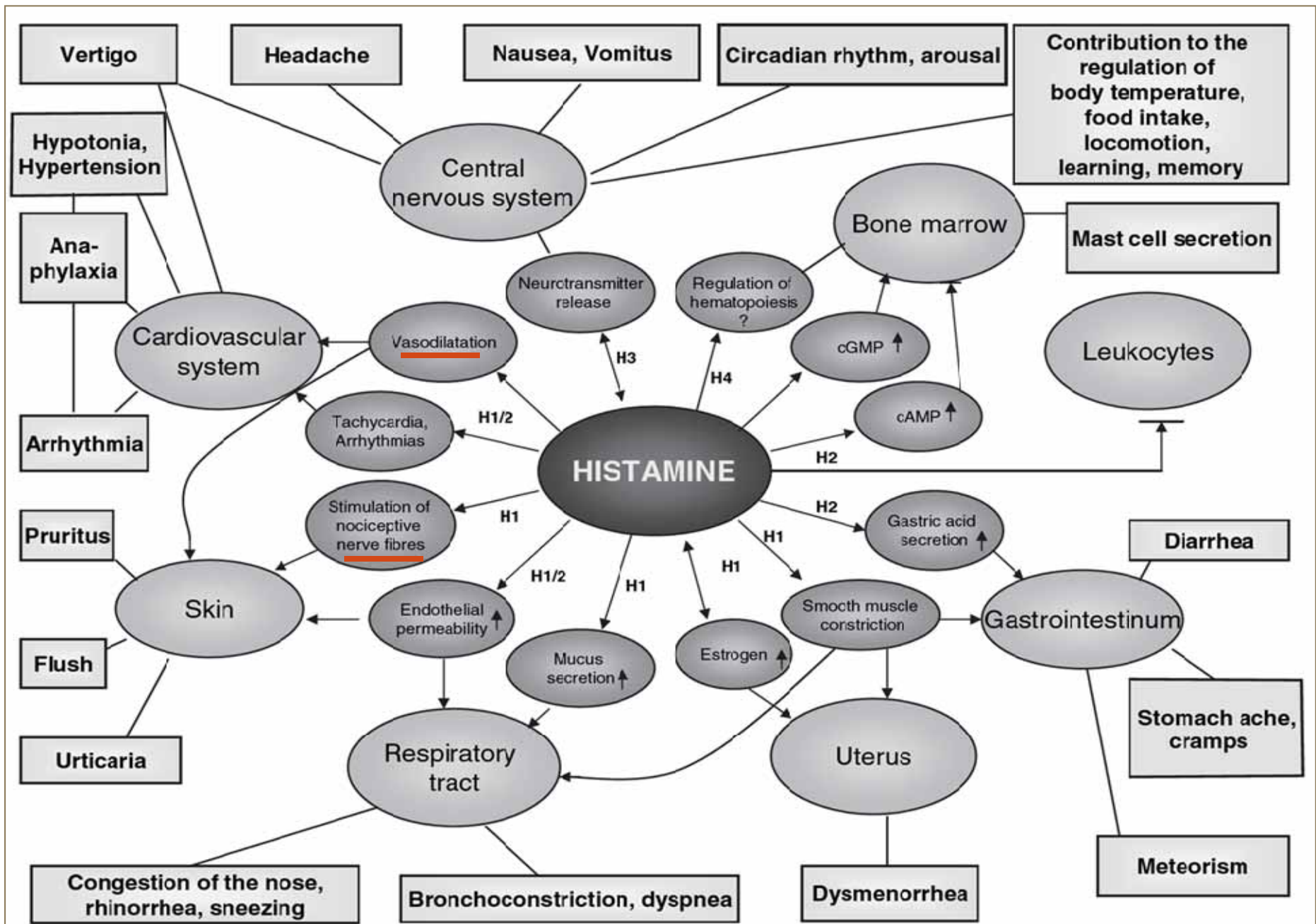


- A. Headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A. bilateral
  - B. frontotemporal location
  - C. pulsating quality
  - D. aggravated by physical activity
- B. Absorption of histamine
- C. Headache develops within 10 minutes after absorption of histamine
- D. Headache resolves within 1 hour after absorption of histamine has ceased

# Histamine and histamine intolerance



- Histamine is a biogenic amine that occurs to various degrees in many foods.
- Persons with low amine oxidase activity are at risk of histamine toxicity.
- Diamine oxidase (DAO) is the main enzyme for the metabolism of ingested histamine (extracellular).
- Histamine-rich food or alcohol/drugs that release histamine or block DAO may provoke symptoms.



Maintz L, Novak N. Histamine and histamine intolerance. Am J Clin Nutr. 2007 May;85(5):1185-96.

# Histamine and histamine intolerance



## Histamine-rich Foods

- Beer and wine
- Anchovies
- Cheeses, especially aged or fermented cheese
- Dried fruits
- Fermented foods
- Processed/ smoked meats/fish
- Sour cream, sour milk, buttermilk
- Soured breads made with large amounts of yeast
- Spinach, tomatoes
- Vinegar or vinegar-containing food

## Histamine-releasing foods

- Alcohol
- Bananas
- Chocolate
- Eggs
- Fish
- Milk
- Papayas
- Pineapple
- Shellfish
- Strawberries
- Tomatoes

### 8.1.9. Calcitonin gene-related peptide (CGRP)-induced HA



- Experimental administration of CGRP causes an immediate headache.
- CGRP is the most potent peptide vasodilator and can function in the transmission of pain.
- During a migraine, activated primary sensory neurons (meningeal nociceptors) in the trigeminal ganglion release CGRP from their peripherally projecting nerve endings located within the meninges causing vasodilation, mast cell degranulation, and plasma extravasation.

## 8.1.10. Headache as an acute adverse event attributed to medication used for other indications



- A.** Headache fulfilling criteria C and D
  - A.** Ill-defined in the literature, but most are dull, continuous, diffuse, and moderate to severe.
- B.** Use of a medication for a therapeutic indication other than headache
- C.** Headache develops within minutes to hours after use
- D.** Headache resolves within 72 hours after cessation of use

## 8.1.10. Headache as an acute adverse event attributed to medication used for other indications



A. Headache has been reported after use of a number of drugs. The following are the most commonly incriminated:

- |                |               |
|----------------|---------------|
| 1. atropine    | 5. imipramine |
| 2. digitalis   | 6. nicotine   |
| 3. disulfiram  | 7. nifedipine |
| 4. hydralazine | 8. nimodipine |

## 8.1.10. Headache as an acute adverse event attributed to medication used for other indications



Acetazolamide	Methaqualone	Caffeine	NSAID
Codeine	Perhexiline	Nifedipine	Thiamazole
Interferons	Barbiturates	Rifampicin	Chloroquine
Ondansetron	Dipyridamole	Calcium	Griseofulvin
Ajmaline	Metronidazole	antagonists	Octreotide
Didanosine	Primidone	Etofibrate	Cimetidine
Isoniazid	Beta-interferon	Nitrofurantoin	Guanethidine
Paroxetine	Disopyramide	Sildenafil	Estrogens
Amantadine	Morphine and	Carbimazol	Triptans
Dihydralazine	derivatives	Gestagens	Clofibrate
Meprobamate	Prostacyclines	Nitrates	Immunoglobulins
Pentoxifylline	Bromocriptine	Theophylline and	Omeprazole
Antihistaminics	Disulfiram	derivatives	Vitamin A
Ergotamine	Nalidixic acid	Chinidine	
	Ranitidine	Glycosides	



## 8.1.10. Headache as an acute adverse event attributed to medication used for other indications



**Google** nimodipine Instant is on ▼ Search

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▶ **Nimodipine (Brand name: Nimotop)**

**Nimodipine** is used to treat symptoms resulting from a ruptured blood vessel in the brain (hemorrhage). It increases blood flow to injured brain tissue. This medication is sometimes prescribed for other uses; ask your doctor or pharmacist for more information. **Nimodipine** comes as a capsule to take by mouth. If a ...

[Side effects](#) - [How to take](#) - [Precautions](#) - [Dietary Instructions](#) - [Missed a dose](#)

[www.nlm.nih.gov](#)

**Nimodipine - Wikipedia, the free encyclopedia**

**Nimodipine** (marketed by Bayer as Nimotop) is a dihydropyridine calcium channel blocker originally developed for the treatment of high blood pressure. ...

[Dosage](#) - [Usage](#) - [Pharmacokinetics](#) - [Mode of action](#)  
[en.wikipedia.org/wiki/Nimodipine](#) - [Cached](#) - [Similar](#)

## 8.2. Medication-overuse headache (MOH)



- A. Headache present on  $\geq 15$  days/month fulfilling criteria C and D
- B. Regular overuse for  $\geq 3$  months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache
- C. Headache has developed or markedly worsened during medication overuse
- D. Headache resolves or reverts to its previous pattern within 2 months after discontinuation of overused medication

## 8.2. Medication-overuse headache (MOH)



1. The headache is variable, even within the same day, from migraine-like to those of tension-type headache.
2. “Overuse” in terms of duration and treatment days per week. Must be both frequently and regularly, (on 2 or more days each week).

Bunching of treatment days with long periods without medication intake is much less likely to cause medication-overuse headache.

## 8.2. Medication-overuse headache (MOH)



- A. Excessively used therapeutic agent + susceptible patient.
- B. The best example is overuse of symptomatic headache drugs causing headache in the headache-prone patient.
- C. Most common cause of migraine-like headache occurring >15 days per month and of a mixed picture of migraine-like and tension-type-like headaches >15 days per month.
- D. Episodic tension-type headache can become a chronic headache through overuse of analgesics.

# Scrubs



“This is the reason why your headache didn't go away: That's actually pronounced analgesic, not anal-gesic. Sir, the pills go in your mouth.”



## 8.2. Medication-overuse headache (MOH)



Intake on  $\geq 10$  days/month on a regular basis for  $>3$  months

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

## 8.2. Medication-overuse headache (MOH)



Intake on  $\geq 10$  days/month on a regular basis for  $>3$  months

- Ergotamine

- ✦ Migranal

- ✦ Cafergot, Migergot (w/ caffeine)

## 8.2. Medication-overuse headache (MOH)



Intake on  $\geq 10$  days/month on a regular basis for  $>3$  months

### ○ Triptan

- ✦ Almotriptan- Axert
- ✦ Frovatriptan- Frova
- ✦ Rizatriptan- Maxalt
- ✦ Sumatriptan- Imitrex
- ✦ Zolmitriptan- Zomig



## 8.2. Medication-overuse headache (MOH)



Intake on  $\geq 10$  days/month on a regular basis for  $> 3$  months

- Opioid

- ✦ Buprenorphine- Buprenex
- ✦ Butorphanol- Stadol
- ✦ Codeine- Tylenol with codeine
- ✦ Fentanyl- Duragesic
- ✦ Hydrocodone- Vicodin
- ✦ Hydromorphone- Dilaudid
- ✦ Methadone- Dolophine
- ✦ Morphine- Astramorph
- ✦ Oxycodone- OxyContin
- ✦ Propoxyphene- Darvon

## 8.2. Medication-overuse headache (MOH)



Intake on  $\geq 10$  days/month on a regular basis for  $>3$  months

- Simple analgesics
  - ✦ Aspirin
  - ✦ Ibuprofen
  - ✦ Naproxen
  - ✦ Acetaminophen
- Combination analgesics

## 8.2. Medication-overuse headache (MOH)

### *Directions*

- **do not take more than directed**
- **the smallest effective dose should be used**

### adults

- take 2 capsules with a glass of water
- if symptoms persist or worsen, ask your doctor
- do not take more than 2 capsules in 24 hours, unless directed by a doctor



## 8.2. Medication-overuse headache (MOH)



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Kirkland Signature™ Ibuprofen  
200mg 1000 Tablets

Two Bottles, 500 Tablets Each

Item # 355400

**Rated** ★★★★★ (out of 2 reviews)

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**\$8.99**

Plus Shipping & Handling

The estimated delivery time will be approximately  
7 - 10 business days from the time of order.

Qty:

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### 8.4.1. Caffeine-withdrawal headache



- A. Bilateral and/or pulsating headache fulfilling criteria C and D
- B. Caffeine consumption of  $\geq 200$  mg/day for  $>2$  weeks, which is interrupted or delayed
- C. Headache develops within 24 hours after last caffeine intake and is relieved within 1 hour by 100 mg of caffeine
- D. Headache resolves within 7 days after total caffeine withdrawal

## 8.4.1. Caffeine-withdrawal headache

Coca-Cola Classic (12oz)	2.9 mg /
Diet Coke (12oz)	3.8 mg
Mountain Dew (12oz)	4.5
standard brewed tea (12	6.0
Amp Energy Drink (160	8.9
Red Bull (8.5oz)	9.5
Pimp Juice (8.3oz)	9.8
ground roasted coffee (12oz)	17.0
Rockstar 2x Energy (12oz)	20.
5 hour Energy (2oz)	69.



## 8.4.2. Opioid-withdrawal headache



- A. Bilateral and/or pulsating headache fulfilling criteria C and D
- B. Opioid intake daily for >3 months, which is interrupted
- C. Headache develops within 24 hours after last opioid intake
- D. Headache resolves within 7 days after total opioid withdrawal

### 8.4.3. Estrogen-withdrawal headache



- A. Headache or migraine fulfilling criteria C and D
- B. Daily use of exogenous estrogen for  $\geq 3$  weeks, which is interrupted
- C. Headache or migraine develops within 5 days after last use of estrogen
- D. Headache or migraine resolves within 3 days





## 9. HEADACHE ATTRIBUTED TO INFECTION



**A DIAGNOSIS THAT IMPROVES WITH  
RESOLUTION OF THE INFECTION  
(IN MOST CASES)**

## 9.2. Headache attributed to systemic infection



- A.** Headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A.** diffuse pain
  - B.** intensity increasing to moderate or severe
  - C.** associated with fever, general malaise or other symptoms of systemic infection
- B.** Evidence of systemic infection
- C.** Headache develops during the systemic infection
- D.** Headache resolves within 72 hours after effective treatment of the infection

## 9.2. Headache attributed to systemic infection



- A. Some systemic infections, particularly influenza, have headache as a prominent symptom along with fever and other symptoms.
- B. The mechanisms include direct effects of the microorganisms themselves.
- C. Infective microorganisms may influence brainstem nuclei, causing headache.
- D. Endotoxins may activate inducible NOS.
- E. The exact nature of these mechanisms remains to be investigated.

# 10. HEADACHE ATTRIBUTED TO DISORDER OF HOMEOSTASIS



**A DIAGNOSIS SECONDARY TO SIGNIFICANT  
SYSTEMIC DISTURBANCES**

## 10.1. Headache attributed to hypoxia, hypercapnia



- A. Headache occurs within 24 hours after acute onset of hypoxia with  $\text{PaO}_2 < 70$  mm Hg or in chronically hypoxic patients with  $\text{PaO}_2$  persistently at or below this level.
- B. It is often difficult to separate the effects of hypoxia and hypercapnia.

### 10.1.1. High altitude headache



- A.** Headache with at least two of the following characteristics and fulfilling criteria C and D:
  - A.** bilateral
  - B.** frontal or frontotemporal
  - C.** dull or pressing quality
  - D.** mild or moderate intensity
  - E.** aggravated by exertion, movement, straining, coughing or bending
- B.** Ascent to altitude above 2,500 m (8,200ft)
- C.** Headache develops within 24 hours after ascent
- D.** Headache resolves within 8 hours after descent

### 10.1.1. High altitude headache



- A. Acute mountain sickness (AMS) involves headache, nausea, anorexia, fatigue, dizziness and sleep disturbances.
- B. Acetazolamide (125 mg, two or three times daily) may reduce susceptibility to AMS.
- C. Preventative strategies include allowing for acclimatization (2 days) prior to strenuous exercise, avoiding alcohol, and liberalizing fluid intake.



<b>Mt McKinley</b>	<b>6194 m</b>
<b>Pikes Peak</b>	<b>4302 m</b>
<b>Telluride, CO</b>	<b>2671 m</b>
<b>Flagstaff, AZ</b>	<b>2135 m</b>
<b>Albuquerque, NM</b>	<b>1865 m</b>
<b>Memphis, TN</b>	<b>59 m</b>



## 10.1.2. Diving Headache



- A. Headache, no typical characteristics known, fulfilling criteria C and D
- B. Diving to depth below 10 m
- C. Headache develops during diving and is accompanied by at least one of the following symptoms of CO<sub>2</sub> intoxication in the absence of decompression illness:
  - A. light-headedness
  - B. mental confusion
  - C. dyspnea
  - D. flushed feeling in the face
  - E. motor incoordination
- D. Headache resolves within 1 hour after treatment with 100% O<sub>2</sub>

## 10.1.2. Diving Headache



- A. Hypercapnia (arterial  $\text{PCO}_2 > 50$  mm Hg) relaxes cerebrovascular smooth muscle leading to vasodilatation and increased intracranial pressure.
- B. Carbon dioxide may accumulate in a diver who skip breathes or takes shallow breaths.
- C. Strenuous exercise increases the rate of  $\text{CO}_2$  production more than 10-fold.
- D. Diving headache usually intensifies during the decompression phase of the dive or upon resurfacing.

### 10.1.3. Sleep apnea headache



- A.** Recurrent headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A.** occurs on >15 days per month
  - B.** bilateral, pressing quality and not accompanied by nausea, photophobia or phonophobia
  - C.** each headache resolves within 30 minutes
- B.** Sleep apnea (Respiratory Disturbance Index  $\geq 5$ ) demonstrated by overnight polysomnography
- C.** Headache is present upon awakening
- D.** Headache ceases within 72 hours, and does not recur, after effective treatment of sleep apnea

### 10.1.3. Sleep apnea headache



- $RDI = (RERA + \text{Hypopnea} + \text{apnea}) / \text{test time (hrs)}$
- Respiratory Disturbance Index (RDI)  $<5$ 
  - No Obstructive Sleep Apnea
- Respiratory Disturbance Index (RDI) 5 to 15
  - Mild Obstructive Sleep Apnea
  - Consider Upper airway resistance syndrome
- Respiratory Disturbance Index (RDI) 16 to 30
  - Moderate Obstructive Sleep Apnea
- Respiratory Disturbance Index (RDI)  $>30$ 
  - Severe Obstructive Sleep Apnea

## 10.3 Headache attributed to arterial hypertension



- Mild (140-159/90-99 mm Hg) or moderate (160-179/100-109 mm Hg) chronic arterial hypertension does not appear to **cause** headache.
- 10.3.1 Headache attributed to phaeochromocytoma
  - Incidence is 2-8 per million
- 10.3.2 Headache attributed to hypertensive crisis
  - paroxysmal rise in systolic (to >160 mm Hg) and/or diastolic (to >120 mm Hg)

## 10.4 Headache attributed to hypothyroidism



- A. Headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A. bilateral
  - B. non-pulsatile
  - C. continuous
- B. Hypothyroidism is demonstrated by appropriate investigations
- C. Headache develops within 2 months after other symptoms of hypothyroidism become evident
- D. Headache resolves within 2 months after effective treatment of hypothyroidism

## 10.4 Headache attributed to hypothyroidism



- A. 30% of patients with hypothyroidism suffer from headache
- B. Early symptoms:
  - A. Being more sensitive to cold
  - B. Constipation
  - C. Depression
  - D. Fatigue or feeling slowed down
  - E. Heavier menstrual periods
  - F. Joint or muscle pain
  - G. Paleness or dry skin
  - H. Thin, brittle hair or fingernails
  - I. Weakness
  - J. Weight gain (unintentional)



## 10.5 Headache attributed to fasting



- A. Headache with at least one of the following characteristics and fulfilling criteria C and D:
  - A. frontal location
  - B. diffuse pain
  - C. non-pulsating quality
  - D. mild or moderate intensity
- B. The patient has fasted for >16 hours
- C. Headache develops during fasting
- D. Headache resolves within 72 hours after resumption of food intake



## 10.5 Headache attributed to fasting



- A. Not related to duration of sleep, to caffeine withdrawal, or to hypoglycemia.
- B. Fasting headache can occur in the absence of hypoglycemia.
- C. Insulin-induced hypoglycemia does not precipitate headache in migraine sufferers.
- D. Headache is not a complaint of patients presenting to the emergency department with symptomatic hypoglycemia

## 10.6 Cardiac cephalalgia



- A. Headache, which may be severe, aggravated by exertion and accompanied by nausea and fulfilling criteria C and D
- B. Acute myocardial ischemia has occurred
- C. Headache develops concomitantly with acute myocardial ischemia
- D. Headache resolves and does not recur after effective medical therapy for myocardial ischemia or coronary revascularization

# Secondary Headache Disorders



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