Chapter 103

# New Daily Persistent Headache

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## DEFINITION OF NEW DAILY PERSISTENT HEADACHE

**International Headache Society (IHS) code and diagnosis:** 4.8 New daily-persistent headache (NDPH)

**World Health Organization (WHO) code and diagnosis:** G44.2 New daily-persistent headache (NDPH)

**Short description:** NDPH is a headache that is daily and unremitting from or almost from the moment of onset, typically in individuals without a prior headache history. NDPH may take either of two subforms: a self-limiting subform, which typically resolves without therapy within several months, and a refractory subform, which is resistant to aggressive treatment.

**Previously used terms:** chronic benign daily headache

## INTRODUCTION

New daily persistent headache (NDPH) was first described by Vanast in 1986 (14) as a benign form of chronic daily headache (CDH) that improved without therapy. In the headache specialist's office NDPH is anything but benign and is felt to be one of the most treatment refractory of all headache conditions. NDPH has now been included in the revised International Classification of Headache Disorders (ICHD-II) as a separate entity (Table 103-1). As there have been only a few studies looking at the clinical characteristics and differential diagnosis of NDPH, these consensus criteria may need to be modified as more data on this syndrome are published. It appears that there are two subtypes of NDPH: a self-limited form, which typically goes away within several months without any therapy, and a refractory form, which remains resistant even to aggressive treatment. NDPH should not be difficult to diagnose in a physician's office based on its profile of headache onset, which should be very precise, and most patients can pinpoint the exact date and some even the exact time their headache began.

## EPIDEMIOLOGY

Even though NDPH has probably been around for centuries, it has only recently been considered a separate diagnosis from chronic tension-type headache, medication-overuse headache, hemicrania continua, or chronic migraine (12). The prevalence of CDH from population-based studies in the United States, Asia, and Europe is about 4 to 5% (12). In those epidemiologic investigations, NDPH was rarely stratified out from the data and the used definition of NDPH varied slightly. Several studies have documented the prevalence of NDPH: Castillo et al. reported that 4.7% of a 2252 population sample from Spain have CDH, of which 0.1% had NDPH (2). Bigal et al.(1) noted that 10.8% of 638 patients with CDH in a headache specialty clinic had NDPH, while Koenig et al. found that 13% of a pediatric CDH population, surveyed from selected pediatric headache specialty clinics, had NDPH (4).

## CLINICAL FEATURES

There are only three case series in the literature dedicated to describing the clinical characteristics of NDPH. Vanast(14) noted a female predominance in 45 patients (26 women and 19 men) and an earlier age of onset in women. Seventy-two percent of the patients stated the pain of NDPH was constant. Pain location was temporal in 9 of 45 patients, temporal plus other areas in 14 patients, occipital and extra sites in 20 patients, and holocranial in 5 patients. "Migrainous" associated symptoms were noted in a large percentage: nausea 55%, vomiting 12%, photophobia 34%, and phonophobia 37%.

Li and Rozen (5) published the largest study to date describing the syndrome of NDPH based on a retrospective chart review. Female:male gender ratio was 2.5:1. Age of onset ranged from 12 to 78 years with a peak age of onset in the second and third decade in women and the fifth decade in men. Eighty-two percent of patients were able to

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**TABLE 103-1 ICHD-II Criteria for New Daily Persistent Headache**

**IHS code and diagnosis:** 4.8 New daily persistent headache

A. Headache for >3 months fulfilling criteria B through D
B. Headache is daily and unremitting from onset or from 3 <days from onset
C. At least two of the following pain characteristics:
   1. Bilateral location
   2. Pressing/tightening (nonpulsating) quality
   3. Mild or moderate intensity
   4. Not aggravated by routine physical activity such as walking or climbing stairs
D. Both of the following:
   1. No more than one of photophobia, phonophobia, or mild nausea
   2. Neither moderate or severe nausea nor vomiting
E. Not attributed to another disorder

pinpoint the exact day their headache started. Headache occurred in relation to an infection or flulike illness in 30%, extracranial surgery in 12%, and a stressful life event in 12%. A prior headache history was found in 38% (episodic migraine 19%, episodic tension-type headache 2%, and unspecific headache 17%). In 79%, the pain was continuous throughout the day. Pain intensity was moderate in 61%, while 21% experienced severe pain. Headache location was bilateral in 64% while almost 60% had some pain localized to the occipital–nuchal region, 44% experienced retroorbital pain, and 18% holocranial pain. Headache quality was described as a throbbing sensation in 55% and pressurelike in 54%. Nausea occurred in 68%, photophobia in 66%, phonophobia in 61%, vomiting in 23%, osmophobia in 23%, and vertigo in 11%. Aura-type symptoms, including visual photopsias and seeing zigzag lines, were present in a small number of patients. Family history of headache was documented in 29%. Takase et al. (13) looked at the clinical characteristics of NDPH in 30 Japanese patients. There was a male predominance (17 men and 13 women), and age of onset ranged from 13 to 73 years. Headache onset was associated with a stressful life event in 20%, while the remainder could not identify a probable cause. Headache intensity was severe in all patients. Headache quality was a pressure or tightening sensation in 73%, pulsating in 10%, and both pressing and pulsating in 5%. Associated symptoms were rare with mild nausea occurring in 10 patients while only 1 patient had photophobia.

## ETIOLOGY OF NEW DAILY PERSISTENT HEADACHE

Because a number of NDPH patients state that they had a cold or flulike illness when their headache began, an infectious cause can be hypothesized. Some authors have linked Epstein-Barr virus (EBV) infection with NDPH. Diaz-Mitoma et al. (3) identified oropharyngeal secretions of EBV in 20 of 32 patients with NDPH compared with 4 of 32 age- and gender-matched controls. A history of mononucleosis was identified in 12 of the patients. Almost 85% of NDPH patients were found to have an active EBV infection as opposed to 8 in the control group. The authors hypothesized that activation of a latent EBV infection may have been the trigger for the development of a chronic daily headache from onset. EBV titers were tested in seven patients from the Li and Rozen (5) investigation, of whom five had positive titers indicating past but not active infection. Santoni and Santoni-Williams (11) demonstrated evidence of systemic infection in 108 patients with NDPH including *Salmonella*, adenovirus, toxoplasmosis, herpes zoster, EBV, and *Escherichia coli* urinary tract infections.

The mechanistic link between an infection and NDPH is elusive. One may hypothesize an activated immune response to a new or reactivated viral infection leading to an autoimmune-triggered headache possibly by setting up a state of continuous neurogenic inflammation. The virus itself could in some way activate or damage the trigeminal system, leading to daily pain. An infectious etiology is not the presumed cause of NDPH in every patient, as almost 40 to 60% of NDPH sufferers have no recognized trigger.

To date, only one study explored causes of NDPH in children (6). Of a cohort of 41 children, 15 had the onset of their headache during a viral infection, and a positive EBV titer was found in 60% (6). Eight developed NDPH after mild head injury, three after a surgical procedure, and one during high altitude camping. Four patients were diagnosed initially with intracranial hypertension but the headache persisted after treatment and normalization of pressures. Finally, five patients had no identifiable inciting event.

## LABORATORY STUDIES

In most instances, laboratory and neuroimaging studies in NDPH are normal. In the Li and Rozen investigation, a brain magnetic resonance imaging or computed tomography scan was completed in 49 patients, of which 66% had normal studies while the remainder had nonspecific imaging findings felt not to be related to the headache condition (5). Cerebrospinal fluid (CSF) data are scant but appear to be normal in adults (5), whereas a low and almost nonexistent CSF protein level was documented in four out of four adolescent patients with NDPH (9). The cause of the low CSF protein level is unknown.

## SECONDARY MIMICS OF NDPH

A diagnosis of primary NDPH is made only after secondary causes have been ruled out. Two disorders in particular can mimic the presentation of NDPH: spontaneous CSF leak

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**TABLE 103-2 Secondary Causes of a Daily Headache From Onset**

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| Cerebral vein thrombosis |
| Low cerebrospinal fluid pressure headache |
| High cerebrospinal fluid pressure headache |
| Carotid or vertebral artery dissection |
| Giant cell arteritis |
| Meningitis |
| Sphenoid sinusitis |
| Cervical facet syndrome |
| Intranasal contact (contact point headache)—pain caused by contact of intranasal structures (e.g., nasal septum and nasal turbinate) |
| Posttraumatic headache |

and cerebral venous sinus thrombosis (7,8). In patients who present with NDPH and are subsequently found to have cerebral vein thrombosis, none of the typical features recognized of the syndrome is present, including history of new onset seizure, focal neurologic deficits, change of consciousness, cranial nerve palsies, and bilateral cortical signs, and there is no evidence of papilledema on funduscopic examination. The differential diagnosis for a daily headache from onset is provided in Table 103-2.

## MANAGEMENT

Generally, no specific treatment strategy can be recognized for primary NDPH. Most headache specialists will treat NDPH with the same medications they use to treat migraine, even though based on response NDPH and migraine are two completely separate syndromes.

Takase et al. evaluated the effect on NDPH of treatments such as muscle relaxants, tricyclic and selective serotonin reuptake inhibitor (SSRI) antidepressants, and valproic acid (13). In 8 of 30 patients, treatment was deemed very effective (daily headache intensity 3/10 or less), 1 patient had a moderately effective response (daily headache intensity 4 to 5/10), 6 patients had a mildly effective response (daily headache intensity 6 to 7/10), and 15 patients showed no response to treatment. Only two patients developed headache-free time after therapy; the remainder continued with daily head pain, although some had an improved quality of life. The authors concluded that NDPH is overall unresponsive to typical headache treatment (13).

Recently, five patients were presented in whom successful treatment of NDPH was obtained with gabapentin or topiramate (10).

## PROGNOSIS

The self-limited form of NDPH has a good prognosis, as patients appear to improve without any intervention. In Vanast et al.'s (14) initial description of NDPH, 30% of affected men were headache free at 3 months, and 86% were headache free at 2 years. In women, 30% were headache free at 3 months, and 73% were headache free at 2 years.

In patients with the refractory form of NDPH, conditions may not remit for years to decades, even with aggressive treatment. Typically, NDPH patients will start to overuse medications because they have a daily headache, but unlike in medication-overuse headache, NDPH patients do not improve once the overused compound is stopped.

## REFERENCES

1. Bigal ME, Sheftell FD, Rapoport AM, Lipton RB, Tepper SJ. Chronic daily headache in a tertiary care population: correlation between the International Headache Society diagnostic criteria and proposed revisions of criteria for chronic daily headache. *Cephalalgia* 2002;22:432–438.
2. Castillo J, Munoz P, Guitera V, Pascual J. Epidemiology of chronic daily headache in the general population. *Headache* 1999;38:497–506.
3. Diaz-Mitoma F, Vanast WJ, Tyrell DL. Increased frequency of Epstein-Barr virus excretion in patients with new daily persistent headaches. *Lancet* 1987;1:411–415.
4. Gumbardella A, Pirritano D, Labate A, et al. Cerebral venous thrombosis and isolated intracranial hypertension without papilledema in CDH. *Neurology* 2001;57:31–36.
5. Koenig MA, Gladstein J, McCarter RJ, Hershey AD, Wasiewski W, and the Pediatric Committee of the American Headache Society. Chronic daily headache in children and adolescents presenting to tertiary headache clinics. *Headache* 2002;42:491–500.
6. Li D, Rozen TD. The clinical characteristics of new daily persistent headache. *Cephalalgia* 2002;22:66–69.
7. Mack K. What causes new daily persistent headache in children? *Cephalalgia* 2003;23:609.
8. Mokri B. Low cerebrospinal fluid pressure syndromes. *Neurol Clin* 2004;22:55–74.
9. Rozen T, Haynes G, Range C, Swidan S. Low cerebrospinal fluid protein levels in adolescents with new daily persistent headache [Abstract]. *Neurology* 2004;62[Suppl 5]:A336.
10. Rozen TD. Successful treatment of new daily persistent headache with gabapentin and topiramate [Abstract]. *Headache* 2002;42:433.
11. Santoni JR, Santoni-Williams CJ. Headache and painful lymphadenopathy in extracranial or systemic infection: etiology of new daily persistent headaches. *Intern Med* 1993;32:530–533.
12. Silberstein SD, Lipton RB. Chronic daily headache, including transformed migraine, chronic tension-type headache and medication overuse. In: Silberstein SD, Lipton RB, Dalessio D, eds. *Wolff's headache and other head pain*. Oxford: Oxford University Press, 2001:247–282.
13. Takase Y, Nakano M, Tatsumi C, Matsuyama T. Clinical features, effectiveness of drug based treatment and prognosis of new daily persistent headache: thirty cases in Japan. *Cephalalgia* 2004;24:955–959.
14. Vanast WJ. New daily persistent headaches: definition of a benign syndrome. *Headache* 1986;26:317.