New daily persistent headache

If you don't ask they won't tell

MICHAEL ELLER MB BS, FRACP

New daily persistent headache (NDPH) is a morbid headache condition that is under-recognised in the community. It is likely more common in the adolescent population. Initial investigations to exclude a secondary cause of headache are appropriate. An accurate diagnosis helps the patient understand their illness and leads to expectations that mirror their real-world experience, strengthening the therapeutic relationship and diminishing risk of harm. A neurologist and other care providers such as a psychologist should be involved early in the course of management to optimise the chance of success.

Unremitting headache without any appreciable response to simple analgesics can motivate people and their families to seek medical attention, particularly when this symptom is novel. Of patients with daily headache of over three months in duration, a proportion describe this symptom as having begun on a specific day. This is defined as new daily persistent headache (NDPH).[1]

First described in 1986, NDPH is a rare headache condition that is likely underdiagnosed, with an estimated one-year prevalence of 0.03% of the adult population.[2,3] Although a personal or family history of headache may be forthcoming, this is not necessary or even typical. The illness can affect both sexes but has a slight female preponderance, and is more common in the adolescent population.[4]

A diagnosis of NDPH unfortunately tends to presage a refractory, difficult and prolonged clinical course. Recognition of the diagnostic entity is important as it truncates the patient's diagnostic journey and alleviates the stress of this phase, hopefully leading to better coping strategies and positive reinforcement of therapeutic relationships. Early involvement of a neurologist once initial investigations and treatment trials have been exhausted is recommended.

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Dr Michael Eller is a Neurologist with international subspecialty training in headache. He practices at Monash Medical Centre, has an appointment at Monash University and is actively involved in the Australia and New Zealand Headache Society (ANZHS).

Key points

- New daily persistent headache (NDPH) presents as an unremitting headache that begins on a given day and is likely more common in adolescents than older adults.
- It requires distinct work-up and management and is therefore important to recognise.
- NDPH can be considered a syndrome in that a secondary cause must be excluded. After adequate work up, NDPH can be considered a primary headache condition.
- The NDPH phenotype can be bland or demonstrate migrainous features such as photophobia.
- Even a small improvement in pain can significantly improve quality of life.
- NDPH tends to be ongoing and refractory to treatment, with a high incidence of psychological comorbidity. A multidisciplinary approach to management is therefore recommended.

History

Headache is a common complaint brought to medical practitioners. Two to 3% of the population suffer from some sort of headache every day although patients will often not volunteer their level of discomfort on days of milder head pain.[5] Discomfort of protean or an unfamiliar nature will not necessarily be relayed by the patient as headache, even if it is an ache in the head: common examples include a sensation of vice-like pressure or bilateral sinus fullness. Therefore, a headache history must be sought – it will not necessarily be provided by the patient. Questions to help elicit such a history are provided in Box 1. Most patients with frequent, intrusive headache have a typical history consistent with chronic migraine. That is, their headache burden began as an intermittent problem that waxed and waned over the years only to become more regular and intrusive over time.[6]

A striking and distinct subset of patients with daily headache are able to describe the onset of their symptoms that began within a specific 24-hour period, typically without having much in the way of prior headache symptoms. Most patients look for a causal link to the most plausible temporal event that could have precipitated the illness from their perspective. Representative examples from my clinical experience have included a trip to Luna Park without any potential acceleration-deceleration injury, the shock of a relative's unexpected death and dental work in the preceding month.

Canonical symptoms typically associated with migraine, such as photophobia and nausea, are not uncommon.[4] Even if present, the corollary is not that migraine is a more correct diagnosis but, rather, a thorough history of the symptoms over time should be sought.

1. Sample questions that should be incorporated into a headache history in order to diagnose new daily persistent headache

- How long has headache been present?
- If present for over three months: Did it begin on a specific day? If so, what were the circumstances of the onset of headache symptoms? Was there any trauma?
- Are there any other associated novel symptoms? Were you unwell in any other way at the time?
- Is there any postural or lateralising aspect to the headache?
- Are there any associated migrainous symptoms such as nausea and photophobia?
- Is there a personal or family history of headache?
- What is the level of discomfort and loss of function associated with this headache? For example, how often are you unable to attend work or do you miss social functions?

Potential secondary causes of persistent headache should be considered when criteria are met for NDPH, as outlined in Box 2. What is particular to NDPH is that headache begins on a specific day. If the patient cannot recall this, NDPH is not the diagnosis. The dichotomy is a primary versus secondary problem; it is important to maintain appropriate suspicion and investigate judiciously in light of the recommendation that common headache complaints such as migraine do not warrant imaging such as an MRI brain.[7,8] Bilateral or holocephalic pain is typical in NDPH, whereas a complaint of unilateral or focal discomfort should represent a prompt to comprehensively exclude an alternative explanation. Symptoms suggestive of an infectious cause may include fever and coryzal complaints. Progressive constitutional symptoms such as weight loss and anorexia may point to a malignant or infectious cause. Reliably worsened headache that comes on with upright posture can be indicative of low intracranial cerebrospinal fluid pressure, while recent weight gain and new headache in a young woman can suggest raised intracranial pressure associated with idiopathic intracranial hypertension. Coincident trauma or surgery suggest other diagnoses as outlined in the *International Classification of Headache Disorders-3* (ICHD-3).[1] A suggested approach to diagnosis is outlined in the Flowchart and in the 'Investigations' section below.

Persistent headache can have a significant impact on quality of life.[4,9] Anxiety and depression are common, especially if symptoms fail to remit over months to years. As such, a holistic approach and early involvement of appropriate care providers such as a social worker, psychologist or school counsellor should be considered.

Physical examination

A neurological examination should be performed in patients who report headache. An impression regarding the patient's interactive quality and style, gait and speech should be made as a matter of course. Tone, power, reflexes, co-ordination and sensation of the upper and lower limbs should be assessed. An eye examination interrogating acuity, fundoscopy and visual field as well as ocular motility is essential. If not confident with fundoscopy, ask a colleague to help or, at minimum, request an optometrist review to help exclude evidence of papilloedema (and associated intracranial pressure). Otherwise, the remaining cranial nerves (CNs) should be examined, particularly the trigeminal (5th CN) and facial (7th CN) nerves.

Blood pressure, temperature and vital signs should be noted. Nuchal rigidity should be excluded. Other systems can be examined if the history is indicative. For example, comorbid cough and weight loss in a particular demographic may prompt a respiratory examination and check for lymphadenopathy – tuberculosis or carcinomatous meningitis may need to be eliminated as a potential cause of headache.

Investigations

As with any headache complaint, novelty, the degree of discomfort and associated signs and symptoms should direct and triage any search to exclude a secondary cause. Unlike patients with history typical of migraine and a normal neurological examination, patients with NDPH should undergo an MRI brain with and without contrast. Simple blood tests should be conducted including a full blood examination; electrolyte, urea and creatinine levels; comprehensive metabolic panel; liver function tests; C-reactive protein level; thyroid stimulating hormone level; antinuclear antibody test and a pregnancy test if relevant. This is not a comprehensive list, of course.

If a viral aetiology is suspected, tests can be ordered, with the caveat that sera can be hard to interpret if acute and convalescent titres are not available for comparison. The index of suspicion regarding a secondary viral aetiology will determine the thoroughness of investigations – liaise with an infectious disease consultant if the clinical suspicion is high.

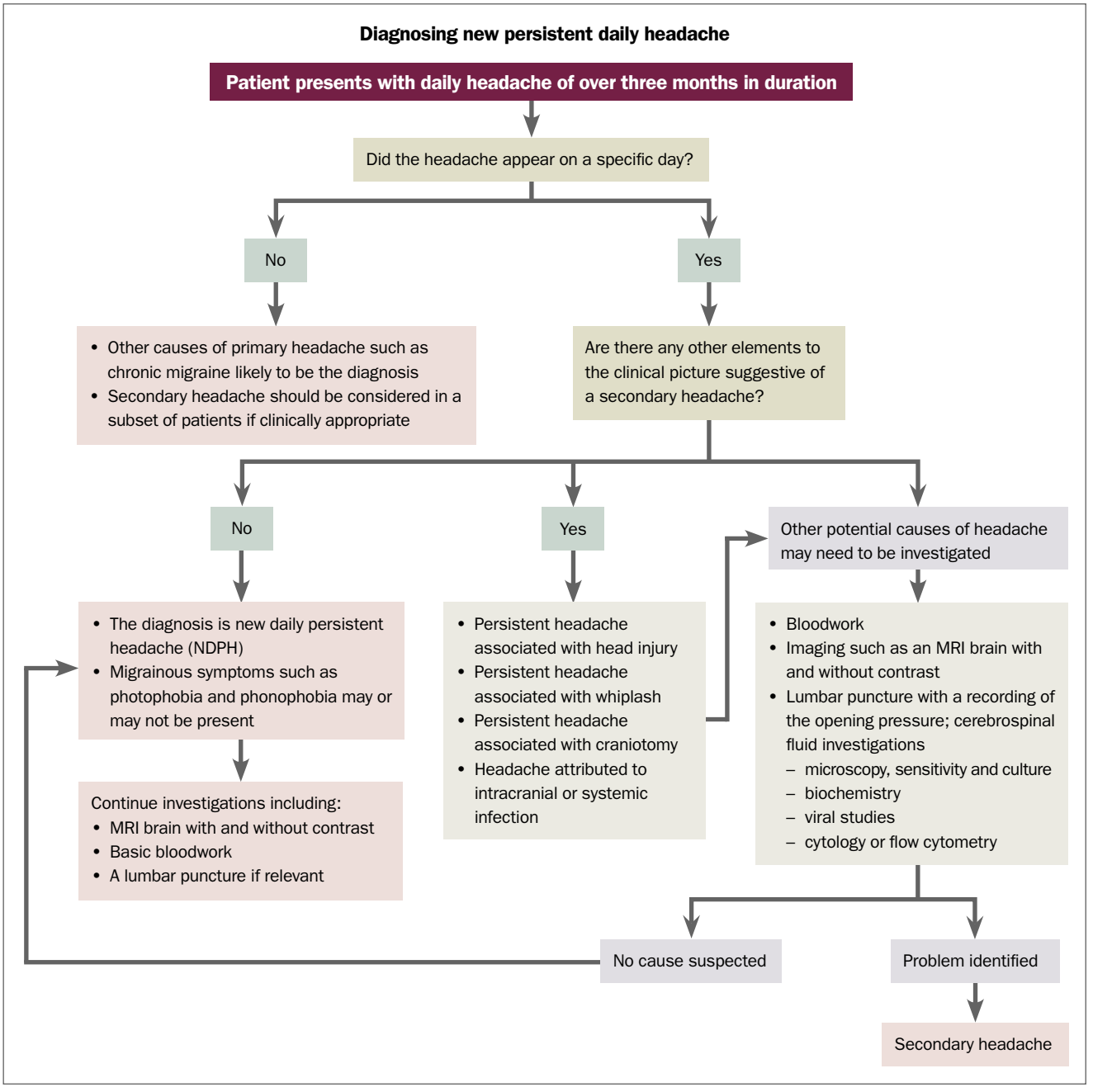
If an infective or malignant aetiology is suspected, assessment of the cerebrospinal fluid is appropriate, as outlined in the Flowchart. The opening pressure should always be checked in this context – it must be requested specifically, as it is not a routine

2. *International Classification of Headache Disorders*-3 (ICHD-3) criteria for new daily persistent headache[1]

Previously used terms
Chronic headache with acute onset; de novo chronic headache

Description
Persistent headache, daily from its onset, which is clearly remembered. The pain lacks characteristic features, and may be migraine-like or tension-type-like, or have elements of both.

Diagnostic criteria
- **A.** Persistent headache fulfilling criteria B and C
- **B.** Distinct and clearly-remembered onset, with pain becoming continuous and unremitting within 24 hours
- **C.** Present for over 3 months
- **D.** Not better accounted for by another ICHD-3 diagnosis



element of this investigation outside of specialist neurological care. This procedure is simply performed with a disposable manometer and can be achieved in any context in which the lumbar puncture is being conducted.

If whiplash injury or other trauma is a likely precipitant and the patient was not imaged contemporaneously, other investigations such as an MRI cervical spine can be considered. Note that if this is the case, there will likely be more appropriate headache designations under the ICHD-3, such as persistent headache associated with whiplash.[1]

Therapies

Once a secondary cause of NDPH has been excluded, or in parallel with the initial work-up, treatment trials should commence to try to ameliorate discomfort. NDPH can be a disabling condition with a potentially enormous impact on patient and family wellbeing, especially when the problem emerges in formative years.

Acute medications such as NSAIDs and triptans – sumatriptan for example – are typically of limited use, although occasionally can be useful for headache exacerbations. Headache tends to be continuous and

relatively uniform in semiology and intensity. Early avoidance of opioids and over-the-counter medications will avoid addiction and/or other sequelae such as medication overuse leading to headache worsening. To reiterate, acute medications tend to be ineffective in NDPH and should be used sparingly, if at all.

Pharmacological strategies for managing NDPH mirror the approach for chronic migraine. It is a question of trial and error in a way that is tailored to the patients' comorbidities and preferences. Many repurposed drugs used in treatment trials for migraine can have significant side effects leading to an early sense of treatment fatigue and futility in the patient and clinician alike.[8] Common pitfalls such as inadequate treatment trials (in terms of duration and dosing), failure to stop unhelpful medications and inadequately conveying potential medication side effects should be avoided.

There is some evidence for the use of botox in NDPH with or without migrainous symptoms.[10] Anecdotally, some patients who have received medications directed at the calcitonin-gene related peptide ligand or canonical receptor, such as galcanezumab or erenumab, respectively, have demonstrated occasional benefit.

Therapeutics that are usually considered 'transitional' and are deployed in managing medication overuse and/or attempting to move a patient from a chronic to an episodic migraine burden can be trialled in NDPH. The impetus is obvious for clinicians who have managed patients with this condition – there is significant morbidity and desperation can emerge. Any improvement will be welcomed, even one to two points on a 10-point verbal analogue scale: for example, a 6/10 headache may enable a teenager to socialise and study whereas an intensity of 8/10 renders them bedbound. As such, quality of life and level of function can improve significantly even with a change of small magnitude.

Transitional therapies that can be considered would typically need the involvement of a pain specialist or neurologist. An outpatient example includes a greater occipital nerve block. Inpatient examples include intravenous lignocaine, dihydroergotamine or ketamine. Although a robust evidence base is lacking, these therapeutics can be of value in the medium term and certainly have a place in managing this condition.

Adolescent healthcare units associated with public hospitals may facilitate access to helpful input from allied health professionals such as a psychologist to help optimise mental health or an exercise physiologist to provide a framework (if needed) to maintain physical activity despite headache. Hospital-based pain units, both private and public, often have associated practitioners who can help, such as physiotherapists (who can provide strategies to maintain physical activity) and social workers, facilitating the benefits of a team approach to patient care. Such support should not replace medication trials but can be a useful and appreciated adjunct in the face of a difficult to treat, chronic problem, especially in younger patients.

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Conclusion

New daily persistent headache is an uncommon, distinctive and often disabling headache condition that is under-recognised in the community. A thorough set of investigations to exclude a secondary cause of headache is appropriate. Treatment trials can be effective, even if less reliably so than in other headache conditions such as chronic migraine. An accurate diagnosis helps the patient and their family plan appropriately and leads to expectations that mirror their real-world experience, allowing them to have a sense of control and understanding of the condition. Appropriate allied health input should be offered. Neurologists should be involved early in the course of management to optimise the chance of successful diagnosis and management. **PMT**

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COMPETING INTERESTS: None.