



## CDH: More than Just a Headache



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Table 1

### Causes of chronic daily headache

#### Primary causes

- Chronic migraine
- Chronic tension-type headache
- New daily persistent headache
- Chronic cluster
- Hemicrania continua

#### Secondary causes

##### Medication-related

- Medication-overuse (rebound) headache
- Drug side-effects

##### Post-traumatic

- Headache attributable to head injury
- Headache attributable to neck injury or whiplash

##### Vascular

- Giant cell arteritis
- Subdural hematoma
- Ischemic or hemorrhagic stroke
- Venous sinus thrombosis
- Arterial dissection
- Severe arterial hypertension

##### Structural

- Headache attributable to cervical spine disorders
- Headache attributable to temporomandibular joint (TMJ)/dental pathology

##### Disorders of intracranial pressure

- Increased intracranial pressure (primary or secondary tumour, idiopathic intracranial hypertension, hydrocephalus)
- Decreased intracranial pressure (spontaneous intracranial hypotension, post lumbar puncture headache)

##### Infectious

- Meningitis (tuberculosis, fungal, parasitic)
- Sinusitis (sphenoid sinusitis)

##### Metabolic

- Obstructive sleep apnea, hypoxia, hypercarbia, carbon monoxide
- Thyroid disease

### Isabelle's Case



- Isabelle, 38, presents with chronic daily headache.
- Her past medical history is notable for asthma and endometriosis.
- She had episodic migraines as a teenager and young adult.
- Over the last five years, her headaches have escalated in frequency, but not necessarily severity. However, for the past three years, she has had daily headaches.
- She takes six to eight tablets daily of over-the-counter acetaminophen with codeine (starting with two tablets first thing in the morning).
- On some days, her headaches resemble her previous migraine attacks and on other days, her headaches resemble chronic tension-type headaches.
- Her physical examination is completely normal.
- Her routine serology at her recent general physical examination was normal.
- A baseline, unenhanced, CT scan completed in the emergency room during a headache exacerbation was also normal.

For more on Isabelle, go to page 72.

### What is CDH?

Chronic daily headache (CDH) is a symptom rather than a diagnosis. CDH simply refers to the presence of a headache on  $\geq 15$  days per month for  $\geq 3$  months. Correspondingly, correctly identifying the underlying cause for the chronic headache (*i.e.*, either a primary or secondary headache disorder) (Table 1) is necessary to direct investigations and to make rational therapeutic decisions.

Table 2

### Chronic daily headache: red flags

- 1) Onset age > 50 years
  - Consider temporal arteritis, brain tumour (primary or secondary) or subdural hematoma
- 2) Presence of fever or systemic symptoms
  - Chronic meningitis (tuberculosis, fungal or parasitic infection)
  - Sinusitis (note sphenoid sinusitis may occur without nasal symptoms)
  - Vasculitis (primary central nervous system or secondary to other inflammatory/rheumatologic conditions)
  - Temporal arteritis (fatigue, polymyalgia rheumatica, jaw claudication, scalp tenderness)
- 3) Focal neurologic symptoms or findings
  - Any accompanying neurologic symptom or neurologic sign (mentation, personality, optic disc swelling, field cut, focal weakness, incoordination etc.) suggests a secondary cause and warrants investigation
- 4) Precipitated or exacerbated by positional changes, valsalva, bending or coughing
  - If worse when standing — think spontaneous intracranial hypotension
  - If worse when supine, or with valsalva - think increased intracranial pressure and/or posterior fossa abnormality
- 5) History of cancer, immunocompromise or HIV
  - Be wary of metastatic disease or intracranial infection
- 6) Progressive headache or escalating medication requirements
  - Re-evaluate original diagnosis and consider a secondary cause
  - Be wary of caffeine and/or medication overuse

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### Helping Isabelle

- Isabelle's headaches are best classified as probable transformed migraine and probable medication overuse headache. If headache persists following the withdrawal of the acetaminophen with codeine tablets, she has definite transformed migraine. However, if the headache disappears following withdrawal of the acetaminophen with codeine tablets, then she has medication overuse headache and underlying episodic migraine headache.
- The first step is to educate Isabelle about migraine and medication overuse headache. Potentially modifiable risk factors should be explored. Furthermore, she should abruptly discontinue the use of acetaminophen with codeine. A prescription, non-steroidal, anti-inflammatory drug (NSAID) may be substituted for seven to 10 days. Migraine prophylactic therapy should be initiated.

### Who does CDH affect?

Worldwide, 3% to 5% of the general population suffers from CDH. CDH can occur in children, adults and the elderly. Notably, patients with CDH have significantly diminished health-related quality of life; as well as a decreased physical, social, occupational functioning and mental health.

### How do you approach a patient with CDH?

Fortunately, the vast majority of CDH is attributable to benign primary headache disorders; nonetheless, clinicians need to be vigilant about looking for secondary causes of headaches in their patients (Table 2). A thorough history is the most critical aspect of evaluation of CDH and it leads to the diagnosis in the vast majority of cases.

## **What are the primary causes of CDH?**

### **Chronic Migraine (CM)**

Chronic migraines represents the transformation of episodic migraine into CDH. Patients with CM often have a history of episodic migraine that began in their teens or twenties and has lasted for 10 to 20 years. In most cases, the transformation from episodic to CM is gradual but the transition can be abrupt in about 10% to 20% of cases. With CM, on some days the headaches and associated symptoms (*i.e.*, nausea, photophobia and phonophobia) retain characteristics of a migraine, while on other days, the headaches may be indistinguishable from tension-type headaches. Often these patients are labeled as having mixed tension and vascular-type headaches.

*Chronic daily headache is a symptom rather than a diagnosis.*

While CM often evolves from episodic migraine due to a medication overuse, many patients with chronic migraine do not overuse analgesics. Repeated migraine attacks may be associated with physiologic changes within the brain resulting in chronic pain. In susceptible individuals, an increased frequency of migraines may result from dynamic physiologic and biochemical alterations in central nociceptive and pain modulatory systems secondary to repeated attacks of migraine. The evolution of episodic migraine to CM may be the consequence of neuronal sensitization, impaired descending inhibitory control of medullary dorsal horn (trigeminal caudalis) neurons, or both, leading to the facilitation of ascending trigeminal nociceptive pathways.

### **Chronic tension-type headache (CTTH)**

CTTH is a rather non-descript, bilateral, mild-to-moderate intensity headache that has a pressure/tight band quality. Given its rather featureless characteristics, CTTH should be a diagnosis of exclusion. Importantly, headaches from brain tumours can be indistinguishable from CTTH.

### **Chronic cluster headache**

Chronic cluster headache is a severely debilitating disorder characterized by repeated episodes (each lasting 15-180 minutes followed by a headache-free interval) of severe pain in the orbital or temporal region and is associated with cranial autonomic features (*e.g.*, conjunctival injection, lacrimation, rhinorrhea, ptosis and/or meiosis). Patients usually can't sit still and are restless or agitated during attacks.

### **New daily persistent headache (NDPH)**

NDPH is characterized by a daily, constant and unremitting headache of acute onset (*i.e.*, developing over less than three days). The headache may be indistinguishable from CTTH and migrainous exacerbations can occur and the headaches may be debilitating. Unlike CTTH or CM, patients can pinpoint the calendar date of onset of their headache. In these patients, an exhaustive search for secondary causes is mandatory.

### **Hemicrania Continua**

Hemicrania continua is characterized by a continuous unilateral, moderately severe headache with exacerbations of severe pain lasting from hours to days. Autonomic features ( $\geq 1$  of conjunctival injection, lacrimation, rhinorrhea, ptosis, meiosis) may accompany the exacerbations and occur ipsilaterally to the pain. Patients typically experience substantial relief after a short therapeutic trial with indomethacin (25 mg, three times daily to 75 mg, three times daily).

Table 3

**Medication overuse headache****Diagnostic criteria:**

1. Headache present on  $\geq 15$  days each month.
2. Medication consumption on a regular basis sufficient to cause rebound headache:
  - Simple analgesics  $\geq 15$  days each month
  - Combination analgesics (with caffeine, codeine and/or butalbital)  $\geq 10$  days/month
  - Triptans or ergotamine  $\geq 10$  days/month
  - Opioids  $\geq 10$  days/month
3. Headache has developed or worsened during the period of medication overuse.
4. Headache resolves or reverts to previous pattern following discontinuation of medication overuse.

**Characteristics of medication overuse headache:**

1. The frequency of the headaches increases insidiously over time.
2. Patients often awake in the morning with headache (even though this was not a feature of their original headache).
3. A proportion of individual headache attacks may become non-descript (losing their characteristic migrainous or autonomic features and phenotypically resembling tension-type headache).
4. The threshold for stress or exertion to precipitate headaches is frequently lowered.
5. Escalating doses of symptomatic medications are required.
6. Headaches occur within a predictable period after the last consumption of symptomatic medication, usually with reduced efficacy (due to rebound or withdrawal phenomenon).

**► What is MOH?**

Medication overuse headache (MOH) is the generation, perpetuation or maintenance of chronic head pain in headache sufferers caused by the frequent and excessive use of immediate symptomatic-relief medications. Frequent use of simple analgesics (acetaminophen), combination analgesics (containing caffeine, codeine or barbiturates), opioids, ergotamine or triptans can transform episodic headaches into a near-daily or daily pattern.

The pathophysiology of MOH is unclear, but potential contributing factors include:

- 1) Psychotropic effects of, and corresponding withdrawal effects from, caffeine, codeine and/or barbiturates
- 2) Downregulation of central inhibitory pathways, resulting in a reduction of descending inhibitory modulation and the facilitation of trigeminal nociceptive pathways and
- 3) Paradoxical pronociceptive effects, whereby frequent opioid administration leads to increased activity of pain facilitation cells (ON-cells) arising in the rostral ventromedial medulla, an area essential to the integration of nociceptive processing and descending pain modulation.

Individuals who suffer from migraines may have an underlying genetic susceptibility to MOH, considering that non-headache patients with other painful disorders requiring daily analgesics do not develop CDH. Interestingly, in a study of 110 patients using daily analgesics for rheumatologic disorders, an increased risk of developing CDH occurred only in susceptible individuals with a pre-existing history of episodic migraine.

**► How do you treat CM and MOH?**

Unfortunately, no formal guidelines exist for the treatment of chronic migraine or medication overuse headache. Evidence from randomized controlled trials is limited and treatment is based on case series, retrospective reviews, anecdotal reports and expert opinion. Table 4 provides clinical pearls for the management of chronic migraine with/without medication overuse.

Table 4

**Management of CM with or without MOH**

- 1. Education:** Patients must be educated about their headaches so they can assume an active role in the treatment process (*i.e.*, direct them to patient resources on the internet such as, the American Council for Headache Education, the National Headache Foundation and/or Headache Network Canada).
- 2. Lifestyle modifications:** Establish a regular and appropriate sleep pattern, avoid skipping meals, initiate regular exercise and eliminate caffeine consumption.
- 3. Bio-behavioural therapy:** Relaxation therapy, biofeedback, stress management and cognitive behavioural therapy is often helpful to allow patients to achieve an internal locus of control.
- 4. Co-morbid disorders:** Co-morbid depression and/or anxiety should be addressed concurrently (note that some patients are depressed *because of* their daily headache).
- 5. Withdrawal of overused medications:** Overused medications should be either abruptly discontinued or tapered off due to the possibility of tolerance, habituation and dependence and due to potential risk of renal, hepatic and/or gastrointestinal side-effects.
  - Abrupt discontinuation— simple analgesics, ergotamines, triptans and most combined analgesics.
  - Taper— to avoid side-effects, withdrawal from opioids and/or barbiturates must be slow rather than abrupt. To alleviate potential side-effects from barbiturate withdrawal, a long-acting barbiturate alternative (*i.e.*, phenobarbital) may be substituted.
  - Acute headache management
    - Withdrawal symptoms typically last from two to 10 days. Symptomatic agents in limited doses (from drug classes other than what the patient is overusing) should be provided to alleviate withdrawal symptoms (headache, nausea, vomiting, arterial hypotension, tachycardia, sleep disturbances, restlessness and nervousness).
    - Options include long-acting NSAIDs, dihydroergotamine, triptans or an oral prednisone taper.
    - For patients requiring more aggressive treatment, several strategies have been advocated: one to three days of subcutaneous, intranasal or IV dihydroergotamine, IV methylprednisolone, IV neuroleptics or IV divalproex.
    - After initial detoxification, acute medications to treat episodic migraine attacks (*i.e.*, NSAIDs or triptans) are provided in limited doses.
- 6. Prophylactic therapy:** There is no solid evidence base upon which to make prophylactic therapy decisions in these patients; however, reasonable options include: antidepressants (*i.e.*, amitriptyline, anticonvulsants (*i.e.*, topiramate, gabapentin and divalproex sodium), beta-blockers (*i.e.*, propranolol), neurotoxins (*i.e.*, botulinum toxin) and possibly anti-spasticity agents (*i.e.*, tizanidine).
- 7. Follow-Up:** Patients should be provided with support and close follow-up and should be provided with realistic expectations (*i.e.*, medication overusers need to realize that during the withdrawal phase they may feel worse before they feel better).
- 8. Referral:** As management of these patients is often time consuming and difficult, early referral to a neurologist and/or a headache clinic is justified.

CM: chronic migraine

MOH: medication overuse headache

## What are the appropriate investigations for CDH?

All patients with CDH require an early unenhanced CT scan of the brain. If there are any red flags (Table 2) on history, any abnormalities on physical examination, or if the headache is not easily classifiable as a primary headache syndrome, further work-up is required (*i.e.*, serology, CT with contrast, MRI plus or minus gadolinium, neurologic and/or ophthalmologic consultation). It is important to remember that many secondary causes of chronic daily headache can be missed if the investigation is stopped after a normal CT scan (*i.e.*, temporal arteritis, intracranial hypertension, intracranial hypotension).

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