

# New Daily Persistent Headache: A Question and Answer Review

A specialist provides clarification on the diagnosis and management of the challenging condition known as NDPH.

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**A**bout four percent of the adult population have one of the primary types of chronic daily headache (CDH). CDH is headache of long duration (more than three months) occurring on at least 15 days per month with untreated headache lasting longer than four hours. Primary types (not related to structural dysfunction or other illness) are diagnosed after the exclusion of the many possible causes of secondary headaches by history, examination, and testing, as indicated, which include chronic migraine, chronic tension-type headache, hemicrania continua, and new daily persistent headache (NDPH). Vanast provided the first description of NDPH in 1986.<sup>1</sup>

## **What are the symptoms of NDPH? What are the diagnostic criteria?**

In order to meet the diagnostic criteria as defined by the International Classification of Headache Disorders 2nd edition (ICHD-2) from 2004, the headache must occur daily and be unremitting from within three days of onset.<sup>2</sup> The onset is often so striking that most patients can identify the exact day that their headache disorder began.<sup>3,4</sup> The headaches can vary greatly in their clinical presentation and duration. Eighty percent of patients experience a

constant headache throughout the day with no pain-free period.<sup>5</sup> For most patients, the baseline level of pain is mild to moderate in intensity and bilateral in up to 94 percent.

The headaches are typically described as throbbing and/or pressure-like, generalized or unilateral in 11 percent, and localized to any head region with migraine symptoms such as nausea, photophobia, phonophobia, and lightheadedness present in over 50 percent with occasional vomiting.<sup>6,7</sup> Cranial autonomic symptoms occur with painful exacerbations in 21 percent, and cutaneous allodynia may be present in 26 percent.<sup>7</sup> There are rare reports of an associated visual aura and unrelated frequent episodic bilateral facial flushing with painful exacerbations (usually lasting for a few minutes).<sup>7</sup> A history of prior depression or anxiety is present in 51 percent, and symptoms of current depression are present in 62 percent.

The ICHD-2 criteria are overly restrictive because they exclude the presence of more than one migraine feature, which are present in about 50 percent of children and adults with abrupt onset chronic daily headaches.

Robbins et al. have proposed a revised version of ICHD-2 criteria, creating a NDPH-ICHD subset (the

current guidelines) and a NDPH-mf subset (those with migraine type features).<sup>7</sup> They further divided these groups into three prognostic subgroups: persisting type with a continuous headache from onset, a remitting type where the headache either resolves completely or occurs less than five days per month for at least three months, and a relapsing-remitting type where pain-free periods are interspersed among times of continuous headaches. The authors found that the two subtypes (NDPH-ICHD and NDPH-mf) had very similar demographic, clinical and prognostic features.

### **What is the epidemiology?**

The age of onset ranges from six to greater than 70 years old, with a mean of 35 years.<sup>6,7</sup> NDPH is more common in females with a 2.5:1 ratio in adults<sup>7</sup> and 1.8:1 ratio in children. NDPH is rare. A population-based cross sectional study of 30,000 persons aged 30-44 years found a one-year prevalence of 0.03 percent. In patients with chronic daily headache seen in tertiary headache clinics, NDPH is diagnosed more often in children and adolescents (13-35 percent)<sup>10</sup> than in adults (1.7-10.8 percent).<sup>9</sup> In one study, 25 percent had a preexisting history of a primary headache disorder (episodic tension type headache in 18.3 percent or episodic migraine seven percent).<sup>7</sup>

### **What is the pathophysiology?**

The pathophysiology of NDPH is unknown. There have been several studies postulating a link between a preceding flu-like or upper respiratory infection in 14-30 percent,<sup>6,7</sup> a stressful life event in 10-12 percent,<sup>5,6,7</sup> or extracranial surgery in seven to 12 percent of patients.<sup>5,6</sup> Cervical joint hypermobility<sup>11</sup> and defective internal jugular venous drainage<sup>12</sup> have also been suggested as causes.

### **What is the differential diagnosis?**

The diagnosis of primary NDPH is one of exclusion as appropriate of a long list of other daily headaches.<sup>13</sup> Remember the definition of NDPH requires a daily unremitting occurrence within three days of onset, which helps distinguish NDPH from chronic migraine and tension-type headache, which begin as episodic

types with gradual escalation. There may be overlap of symptoms with hemicrania continua as, 11 percent of cases of NDPH may be unilateral and cranial autonomic symptoms may be present with exacerbations. However, indomethacin produces complete and sustained pain relief in hemicrania continua but not in NDPH.

A few series provide information on the potential yield of neuroimaging. For example, Wang et al.<sup>14</sup> retrospectively reviewed the medical records and MRI images of 402 adult patients (286 women and 116 men) who had been evaluated by the neurology service with a primary complaint of chronic headache (a duration of three months or more) and no other neurologic symptoms or findings. Major abnormalities (a mass, caused mass effect, or was believed to be the likely cause of the patient's headache) were found in 15 patients (3.7 percent), including a glioma, meningioma, metastases, subdural hematoma, arteriovenous malformation, three cases of hydrocephalus, and two Chiari I malformations. Major abnormalities were found in 0.6 percent of patients with migraine, 1.4 percent of those with tension headaches, 14.1 percent of those with atypical headaches, and 3.8 percent of those with other types of headaches.

NDPH mimics or secondary headaches to consider include the following: medication overuse, postmeningitis headache, chronic meningitis, sphenoid sinusitis, neoplasms, chronic subdural hematoma, posttraumatic headaches, hypertension, spontaneous intracranial hypotension, pseudotumor cerebri (idiopathic and secondary intracranial hypertension), cervical artery dissections, cerebral venous thrombosis, arteriovenous malformation, dural arteriovenous fistula, unruptured intracranial saccular aneurysms (possibly), Chiari malformation, temporal arteritis, cervicogenic, and temporomandibular joint dysfunction.

For example, spontaneous intracranial hypotension (SIH) syndrome often presents with a headache that is present when a patient is upright but is relieved by lying down, or by an orthostatic headache. However, as SIH syndrome persists, a chronic daily headache may be present without orthostatic features. Neck or interscapular pain may

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precede the onset of headache in some cases by days or weeks. MRI abnormalities of the brain and spine are variably present in perhaps 90 percent of cases. An MRI scan of the brain may reveal diffuse pachymeningeal (dural) enhancement with gadolinium without leptomeningeal (arachnoid and pial) involvement and, in some cases, subdural fluid collections, which return to normal with resolution of the headache.<sup>15</sup>

Cervical artery dissections, which can present with headache or neck pain alone,<sup>16</sup> can be a rare cause of new daily headaches. Occasionally, the headaches can persist intermittently for months and even years and can lead to a pattern of chronic daily headaches especially after cervical carotid artery dissection. Magnetic resonance angiography is the study of choice for detection, as carotid ultrasound is operator dependent and less sensitive.

Temporal arteritis should always be considered with new onset headaches over the age of 50. As the rare exception, in a Canadian study of 141 consecutive patients presenting to a neuro-ophthalmology practice, there was one patient under the age of 50 (age 47).<sup>17</sup>

### **What is the treatment?**

There are no prospective placebo controlled trials of preventive treatment. NDPH is typically treated empirically using the same preventive medications for chronic tension type<sup>18</sup> or chronic migraine alone or in combinations. Muscle relaxants such as baclofen or tizanidine may be helpful.<sup>5</sup> For some patients, headache escalations may respond to triptans.<sup>7</sup> In children and adolescents, the most commonly used medications include the tricyclic antidepressants (amitriptyline) and antiepileptics (topiramate, valproic acid, gabapentin) and less often propranolol, selective serotonin reuptake inhibitors and muscle relaxants.<sup>19</sup> Medication overuse can be present in up to 45 percent of patients.<sup>7</sup> In a small series of patients, Grosberg has found clonazepam 0.5mg qhs up to 1mg bid with an extra 0.5-1.0mg prn for breakthrough pain effective (Brian Grosberg, MD, personal communication). Although continuous opioid therapy is sometimes used for refractory

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headaches including NDPH, this therapy is usually not effective and needs to be carefully monitored by experienced physicians for adverse events.

An inpatient regimen of IV DHE may be of benefit.<sup>20</sup> Intravenous haloperidol<sup>21</sup> and intravenous magnesium may be efficacious. Some patients may benefit with greater occipital nerve blocks.<sup>22</sup> Some patients anecdotally benefit from cervical trigger point injections and physical therapy. It is not known whether Botox injections are efficacious, as there is only a single case report published. Intravenous methylprednisolone (1,000mg daily for five days) in nine patients followed by oral steroids (60mg of prednisolone daily) for two to three weeks in six of the nine was reported as producing complete resolution in all patients with NDPH and a history of antecedent extracranial infection but none of two without.<sup>23</sup> However, only four of nine cases had the NDPH for three months or longer.

Alternative therapies are sometimes tried without evidence of efficacy, including riboflavin, butterbur, coenzyme Q10, magnesium, massage, acupuncture, exercise, physical therapy, chiropractic manipulation, weight loss, and yoga. Some patients undergo surgical procedures, such as septoplasty and occipital nerve decompression without reports of efficacy. Although neuromodulation, especially occipital nerve stimulation may be of benefit for some primary headaches, I can find no reports of efficacy for NDPH although this would be of interest.

### **What is the prognosis?**

Robbins, et al.'s study of 71 patients found three prognostic categories of NDPH patients: 76.1 percent with persistent headaches, 15 percent with remission (time to remission ranged from four months to 54 years with a median duration of 21 months), and eight percent with a relapsing-remitting type (range to first remission three-24 months).<sup>8</sup> In a study of 28 children and adolescents, 20/28 continued to have headache six months to two years later, and only eight of 28 were headache free (three within one year and four within two years).<sup>24</sup> NDPH can be one of the most difficult to treat headache types, which can

result in impairment and disability. Better treatments are clearly needed. ■

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