NEW DAILY PERSISTENT HEADACHE

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Chronic daily headache, defined as headache on 15 days or more per month for more than three months, is covered generally in another section of this supplement. However, because the syndrome of "new daily persistent headache" (NDPH) is so clinically distinct (table 1), and has an interesting range of secondary possibilities that are curable, we have elected to highlight the problem here. This is not to imply any linked pathophysiology but simply to highlight what is a clinically useful concept. From a nosological point of view most of what is covered here could be placed in the various parts of the classification system of the International Headache Society.[1] It serves both patients and clinicians to highlight this syndrome because the implications of missing the diagnosis can be so profound. NDPH can have both primary[2] and secondary forms (table 2). More general texts address the many surrounding issues of headache diagnosis and management.[3 4]

CLINICAL PRESENTATION

The patient with NDPH presents with a history of headache on most if not all days that began from one day to the next. The onset of headache is abrupt, often moment-to-moment, but at least in less than a few days (where three is suggested as an upper limit).[4] The classical history, if that term is yet appropriate, will be for the patient to recall the exact day and circumstances, so from one moment to the next a headache develops that never leaves them. This presentation triggers certain key questions about the onset and behaviour of the pain. These need to be woven with the more generic questions that one asks a patient with persistent headache, to form a provisional diagnosis. The pressing issues arise from considering the differential diagnosis, particularly of the secondary headache forms. Although subarachnoid haemorrhage is listed for some logical consistency, as the headache may certainly come on from one moment to the next, it is not likely to produce diagnostic confusion in this group of patients.

Others have covered the diagnosis[5] and the pitfalls in diagnosis,[6] and the issues surrounding late imaging and management of unruptured aneurysms are beyond the scope of this article.[7 8] Suffice to say that subarachnoid haemorrhage is so important that it must always pass by the clinicians diagnostic formulation if only to be excluded, either by history or appropriate investigation.

SECONDARY NDPH

The secondary causes of the syndrome of NDPH are worthy of consideration, as they have a distinct clinical picture that can guide investigation.

Low CSF volume headache

The syndrome of persistent low cerebrospinal fluid (CSF) volume headache is an important diagnosis not to miss. Again the more immediate version of this problem is commonly encountered in neurology after lumbar puncture. In that setting the headache settles rapidly with bed rest. In the chronic situation the patient typically presents with a history of headache from one day to the next. The pain is generally not present on waking, worsens during the day, and is relieved by lying down. Recumbency usually improves the headache in minutes, and it takes only minutes to an hour for the pain to return when the patient is again upright. The patient may give a history of an index event: lumbar puncture or epidural injection, or a vigorous Valsalva, such as with lifting, straining, coughing, clearing the eustachian tubes in an aeroplane or multiple orgasm. Patients may volunteer, or a history may be obtained, that soft drinks with caffeine provide temporary respite. Spontaneous leaks are recognised, and the clinician should not be put-off the diagnosis if the headache history is typical when there is no obvious index event. It is our experience that as time passes from the index event the postural nature may be less obvious; certainly we have seen cases whose index event was several years before the eventual diagnosis. This can make the diagnosis even more of a challenge. The term "low volume" rather than "low pressure" is used, since there is no clear evidence at which point the pressure can be called low.[9] While low pressures, such as 0–5 cm CSF, are usually identified, a pressure of 14 cm CSF has been recorded with a documented leak.

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Table 1 Proposed diagnostic criteria for new daily persistent headache

A. Headache frequency of 15 days or more per month (on average) for 3 months
B. Duration of headache 4 or more hours per day
C. Acute onset of headache in less than 3 days
D. Excludes trigeminal autonomic cephalgias
E. At least one of the following:
1. Excludes sections 5–12*
2. Disorders in 1 excluded by appropriate investigations
3. If a disorder from 1 exists, it is unlikely to account for the new headache

Trigeminal autonomic cephalagias[20] make up section 3 of the revised International Headache Society classification,[1] previously called cluster headache and related syndromes.
*Refers to International Headache Society classification categories.[1]

Table 2 Differential diagnosis of new daily persistent headache

Primary	Secondary
► Migrainous type	► Subarachnoid haemorrhage
► Featureless (tension type)	► Low CSF volume headache
	► Raised CSF pressure headache
	► Post-traumatic headache*
	► Chronic meningitis

*Includes postinfective forms.
CSF, cerebrospinal fluid.

The investigation of choice is magnetic resonance imaging (MRI) with gadolinium (fig 1), which produces a striking pattern of diffuse pachymeningeal enhancement,[10] although leaks have been documented without such enhancement.[11] This may occur in as many as 10% of cases (B Mokri, personal communication). The finding is so typical that in clinical context we move next to treatment. It is also common to see Chiari malformations on MRI with descent of the cerebellar tonsils being a robust finding.[12] This is important from the neurologist's viewpoint since surgery in such settings simply makes the headache problem worse. It seems appropriate that a neurologist should review any patient considered for such surgery for a headache indication preoperatively. Alternatively the CSF pressure may be determined, or a leak sought with ^{111}In-DPTA CSF studies that can show the leak and any early emptying of tracer into the bladder, indicative of a leak.

Treatment is bed rest in the first instance. We have seen false positive transient improvement in persistent low CSF volume headache with chiropractic and other similar therapies, where the treatment necessitated the patient lying down for some prolonged period. Intravenous caffeine (500 mg in 500 ml saline administered over two hours) is the usual,[13] often very efficacious, treatment. The ECG should be checked for any arrhythmia before administration. Our practice is to move to at least two infusions separated by four weeks after obtaining the clinical history and MRI. Since intravenous caffeine is safe, and can be curative, by an unknown mechanism, it spares many patients the need for further tests. If that is unsuccessful, an abdominal binder may be helpful. If a leak can be identified, either by radioisotope study, computed tomographic (CT) myelogram or spinal T2 weighted MRI, an autologous blood patch is usually curative. In more intractable situations theophylline is a useful alternative that offers outpatient management.[14]

There remains a small group of patients who have the typical history as outlined above in whom a leak is not identified, so that blood patch is inappropriate, or blind blood patch fails. Such patients may have sustained CSF leaks at one point that have resolved, leaving altered CSF dynamics, with perhaps a lowered pressure setting in the choroid plexus, and sensitisation of meningeal afferents. This results in these patients having postural headache without a demonstrable leak. Such cases are therapeutically very challenging, and our approach is to treat the headache as if it were, in the broadest sense, a post-traumatic headache.

Raised CSF pressure headache

As is the case for low CSF pressure states, raised CSF pressure as a cause of headache is well recognised by neurologists. Brain imaging can often reveal the cause, such as raised pressure caused by a space occupying lesion. The particular setting in which patients enter the spectrum of NDPH are those with idiopathic intracranial hypertension who present with headache without visual problems, particularly with normal fundi. It is recognised that intractable chronic migraine can be triggered by persistently raised intracranial pressure.[15] These patients typically give a history of generalised headache that is present on waking, and gets better as the day goes on. It is generally worse with recumbency. Visual obscurations are frequently reported. Fundal changes on raised intracranial pressure would make the diagnosis relatively straightforward, but it is in those without such changes that the history must drive investigation.

If raised pressure is suspected brain imaging is mandatory, and it is most simple in the long run to obtain an MRI, and to include MRV. The CSF pressure should be measured by lumbar puncture, taking care to do so when the patient is symptomatic, so that both the pressure and response to removal of 20 ml of CSF can be determined. A raised pressure and improvement in headache with removal of CSF is diagnostic of the problem. Our practice is to have the fields formally documented even in the absence of overt ophthalmic involvement. Initial treatment will be with acetazolamide (250–500 mg twice daily). The patient may respond in weeks with improvement in headache. If this is not effective we turn to topiramate, which has many actions that may be useful in this setting: carbonic anhydrase inhibition, weight loss, and neuronal membrane stabilisation probably through actions on phosphorylation pathways.[16] A small number of severely disabled patients who do not respond to medical treatment will come to intracranial pressure monitoring and even shunting. This is exceptional and not undertaken without careful work up.

Post-traumatic headache

The issue of post-traumatic headache is a vexed one. The International Headache Society accepts the existence of such a syndrome.[1] Much of the discussion degenerates because of the often quoted medico-legal morass. We use the term to indicate trauma in a very broad way. We have seen NDPH after a blow to the head but more commonly after an infective episode, typically viral, or in one case malarial meningitis. A recent series identified one third of all patients with NDPH reported the headache starting after a flu-like illness.[17] The patient may note a period in which they had a significant infection: fever, neck stiffness, photophobia, and pronounced malaise. The headache starts during that period and never stops. Investigation reveals no current cause for the headache. It has been suggested that some patients with this syndrome have a persistent Epstein-Barr infection,[17 18] but this syndrome is anything but clearly delineated. A complicating factor will

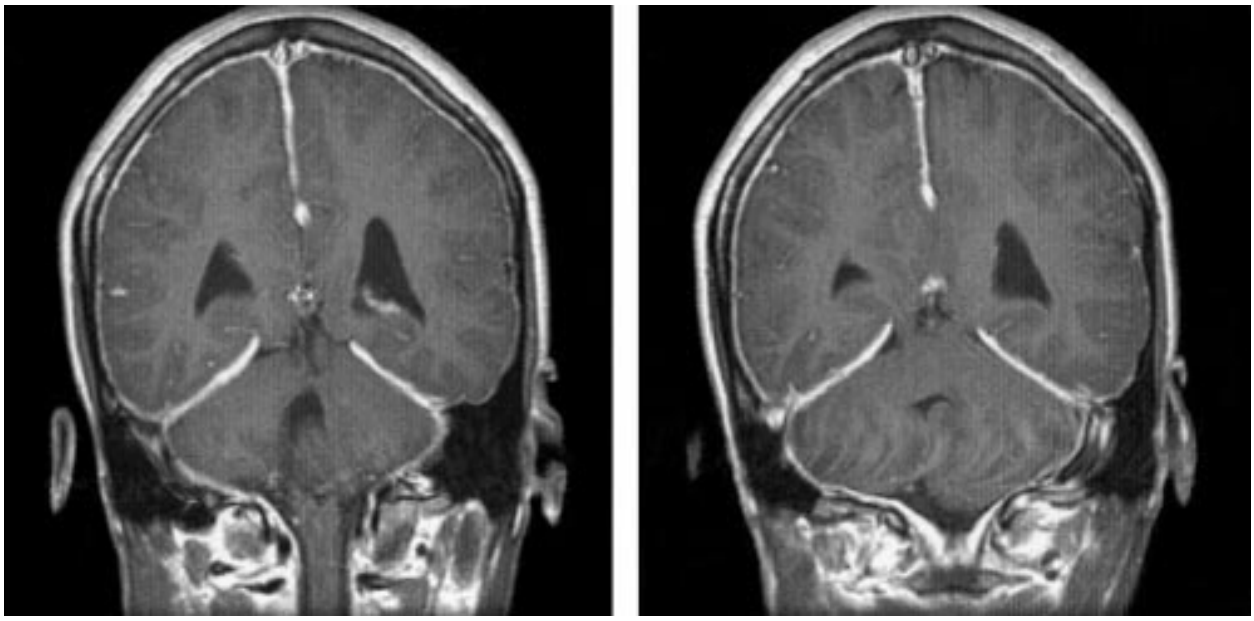

Figure 1 Magnetic resonance image showing diffuse meningeal enhancement after gadolinium administration in a patient with low CSF volume (pressure) headache.

often be that the patient had a lumbar puncture during that illness, so a persistent low CSF volume headache needs to be considered first. We have also seen this syndrome after carotid dissection, subarachnoid haemorrhage, and following intracranial surgery for a benign mass. The underlying theme seems to be that a traumatic event involving the dura mater can trigger a headache process that lasts for many years after that event.

The treatment of this form of NDPH is substantially empirical. We have used tricyclics, notably amitriptyline, and anticonvulsants, valproate and gabapentin, with good effects in a number of patients. In many fewer patients we have found the monoamine oxidase inhibitor phenelzine useful. This group of patients are often rather resistant to treatment. On the positive side the headache seems to run a limited course of 3–5 years,[19] so it will eventually settle. It can certainly be very disabling in that period.

PRIMARY NDPH

Initial descriptions of primary NDPH[2] recognised it to occur in both males and females. Migrainous features were common, with unilateral headache in about one third and throbbing pain in about one third. Nausea was reported in about half the patients, as was photophobia and phonophobia observed again in about half. A number of these patients have a previous history of migraine but not more than one might expect given the population prevalence of migraine.[17]

It is remarkable that the initial report noted that 86% of patients were headache-free at 24 months.[2] It is general experience among those interested in headache management that NDPH of this type is perhaps the most intractable and least therapeutically rewarding forms of headache. In general we classify the dominant phenotype, migraine or tension-type headache, and treat with preventatives according to that subclassification, as for patients with chronic daily headache (see above).

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New daily persistent headache: key points

- New daily persistent headache (NDPH) is a clinical syndrome that identifies patients who were previously headache-free and who, from one day to the next, or over just a few days, develop a persistent headache syndrome
- NDPH has both primary and secondary forms
- All patients with NDPH need a careful history for medication misuse, particularly of over-the-counter medicines
- Important forms of secondary NDPH include cerebrospinal fluid (CSF) pressure abnormalities, either raised CSF pressure or low CSF volume headaches; these need vigorous diagnostic pursuit
- Primary forms of NDPH either have exacerbations that fulfil diagnostic criteria for migraine or are dominated by featureless (tension type) headache
- Primary NDPH is best treated with preventative medications as one would treat the phenotypic presentation of the headache—that is, as chronic migraine or chronic tension-type headache

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WORLD WIDE WEB

Surfing for headache

Web sites for headache vary tremendously in their usefulness to physician and patient. There are those set up by national and international organisations aimed at the clinician and concerned with the structure and organisation of the relevant organisation and management issues. These include the site for the British Association for the Study of Headache (BASH) (http://www.bash.org.uk/), the most useful section of which is probably the British migraine management guidelines. The US equivalent, the site of the American Headache Society (http://www.ahsnet.org/), is more comprehensive with links to useful topics on migraine management. The International Headache Society site (http://www.i-h-s.org/) is aimed particularly at those in clinical headache research with guidelines for drug trials and notice of meetings, but does have some sections of practical use, notably that on recommendations on the risk of stroke in women on the oral contraceptive pill and hormone replacement therapy. The American Academy of Neurology has produced a less dry format and a reasonable headache section aimed more at the patient than physician (http://www.aan.com/), although some advice to patients is somewhat at odds with current thinking—for example, the advice on avoidance of cheese.

For an update on research for the clinician and patient the Institute of Neurology Headache group web site is worth a visit (http://www.ion.bpmf.ac.uk/~headache/headache.html).

It is of no surprise that such a prevalent condition with active patient support groups has generated many patient centred sites. The British sites of note are those of the Migraine Trust (http://www.migrainetrust.org/) and Migraine Action (http://www.migraine.org.uk/). The former is easy to navigate, management centred, emphasising what patients can do to help themselves, including migraine and drug diary cards. The information is by and large accurate and clear cut and probably more up to date than some US sites. The Migraine Action site has detailed and accurate information for the patient who wants to know a bit more and take greater responsibility for their own care. However, I couldn't get some sections of the site to work correctly and many sections are only available to members. The American Council for Headache Education site (http://www.achenet.org/) is easy to navigate and full of useful resources including an interesting migraine art museum. It is particularly good for women and migraine with advice on pregnancy and contraception. The World Headache Alliance site (http://www.w-h-a.org/wha/index.asp) is not as user friendly, but has links to migraine research articles that may be of interest to the patient.

Cluster headache patients tend to be more proactive in patient support groups and interested in research, a reflection no doubt of the severity of the condition and lack of information offered by the medical community. This is reflected in their websites that generally provide much needed support and advice for sufferers and their supporters. The British site for OUCH (uk) (Organization for the Understanding of Cluster Headache) is at http://www.clusterheadaches.org.uk/. This is for patients and operated by patients, offering excellent support for the cluster headache sufferer who often feels abandoned and misunderstood with this terrible condition, including rather poignantly a link to The Samaritans web site. Other useful topics include those on prophylactic medication, an update on current research and, of practical value, details of how to obtain an oxygen regulator through the OUCH loan scheme. The best US cluster headache site is http://www.clusterheadaches.com/. This is a comprehensive site with detailed (and referenced) treatment information, although a notable omission is the optimal use of verapamil. For the medic, the stunning personal experiences of cluster attacks on this site are an invaluable insight into the pain that our patients experience. There is a chat room for sufferers and many useful links for the patient to other cluster sites.

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