AN OVERVIEW OF CHRONIC DAILY HEADACHE*

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ABSTRACT

Although it is surely one of the oldest and most common complaints prompting patients to consult their physicians, chronic daily headache (CDH) was not officially recognized in early 20th century descriptions of headache or even mentioned in the first International Headache Society (IHS) Classification of headaches developed in 1988. Patients with symptoms of CDH would be categorized as falling into 1 of the other major diagnoses, such as migraine or tension headache, but very often these individuals did not fit into any clear-cut category. Finally, in 2004, the IHS published the second edition of the International Classification of Headache Disorders (ICHD-II), in which there are several classifications for chronic primary headaches that address those patients who suffer from headaches of more than 4 hours’ duration on 15 or more days out of the month. Although it is estimated that the incidence of CDH may be as high as 2% to 8% of the general population, which translates into millions of individuals around the world, historically, these patients have been the most difficult to treat and often have found themselves visiting practitioner after practitioner in search of headache relief, only to be faced with frustration and continued symptoms as a result of the lack of effective and available therapies and management guidelines. Even today, the US Food and Drug Administration (FDA) has not approved any medication for use in patients with the diagnosis of CDH; therefore, every pharmacologic therapy in use for these patients is being used off label and is drawn from a variety of other subspecialties within medicine, including cardiology, psychiatry, and even gastroenterology and endocrinology. To begin to understand how to treat these patients, it is first essential to know the population who are afflicted and comprehend the risk factors.

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Epidemiology and Risk Factors

In 2003, Scher et al studied predictors of the onset and/or remission of CDH in an adult population \((n = 1134)\). The investigators demonstrated that over the course of 1 year, \(3\%\) of individuals with episodic headaches \((2 \text{ to } 104 \text{ days/year}, n = 798)\) progressed to CDH \((\text{frequency of } >180 \text{ days/year})\). Factors associated with CDH prevalence at baseline were evaluated, as were those in patients who progressed to more than 180 headaches per year and for those patients whose number of episodes decreased over the course of the year. The authors of this report found that CDH was more common in women, whites, and among those individuals who reported less education. People with CDH were more likely to be previously married (ie, divorced, widowed, or separated), obese, and to have had a physician diagnose them as having diabetes or arthritis. The most significant risk factors seemed to be obesity and having frequent headaches at baseline.\(^5\) In another study by Katsarava et al, 532 patients with episodic migraine \((\text{EM; headache incidence } <15 \text{ days/month})\) were followed for 1 year.\(^6\) A much higher rate of progression was found in this study population, with \(14\%\) of these patients developing CDH \((>15 \text{ days/month})\), in particular, those patients who had more frequent headaches at the onset \((\text{ie, } 10 \text{ to } 14 \text{ days/month})\).\(^6\)

Minor head trauma also predicts the development of CDH. There are many individuals who present to headache clinics and neurologists after what appears to be a trivial incident, such as a minor automobile accident or an accident in a department store where a box hit them on the head. Although there was no fracture, concussion, and possibly not even a laceration of the scalp, debilitating headaches may result. Whereas the question of whether the foundation for their headaches is the resulting litigation, very often, legal issues are not involved. To summarize, the peak incidence for CDH seems to be among women in their 30s and 40s, particularly, among those who have a history of migraine without aura \((\text{ie, } 90\% \text{ of cases})\), and seems to decrease in line with age.\(^5\)\(^6\)

Classification and Criteria for Primary Headache Disorders

Headache disorders are generally classified as primary or secondary, and these classifications are further divided into specific headache types. Of the primary headache disorders, the CDH seems to be unrelated to structural or systemic illnesses and encompasses several types, including chronic migraine \((\text{formerly referred to as } \text{"transformed migraine" \([\text{TM}])})\), chronic tension-type headache \((\text{CTTH})\), cluster headache, and hemicrania continua, which is a relatively rare disorder that is somewhat unique in its response to an infrequently used but potent anti-inflammatory agent, indomethacin. Secondary headache disorders are defined as those attributed to an underlying pathologic condition, such as infection, neoplasm, or a vascular or drug-induced pain. Many patients with CDH who do not have an organic disorder may be suffering from a rebound headache from the use of excessive amounts of caffeine or combination pharmacologic compounds, with ergot being particularly incriminating as

<table>
<thead>
<tr>
<th>IHS ICHD-II Code</th>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>1.5.1</td>
<td>Chronic migraine (previously, transformed migraine)</td>
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<tr>
<td>1.6.5</td>
<td>Probable chronic migraine</td>
</tr>
<tr>
<td>2.3</td>
<td>Chronic tension-type headache</td>
</tr>
<tr>
<td>2.3.1</td>
<td>Associated with pericranial tenderness</td>
</tr>
<tr>
<td>2.3.2</td>
<td>Not associated with pericranial tenderness</td>
</tr>
<tr>
<td>2.4.3</td>
<td>Probable chronic tension-type headache</td>
</tr>
<tr>
<td>3.1.2</td>
<td>Chronic cluster headache</td>
</tr>
<tr>
<td>3.2.2</td>
<td>Chronic paroxysmal hemicrania</td>
</tr>
<tr>
<td>4.7</td>
<td>Hemicrania continua</td>
</tr>
<tr>
<td>4.8</td>
<td>New daily persistent headache</td>
</tr>
<tr>
<td>5.2</td>
<td>Chronic posttraumatic headache</td>
</tr>
<tr>
<td>5.2.1</td>
<td>Attributed to moderate or severe head injury</td>
</tr>
<tr>
<td>5.2.2</td>
<td>Attributed to mild head injury</td>
</tr>
<tr>
<td>5.4</td>
<td>Chronic headache attributed to whiplash injury</td>
</tr>
<tr>
<td>5.6.2</td>
<td>Chronic headache attributed to other head/neck trauma</td>
</tr>
<tr>
<td>5.7.2</td>
<td>Chronic postcraniotomy headache</td>
</tr>
</tbody>
</table>

ICHD-II = International Classification of Headache Disorders (second edition); IHS = International Headache Society. Adapted with permission from Mathew and Ward. Treatment of primary headache: chronic daily headache. In: Standards of Care for Headache Diagnosis and Treatment. Chicago, Ill: National Headache Foundation; 2004:73-80; Data from Headache Classification Subcommittee of the International Headache Society.\(^1\)
a cause of rebound headache if a patient attempts to stop his or her therapy.

The most recent IHS classification of headaches was published in 2004, and although it is somewhat controversial, it does serve as a solid foundation for clinicians on an international level. As such, it may be helpful in terms of research efforts, because it standardizes the definitions for distinguishing among patients with various types of headaches to be studied in clinical trials regardless of where in the world that trial is taking place. Again, subclassifications that fall under CDH include chronic migraine, CTTH, chronic cluster headache, and chronic posttraumatic headache, which is attributed to whiplash injury or other head and neck trauma or postcraniotomy (Table 1).

Because it is such a common cause of CDH (and the usual progression from episodic events), it is important to briefly describe the criteria for chronic migraine. These are headaches that are unilateral, pulsating in quality, accompanied by nausea and/or vomiting and/or photophobia and phonophobia, and are moderate to severe in pain intensity to the extent that they interfere with routine activity. Mathew noted that when patients with EM developed chronic migraine, there was some change in the symptoms. Although initially experiencing autonomic and gastrointestinal complaints, the accompanying symptoms patients developed with chronic migraine now more commonly included musculoskeletal and psychological symptoms, such as depression. In addition, medication use became central to their lifestyle, and often excessive, with patients commonly taking daily combination drugs containing acetaminophen, aspirin, and caffeine up to 5 times in a single day for months until finally needing professional treatment for dependence on the drug, in addition to treatment of the headache problem.

Also common among CDHs are those that arise from episodic tension-type headache (TTH) and are possibly associated in some patients with heightened muscle contraction. Again, TTHs occur more than 15 days per month for an average of more than 3 months. They generally last for hours or may be continuous. Contrary to chronic migraine, CTTHs are bilateral, pressing, or tightening (ie, nonpulsating) in quality. They are associated with only mild nausea (if at all); photophobia or phonophobia may be present. CTTHs are mild to moderate in intensity and are not aggravated by routine physical activity or activities of daily living.

Two more additions to the IHS 2004 classification of headaches are daily persistent headache and hemicrania continua. The sudden onset of a daily headache can be quite disturbing to patients who experience a daily, unremitting headache for more than 3 months that is bilateral and bandlike (ie, pressing or tightening) in quality. Daily persistent headache resembles TTH more closely than it does migraines, causing mild-to-moderate pain that is unaffected by activity, is not accompanied by photophobia, phonophobia, and nausea, and is not attributed to another underlying disorder. Hemicrania continua has to be present for more than 3 months, be unilateral, and usually stays on the same side of the head. It is continuous without pain-free intervals. Some of the elements of hemicrania continua resemble cluster headaches. Hemicrania continua are of moderate intensity, but with exacerbations of severe pain accompanied by at least 1 of the following autonomic features on the ipsilateral side to the pain: conjunctival injection and/or lacrimation, nasal congestion and/or rhinorrhea, or ptosis and/or miosis.

**RULING OUT SECONDARY CAUSES**

Clinicians must be familiar with some of the secondary etiologies, shown in Table 2, that mimic CDH, such as those that arise from a mild head trau-

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**Table 2. Secondary Causes of Chronic Daily Headache**

- Post-traumatic (may mimic any primary headache)
- Cervicogenic (especially C2, C3 upper root entrapment)
- Temporomandibular joint syndrome
- Sinus disease
- Arteriovenous malformation
- Arteritis (including giant cell arteritis)
- Subdural hematoma
- Vascular dissection
- Neoplasm
- Infections
- Intracranial hypertension
- Intracranial hypotension

Note: All diagnoses may be confounded by medication overuse.

ma (and even without cerebral concussion), cervicogenic upper nerve root entrapment at level C2 or C3, temporomandibular joint syndrome, sinus infection, arteriovenous malformation, and inflammatory conditions, such as giant cell arteritis. Other serious secondary causes of CDH may include subdural hematoma, vascular dissection, neoplasm, infections, and intracranial hypertension and hypotension. All of these secondary causes may be confounded by medication overuse. Physicians should be alert for changes to an individual patient’s usual headache scenario. For example, an individual who has had EM for years but is now older (ie, >50 years) and suddenly starts experiencing a daily headache requires a thorough evaluation for the possible onset of some organic cause, especially if the headache is associated with systemic symptoms, such as fever, weight loss, or jaw claudication. These systemic symptoms warrant a search for giant cell arteritis, which is commonly known as temporal arteritis.

Other characteristics that may alert the physician to a serious, secondary etiology is the sudden onset of an extremely severe headache—a so-called thunderclap headache—which is described as the worst headache the patient has ever had and peaks in intensity in seconds to minutes. The patient also may experience focal neurologic signs and symptoms, such as papilledema, motor weakness, memory loss, pupillary abnormalities, or sensory loss. Unfortunately, these may be the red flags signaling a subarachnoid hemorrhage or ruptured aneurysm.

**Pathophysiology of Chronic Daily Headache**

The pathophysiology of CDH is still poorly understood and may depend on the type of disorder. For example, if the diagnosis is of chronic migraine, the pathophysiology may be similar to that of EM, but because of a progression of what is happening neurologically and centrally, the end result may be CDH. There may be a diminished threshold for trigeminovascular neuronal activation, hyperexcitability of brain neurons related to the individual with EM, enhanced ascending facilitation resulting in more headache activity, and/or decreased, impaired, descending inhibition from higher pain modulating centers affecting the individual, resulting in a very low threshold for developing headache and pain that is unremitting.

Burstein et al has alluded to the development of early allodynia in EM. If it is untreated, the patient may develop a chronic alldynia, and this may represent one of the pathophysiologic findings in chronic migraine. An individual may have a chronic alldynia that has progressed from the episodic type. Specifically, the authors reported that animal studies on the mechanism of migraine show that intracranial pain is accompanied by increased periorbital skin sensitivity. These findings suggest that the pathophysiology of migraine involves not only irritation of meningeal perivascular pain fibers but also a transient increase in the responsiveness (ie, sensitization) of central pain neurons that process information arising from intracranial structures and skin. The authors evaluated whether the increased skin sensitivity observed in animals also develops in humans during migraine attacks. The investigators found that in 79% of the patients, migraine was associated with cutaneous alldynia, suggesting that hyperexcitability of a specific central pain pathway plays a role in migraine.

Some of the changes to brain tissue that have been noted and may play a role in CDH include iron deposition, which may lead to neuronal damage and progressive disease, thus making these individuals more susceptible to a daily headache. Specifically, Welch et al examined the periaqueductal gray matter (PAG), which is central to the functioning of the descending antinociceptive neuronal network. The authors studied iron homeostasis in the PAG as an indicator of function in patients with EM between attacks and patients with CDH during headache. They used magnetic resonance imaging (MRI) for mapping in 17 patients with EM, 17 patients with CDH and medication overuse, and 17 normal adults. The authors concluded that iron homeostasis, which was impaired in those patients with both migraine and CDH but not in control subjects, may be a “generator” of migraine attacks, potentially by causing dysfunctional control of the trigeminovascular nociceptive system.

Finally, a recent neuroimaging study by Kruit et al conducted on Dutch adults with CDH determined that in the cerebellar region of the posterior circulation territory, patients with migraine had a higher prevalence of infarct than control subjects (5.4% vs 0.7%; \( P = .02 \); adjusted odds ratio, 7.1; 95% confidence interval, 0.9–55). The highest risk was in patients with migraine with aura who had 1 attack or more per month. Women were at highest risk for deep white matter lesions, and the risk increased as headache frequency increased. Still, many unanswered questions concern-
ing the pathophysiology of CDH remain, including whether perhaps the presence of a patent foramen ovale is yet another risk factor or a mere association.\textsuperscript{12,13}

**The Personal and Societal Impact of Chronic Daily Headache**

There can be no doubt that living with chronic pain on a daily basis takes a toll on an individual and his or her family, friends, coworkers, and employer. The psychiatric comorbidities, issues related to disability and economics, are fraught with consequences of a personal and societal nature. For example, D’Amico et al assessed functional disability and health-related quality of life (QOL) among 150 Italian patients suffering from chronic migraine and medication overuse headaches and 22 subjects with chronic cluster headaches.\textsuperscript{14} They used the Migraine Disability Assessment (MIDAS) questionnaire, shown in the Figure,\textsuperscript{15} and the 36-Item Short-Form Health Survey (SF-36) to determine the impact of the headaches. Patients with both conditions had significantly lower scores on most SF-36 scales. MIDAS scores also revealed that patients had impairment of functioning and productivity with effects on their well-being and ability to fulfill their usual roles as student, worker, and/or family member.\textsuperscript{14}

In the United States, Bigal et al found similar results using the MIDAS questionnaire to evaluate 182 patients with chronic migraine compared to 86 patients with episodic symptoms.\textsuperscript{16} The group with chronic migraine had more total headache-days over 3 months (66.7 vs 15.5, \textit{P} < .001), missed more days of work or school (5.3 vs 2.3, \textit{P} = .0007), had more reduced effectiveness days at work or school (11.9 vs 4.6, \textit{P} = .0001), missed more days of housework (16.5 vs 3.3, \textit{P} < .0001), and missed more days of family, social, or leisure activities (7.0 vs 5.5, \textit{P} = .03). The group with chronic migraine was more likely to be in MIDAS grade IV (64.3\% vs 43.2\%, \textit{P} = .001), reflecting severe disability. Therefore, the authors concluded that patients with chronic migraine demonstrate “remarkable impairment of their daily activities and are severely burdened by their headache syndrome.”\textsuperscript{16}

Indeed, several studies now reveal impaired QOL from not only the United States and Europe, but also Asian

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**Figure. Migraine Disability Assessment Questionnaire**

Available at: http://www.midas-migraine.net/About_Midas/questionnaire5.pdf

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

Your rating: Total: ___ days

A On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 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.) ___

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Score</th>
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<tbody>
<tr>
<td>I</td>
<td>Minimal or infrequent disability</td>
<td>0–5</td>
</tr>
<tr>
<td>II</td>
<td>Mild or infrequent disability</td>
<td>6–10</td>
</tr>
<tr>
<td>III</td>
<td>Moderate disability</td>
<td>11–20</td>
</tr>
<tr>
<td>IV</td>
<td>Severe disability</td>
<td>21+</td>
</tr>
</tbody>
</table>

countries. Depression scores in patients with CDH are worse, and the likelihood of hypertension, ingestion of caffeine, and analgesic overuse resulting in medication overuse headache are all greater with CDH.17-20

CONCLUSIONS

Chronic daily headache is a fairly common disorder throughout the world and is often associated with medication overuse. Migraine of an episodic nature may progress to CDH, affecting individuals during their most potentially productive years. The revised IHS 2004 classification adds some flexibility to classifying these disorders and includes many new disorders to the taxonomy. Several new disorders are characterized and need to be distinguished within CDH, such as hemicrania continua, new daily persistent headache, and minor head injury posttraumatic headache. Diagnosis of the specific disorder is helpful and important for effective therapy; for example, the use of indomethacin is extremely effective, but also extremely selective, to the disorder of hemicrania continua. Some inroads have been made with regard to pathogenesis, including the hypothesis that there is hypersensitivity of neurons in the central nervous system and that neurotransmitters and neuromodulators play roles in chronic pain mechanisms. Phenomena, such as iron deposition in the midbrain, and the association of chronic migraine with structural change on MRI of the brain, also are interesting findings that may have a role in this disorder. Whichever cause is ultimately held accountable, it is certain that the CDH has a major impact on the individual, family, and society, with major economic costs and significant comorbidity. New treatment modalities will hopefully offer greater benefit to patients with CDH and are urgently needed.

REFERENCES