Chapter 4
Diagnosis of Primary Chronic Daily Headaches

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Introduction

Chronic daily headache (CDH) is a term of art, rather than an International Classification of Headache Disorders, 3rd edition, beta version (ICHD-3) diagnosis. It is defined as headaches present at least 15 days per month for at least 3 months for at least 4 h per day treated or untreated. Elimination of secondary causes, for example space-occupying lesions, infections, or metabolic causes such as hypothyroidism, is always the first step when a patient with CDH presents in the office of the physician. Once these are eliminated, there are only four primary CDH types. However, by convention, medication overuse headache (MOH, rebound) is often included in CDH, even though it is a secondary headache (see Table 4.1). ICHD-3 states that both chronic migraine (CM) and MOH can be diagnosed at the same time.

Short daily headaches, 3 h or less per day, are generally placed into the trigeminal autonomic cephalalgias (TACs), covered in Chapter 2.

The Four Primary Chronic Daily Headaches

The four CDHs are: Chronic Tension-Type Headache (CTTH), Hemicrania Continua (HC), New Daily Persistent Headache (NDPH), and Chronic Migraine (CM) (see Table 4.2). There are controversies about the diagnosis, and inclusion and exclusion criteria for each of the long daily headaches.

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Table 4.1 The definition of chronic daily headache

1. Headaches present at least 15 days per month
2. Headaches last at least 4 h per day treated or untreated
3. Daily or near-daily headaches have been present at least 3 months in a row
4. CDH is generally primary, but many clinicians include medication overuse headache (MOH) in the term
5. CDH is not an ICHD-3 diagnosis

Table 4.2 The four primary Chronic Daily Headaches (CHD)

1. Chronic Tension-Type Headache (CTTH)
2. Hemicrania Continua (HC)
3. New Daily Persistent Headache (NDPH)
4. Chronic Migraine (CM)

Table 4.3 Chronic Tension-Type Headache (CTTH), ICHD-3 criteria

A. Headache occurring on ≥15 days/month on average for >3 months (≥180 days per year)
B. Headache lasts hours or is continuous
C. Headache has ≥2/4 of the following:
1. Not unilateral (bilateral location)
2. Not throbbing (pressing/tightening, non-throbbing)
3. Not severe (mild or moderate)
4. Not aggravated by routine physical activity (e.g., walking or climbing stairs)
D. Both of the following:
1. No more than one of photophobia, phonophobia, or mild nausea (can have none of these)
2. Neither moderate or severe nausea nor vomiting
E. Not secondary

Chronic Tension-Type Headache

Clinically, CTTH is a featureless, low-level headache that is never severe and generally lacks migrainous features. The ICHD-3 criteria do not call for neck pain as a criterion, a frequently mistaken quality ascribed to this diagnosis. Location does not define tension-type headache (TTH), although bilaterality is one of four listed criteria, the others being a pressing or tightening quality, mild to moderate intensity, and not aggravated by usual activities. Two of these criteria must be met for TTH.

In keeping with the "not migraine" approach described in Chapter 1, CTTH is not throbbing, not severe, not unilateral, not worsened by activity, and generally has no nausea or photophonophobia. The ICHD-3 criteria have some unexpected diagnostic rules for CTTH. Patients are allowed no more than one of photophobia, phonophobia, or mild nausea, or none of these. Patients with CTTH are not allowed to have moderate or severe nausea or vomiting (see Table 4.3).

Table 4.4 Clinical pearls on diagnosing Chronic Tension-Type Headache (CTTH)

- No migrainous features: a continuous, low-level CDH
- Minimal impact from the headaches
- Gradual onset

It is far more clinically frugal and apt to simply require no migrainous features for the diagnosis of TTH. CTTH, besides being featureless, is also usually without impact or disability.

No requirement is made for a previous history of Episodic Tension-Type Headache (ETTH) in order for a patient to be diagnosed with CTTH. Clearly, by ICHD-3 criteria, CTTH and migraine can coexist, with migraine occurring on days that do not meet CTTH criteria. This is the Danish view of CDH, that migraine and TTH can always be distinguished, that it is worth doing so, and that there are therapeutic and pathophysiologic bases for separating them.

The American view, for the most part, is that migraine can turn into CDH, but the transformed headache remains a migraine disorder. Thus, patients with transformed migraine have a primarily migrainous disorder, with bad and not-so-bad days.

There are patients who have "pure" CTTH who never have any migrainous symptoms. These patients are rare.

No mention is made in the ICHD-3 criteria of the manner of presentation of CTTH. However, since NDPH is defined as the abrupt onset of CDH, it follows that to truly diagnose CTTH or CM, patients should have a gradual onset.

So, remember the three pearls on diagnosis of CTTH: no migrainous features, generally no individual impact, and gradual onset. These are included in Table 4.4.

Hemicrania Continua (HC)

Hemicrania Continua (HC) is characterized as a TAC in ICHD-3 and is a primary, continuous, strictly one-sided, moderate to severe headache with cranial autonomic symptoms and periodic moderate or greater intensity exacerbations. By definition, this headache is exquisitely indomethacin-responsive.

Because of the autonomic features, it overlaps more with TACs than CTTH or CM. For these reasons, the main section on HC is now included in Chapter 2 on the TACs. However, for completeness, the ICHD-3 criteria for HC are also in Table 4.5.

Differential Diagnosis on Hemicrania Continua

A few clinical pearls are noted below on differential diagnosis for HC. If you have not read the section in Chapter 2, do so now before reading on.

Table 4.5 Hemicrania continua (HC), ICHD-3 criteria

A. Unilateral continuous CDH for > 3 months with moderate to severe exacerbations
B. At least one of the following, ipsilateral to the side of pain:
   1. Conjunctival injection
   2. Lacrimation
   3. Nasal congestion
   4. Rhinorrhea
   5. Ptosis
   6. Miosis
   7. Eyelid edema
   8. Forehead or facial sweating or flushing
   9. Sense of fullness in the ear
   10. Restlessness or agitation or worsening of pain with movement
C. Complete response to therapeutic doses of indomethacin, with a trial up to at least 225 mg/day
D. Not secondary

- *Remitting subtype:* Interruptions of pain for ≥ 1 day without treatment
- *Unremitting subtype:* Continuous pain with no remission periods of pain for ≥ 1 day for ≥ 1 year

In a patient with continuous side-locked daily headache, the first step is to exclude secondary causes. Side-locked headaches in and of themselves merit a work-up. Switching sides is reassuring for primary or benign diagnosis.

The differential on a continuous *primary* side-locked headache includes HC, cervicogenic headache, CM with or without MOH, and other TACs which can have interictal continuous headache such as Cluster Headache (CH) and Paroxysmal Hemicrania (PH).

The late Dr. John Edmeads of Toronto listed many of his criteria for cervicogenic headache, and although not part of ICHD-3, they are worth repeating here: (1) the headache should be unilateral and the pain should move from the neck forward, (2) the patient should note the neck is a significant component of the pain, (3) the headache should not meet ICHD criteria for a different definable headache disorder, and (4) the headache should respond to differential or placebo-controlled upper cervical, medial branch, or facet blocks. Since HC generally has autonomic features, would not respond to the blocks, and is indomethacin-responsive, these disorders can be distinguished with an indomethacin trial.

Remember, the indomethacin should be 100 % effective, like a key in the lock, for HC. In degenerative conditions such as cervicogenic headache, the anti-inflammatory properties of indomethacin can provide partial relief. Invasive upper cervical blocks do not help HC, although partial relief can occur with occipital nerve blocks in HC.

CM with or without medication overuse will not be 100 % responsive to indomethacin and is treatable with onabotulinumtoxinA (onabot). There is no prospective controlled evidence that onabot works for HC.

Also, the remarkable response to indomethacin in HC occurs with or without a wean of overused medications. Once the indomethacin is working, the wean of inef-

Table 4.6 Clinical pearls on the differential diagnosis of Hemicrania Continus (HC)

- Foreign body sensation in the ipsilateral eye or itchy eye—this generally does not occur in CM with or without MOH, in cervicogenic headache, or in the other TACs
- Overuse of other NSAIDs—this can occur in PH, cervicogenic headache, or MOH, but does raise the question of HC
- Average baseline headache intensity is 6/10, which often helps distinguish HC from the "ghost headache," the mild interictal continuous pain of CH or PH
- Exacerbations can mimic migraine instead of cluster, and the exacerbations can be triptan-responsive. Exacerbations occur frequently, often daily or near daily. This can make distinguishing HC from CM or the other TACs more difficult
- An indomethacin trial may be the only way to distinguish HC with migrainous exacerbations from CM with MOH or even cluster
- Agitation and aggression during the exacerbations is common, as in cluster, but not PH, cervicogenic headache, or CM
- Dislike of light and noise can be ipsilateral and entirely unilateral in all of the TACs, but unilaterality of photophonophobia is very rare in CM and nonexistent in cervicogenic headache
- The indomethacin trial should be to at least 225 mg/day. 1/3 of patients in the Cittadini and Goadsby case series required at least 300 mg/day
- Indomethacin responsiveness does not prove that a patient has primary HC, and an imaging study is necessary

fective overused medications in HC patients can be done easily, generally with great patient cooperation and enthusiasm, unlike the more challenging MOH situation.

The exacerbations of severe headache in HC can be more migrainous than cluster-like, sometimes adding to the diagnostic dilemma. These exacerbations can even be triptan-responsive. When in doubt, an indomethacin trial is in order.

As noted in Chapter 2, CH and PH can manifest continuous interictal pain in as many as 1/3 of patients. This continuous pain in the other TACs is generally of lower intensity compared with the 6/10 average intensity of the continuous unilateral pain of HC.

However, overlap can occur. The attacks in CH and PH can look just like the severe exacerbations in HC, and the continuous one-sided headache can be of intermediate pain levels in any of the three disorders. If the exacerbations are short, as in PH, since PH and HC are both indomethacin-responsive, it can be impossible to distinguish them clinically. This is rare, however. Generally, the short, frequent exacerbations in PH and the higher intensity continuous pain and longer exacerbations of HC tell the clinician which is which (see Table 4.6).

New Daily Persistent Headache

The ICHD-3 criteria for NDPH are the abrupt onset of a primary CDH with no specified features at a specific time remembered by the patient. The requirement is that the onset of CDH occurs within 24 h (see Table 4.7). The diagnosis should be made on the basis of the sudden onset of CDH of any phenotype with no secondary cause.

Table 4.7 New Daily Persistent Headache (NDPH), ICHD-3 criteria

A.	Abrupt onset, a clear and remembered beginning within 24 h, of continuous chronic daily headache and no remissions, no pain-free periods
B.	Headache is continuous for > 3 months
C.	Not secondary

NDPH was covered in Chapter 3, Diagnosis of Other Primary Headaches, because that is where it is placed in the ICHD-3. However, as it overlaps with CM and CTTH and is so problematic, it is discussed again here.

A case series in 2010 by Robbins and colleagues of 71 patients with abrupt onset of CDH found that more than half of them had migrainous features. Two groups of NDPH, those with abrupt onset resembling CTTH and those resembling CM, did not differentiate prognostically or therapeutically.

The key to the diagnosis lies more with the patient's recollection of abrupt onset, and not with the character of the daily headaches. Robbins and colleagues noted three temporal profiles: continuous headache from onset and not remitting, complete remission or with residual headache < 5 days/month for ≥ 3 months, and a relapsing/remitting form, with runs of daily headache and periods of headache freedom.

Additional features that could be useful diagnostically include that almost half of the patients with abrupt-onset CDH had family histories of frequent headaches. Also, almost half remembered a specific trigger such as an antecedent respiratory illness or a stressful life event.

Clinically, one of the key points in diagnosing patients with daily headache is to ask if they had a period of transformation, of gradually increasing frequency of headache days, or if they had a sudden and precipitous onset. Unless explicitly asked, clinicians run the risk of missing the diagnosis of NDPH, a diagnosis necessary to make because of its difficulty in treatment.

The more recent the onset of NDPH, the more concern there should be for a secondary cause. The ICHD-3 requires at least 3 months of continuous headache, and a primary NDPH is obviously more likely in those patients who have had years of continuous daily headache and who had the required abrupt onset.

Potential secondary causes of NDPH include infection (such as HIV or Lyme), cerebrospinal fluid (CSF) leak, vascular causes, metabolic causes, and neoplasm (see Table 4.8).

A clinical history of positional headache (better lying down), tinnitus, photophobia, neck pain, and hyperacusis suggests CSF leak, even without antecedent trauma. MRI without and with contrast, to look for the pachymeningeal enhancement or brain sag associated with CSF leak, is necessary before diagnosing relatively recent-onset NDPH.

Vascular causes, when the NDPH duration is on the short side, that is, months' not years' duration, include dissection, vasculitis, pituitary apoplexy, arterial bleed from aneurysm or arteriovenous malformation (AVM), or cortical vein thrombosis. These vascular causes of abrupt-onset daily headache are often associated with

Table 4.8 Potential secondary causes of abrupt onset of daily headache

• CSF leak should be suggested by positional headache, tinnitus, photophobia, hyperacusis, and neck pain. Diagnosis can be established with an MRI without and with contrast showing pachymeningeal enhancement and/or brain sag
• Infection can present abruptly, so remember HIV and Lyme and other subacute meningo-encephalitides
• Vascular causes can include dissection, pituitary apoplexy, vasculitis, arterial bleed from aneurysm or AVM, or cortical vein thrombosis, so MRA/MRV may be necessary, depending on how close the patient is to the onset of the daily headache
• In the elderly, think subdural hematoma

Table 4.9 Clinical pearls in diagnosing New Daily Persistent Headache (NDPH)

• Patient should remember the approximate date of onset
• Any phenotype
• Some NDPH remits or is relapsing/remitting
• Almost half of NDPH patients remember a trigger such as a preceding respiratory illness or stressful life event
• Almost half of NDPH patients have family histories of frequent headaches

thunderclap onset. Magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) may be necessary, depending on how close the patient is to the onset of the daily headache.

Metabolic causes for daily headache, such as thyroid disease, rarely can have abrupt onset. In the elderly, consideration for a subdural hematoma, even in the absence of trauma should always be given.

Some clinical pearls for diagnosing NDPH are included in Table 4.9.

Chronic Migraine

Unlike the other three CDHs, CM is a controversial diagnosis, with multiple suggestions and positions on diagnostic criteria vying for position. The history of the terms used in diagnosis helps the clinician attempting to accurately diagnose this group of patients.

CM is often used to mean CDH. Thus, many clinicians include both *primary* CDH and *secondary* CDH (MOH, analgesic rebound) in the definition of CM. This was done historically and is based on the similarity of presentation in patients with CDH. Rebound headache has often been telescoped into CM, so diagnosis of MOH is also briefly covered here.

Silberstein, Mathew, Lipton, and colleagues, in 1994, suggested that since episodic migraine transforms into CDH, the term for the daily headache patient should be transformed migraine, with or without medication overuse. The term transformed migraine is still in widespread use and simply means a patient with

Table 4.10 Criteria for transformed migraine. (Silberstein–Lipton, 1994)

1. The headache is not a CDH that develops de novo in a previously headache-free subject, that is, it is not NDPH
2. One of the following three exists:
   a. A prior history of ICHD-defined migraine
   b. A period of escalating headache frequency
   c. Concurrent superimposed attacks of migraine that fulfill ICHD criteria for episodic migraine
3. The patient has CDH, that is, headache > 4 h/day untreated for at least 15 days/month for > 3 months in a row
4. TM can occur with or without medication overuse

Table 4.11 ICHD-3 criteria for chronic migraine

A. Headache (tension-type and/or migraine) on ≥ 15 days per month for > 3 months
B. Occurring in a patient who has a preexisting diagnosis of migraine
C. On ≥ 8 days per month for > 3 months headache at least with one of the following:
   1. Criteria for migraine
   2. The patient feels it is migraine
   3. Successfully treated by triptan(s) or ergot
D. No other cause
E. If medication overuse is present, the ICHD-3 states, "patients meeting criteria for both chronic migraine and for medication-overuse headache should be given both diagnoses. After drug withdrawal, migraine will either revert to the episodic subtype or remain chronic, and be re-diagnosed accordingly"

Table 4.12 ICHD-3 criteria for medication overuse headache

1. Headache on ≥ 15 days/month in a patient with a previously established headache disorder
2. Regular overuse for > 3 months of ≥ 1 acute headache drugs

preexisting episodic migraine has gradually transformed to primary or secondary CDH (see Table 4.10).

The ICHD-2 declared that since MOH is a secondary headache, the term CM should be reserved for primary transformation to daily headache. In what turned out to be an ill-fated and short-lived mistake, the official ICHD-2 criteria required the patient to have headache meeting criteria for migraine at least 15 days/month, that is, reaching a migraine level almost daily without medication overuse.

The ICHD-3 criteria for CM require the patient with CDH to reach migraine level or respond to migraine-specific treatment at least 8 days per month out of their daily headaches. Once again, rebound patients are excluded, as they have secondary CDH (see Tables 4.11 and 4.12).

The ICHD-3 criteria for MOH are CDH with enough acute medication intake to propagate the rebound. Criteria are simply taking enough acute medication for more than 3 months to be associated with CDH (see Table 4.12).

The ICHD-3 continues to separate the number of days of intake necessary to generate MOH for different medications. While it turns out there is a hierarchy of

Table 4.13 Clinical pearl on medication overuse headache

• Patients with MOH develop a new headache or a marked worsening of their preexisting headache with their medication overuse

susceptibility to acute medications in terms of likelihood for initiating rebound, it is not the same as listed in ICHD-3. This discussion of rebound will be covered more extensively in Chapter 13.

A good rule of thumb is that if a patient has CDH and is taking acute medications at least 10 days per month, that patient likely has MOH. Fewer days of butalbital (5 days or use or more per month) or opioids (8 days of use or more per month) can also cause MOH (see Table 4.13).

The discussion section under MOH in the ICHD-3 states that these patients "develop a new headache or a marked worsening of their pre-existing headache" with their medication overuse. While not part of the ICHD-3 criteria, this finding is extremely helpful diagnostically in diagnosing MOH.

The ICHD-3 diagnostic issue is how to proceed in a patient with CDH and medication overuse. The patient could have primary CM, and the medication overuse is not playing a role. Or the patient could have MOH, and with a wean reverts to episodic migraine.

The way the ICHD-3 works is seen in the following two diagnostic scenarios:

Scenario 1. You have a patient with episodic migraine who overuses combination analgesics and starts to rebound and develops daily headache. Per ICHD-3, you diagnose both CM and MOH at that first visit.

You take the patient off the analgesics, and the patient goes back from daily headache to discrete episodes of migraine with no headache at all in between. Now you know, the patient initially had MOH and currently has episodic migraine without aura, so you change your diagnosis once this pattern has established itself.

Scenario 2. You have a patient with episodic migraine who overuses combination analgesics and develops daily headache. Per ICHD-3 you diagnose both CM and MOH at that first visit.

You take the patient off the analgesics and the patient continues to have daily headache 6 months later, but is taking no acute medications. Now you know, the patient actually has primary CM and has daily headache without rebound acute medications provoking and continuing the daily headache. You can remove the diagnosis of MOH; this patient has just CM.

In 2010, regulatory randomized controlled studies on the use of onabotulinumtoxinA (onabot, BOTOX) were published in which onabot or vehicle was given subcutaneously for CDH. In those studies, a mixture of patient diagnostic criteria was used for inclusion, including primary CM and MOH for the most part excluding opioid and butalbital rebound. Patients were required to have headache-free periods each month (not a requirement for any CDH diagnosis), and NDPH patients were also excluded. The reason given for studying the treatment of this mixture of primary and secondary headaches was that the phenotype of these patients is similar.

Table 4.14 Criteria for CDH/"chronic migraine" as studied in the onabotulinumtoxinA prevention studies

1. CDH
2. Must have ≥ 4 distinct headache episodes, each lasting ≥4 hours. (cannot be continuous 24/7 headache)
3. MOH allowed but not overuse of butalbital or opioids
4. NDPH excluded

The investigators of onabot lumped all of the subjects into what they called "chronic migraine." This was not CM by ICHD-3 criteria, as it included both secondary CDH (MOH) and primary CM, and also required times of clearing of headache per month, not in the ICHD-3 criteria for CM. These studies served as the regulatory submission for onabot for CDH, but the request was approval for onabot for CM.

Onabot was approved for CM in the USA in October of 2010. The US prescribing information approved by the Food and Drug Administration (FDA) defines CM as headache present for at least 15 days per month for at least 4 h per day, which is CDH.

The reason for belaboring this point is diagnostic: The "chronic migraine" studied in the onabot studies does not correlate with true primary CM by strict ICHD-3 criteria. It also does not include all MOH by ICHD-3 criteria. The "chronic migraine" of the onabot studies is actually a blend of diagnoses and requirements not fitting any one of the established and validated ICHD diagnoses of either primary or secondary CDH (see Table 4.14). The FDA-approved onabot prescribing information definition of "chronic migraine" is just CDH with or without medication overuse, which may be liberating, in terms of diagnosing and treating the phenotype of CDH (see Table 4.15).

Conclusions on Diagnosis of Chronic Daily Headache

There are 4 primary types of CDH, and they are HC, CTTH, NDPH, and CM. There is not much controversy over diagnosing the first two. The diagnosis of NDPH is made on the basis of abrupt onset (within 24 h) of primary CDH of any phenotype, continuous from onset (see Table 4.16).

When diagnosing CM, it is important to make clear whether the clinician is diagnosing the primary CM of the ICHD-3, that is, transformed migraine without medication overuse, or whether one is diagnosing a phenotype of CDH including MOH. Technically, the ICHD-3 diagnosis of CM should not include secondary causes of CDH, but it is allowed to diagnose both CM and MOH prior to weaning overused medication in the setting of CDH.

It is also important to note that some therapy trials, such as that for onabotulinumtoxinA, used hybridized inclusion criteria, involving some features of the

Table 4.15 FDA-approved definition of chronic migraine in onabot prescribing information

• Chronic migraine is headache ≥ 15 days/month for ≥ 4 h/day (= chronic daily headache with or without medication overuse)

Table 4.16 Concluding pearls on diagnosis of primary chronic daily headache

• There are only 4 validated forms of primary CDH according to the ICHD-3: CTTH, HC, NDPH, and CM
• CTTH is a low-level featureless headache, with minimal impact
• HC is a unilateral moderate headache with periodic severe exacerbations, accompanied by autonomic signs. HC is defined by its indomethacin responsiveness
• NDPH is diagnosed as abrupt-onset primary CDH of any phenotype
• Pure ICHD-3 CM is a primary CDH in which a patient transforms from episodic migraine to CDH without secondary causes, including MOH
• MOH is not a primary CDH; it is characterized by overuse of enough acute medication to transform a patient to secondary CDH
• The term "Chronic Daily Headache" (CDH) is not an ICHD-3 term and generally refers to the phenotype of CM + MOH
• The FDA-approved definition of "chronic migraine" is CDH, both primary and secondary, with any phenotype of CDH

ICHD criteria for CM and some secondary MOH criteria. The diagnostic description of CM in the prescribing information for onabotulinumtoxinA for "chronic migraine" is that it is just CDH, primary or secondary. When evaluating a patient, it may be useful to use pure diagnostic criteria to plan treatment. On the other hand, there is a liberating aspect to just using these FDA-approved criteria in lumping all patients with CDH into CM (see Table 4.15). Treatment of MOH will be covered in Chapter 13; treatment of CM is covered in Chapters 14 and 15.

Suggested Reading

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