Primary chronic headaches of long duration include chronic migraine, chronic tension-type headache, new daily persistent headache, and hemicrania continua. This article reviews the utility of neuroimaging and other testing for diagnosis of these headaches. The presentation and diagnosis of the many secondary headaches that can mimic primary headache types are also discussed, including arteriovenous malformations, spontaneous intracranial hypotension, neoplasms, pseudotumor cerebri, cervical artery dissections, cerebral venous thrombosis, Chiari I malformation, and temporal arteritis. Although the yield of diagnostic testing is low, serious pathology as a cause of chronic headaches can be easily overlooked.

Introduction
The 2004 International Headache Society (IHS) second edition classification [1] of primary chronic daily headaches (CDHs) of long duration includes the following types: chronic migraine (CM; with a recent revision in the definition by the IHS) [2], chronic tension-type (CTT) headache, new daily persistent headache (NDPH), and hemicrania continua (HC). CM and CTT headache occur 15 or more days per month, whereas NDPH and HC are daily. The definitions require that all headache types be present for more than 3 months. The prevalence of CDH is approximately 4% of the general population [3] but includes up to 80% of those who are patients at headache clinics in the United States, most of whom are diagnosed with transformed or chronic migraine.

The diagnosis of these disorders is one of exclusion of secondary disorders based upon the history and a normal examination, and the judicious use of diagnostic testing. For headaches meeting primary criteria, the yield of diagnostic testing decreases with increasing duration of the headache (eg, less for headache present for 3 months and significantly less for headache present for 1 year).

Neuroimaging for CDH
There are a few studies on diagnostic testing specifically for CDH. The yield of CT scan or MRI in patients with any headache and a normal neurologic examination is perhaps 2% [4]. In the case of CTT headache, the US Headache Consortium, which published an evidenced-based guideline, concluded that there was not sufficient information to estimate the probability of important intracranial pathology among patients with nonmigrainous headache and a normal neurologic examination, and recommended comparative studies between MRI and CT [5].

Tsushima and Endo [6] retrospectively reviewed the clinical data and magnetic resonance studies of 306 adult patients (136 men and 170 woman), all of whom were referred for MRI evaluation of chronic or recurrent headache with a duration of 1 month or more, no other neurologic symptoms or focal findings at physical examination, and no prior head surgery, head trauma, or seizure. A total of 55.2% had no abnormalities, 44.1% had minor abnormalities, and 0.7% (two) had clinically significant abnormalities (pituitary macroadenoma and subdural hematoma). Neither contrast material enhancement (n = 195) nor repeated MRI (n = 23) contributed to the diagnosis.

Wang et al. [7] retrospectively reviewed the medical records and MRIs 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 3 months or more) and no other neurologic symptoms or findings. Major abnormalities (a mass, caused mass effect, or if thought to be the likely cause of the patient's headache) were found in 15 patients (3.7%), including a glioma, meningioma, metastases, subdural hematoma, arteriovenous malformation, hydrocephalus (three patients), and two Chiari I malformations. These were found in 0.6% of patients with migraine, 1.4% of those with tension headaches, 14.1% of those with atypical headaches, and 3.8% of those with other types of headaches.

Sempere et al. [8•] reported a study of 1876 consecutive patients aged 15 years or older with a mean age of
38 years who presented to a neurology clinic in Spain with nonacute headache. The types of headache included migraine (49%), tension-type headache (35.4%), cluster headache (1.1%), post-traumatic headache (3.7%), and indeterminate headache (10.8%). One third of the patients had new-onset headache, whereas the other two thirds reported headaches for more than 1 year. Neurologic examination was normal in 99.2% of patients. All patients underwent either an MRI or CT scan. Neuroimaging studies detected significant lesions in 1.2%. Significant intracranial abnormalities were detected in those with headaches and a normal neurologic examination (0.9%; 17 patients). The diagnoses in these patients were pituitary adenoma (three), large arachnoid cyst (two), meningioma (two), hydrocephalus (two), Chiari type I malformation, ischemic stroke, cavernous angioma, arteriovenous malformation, low-grade astrocytoma, brain stem glioma, colloid cyst, and posterior fossa papilloma. Eight of these 17 patients were treated surgically.

Severe, progressive, and new-onset headaches were not associated with higher rates of significant intracranial lesions. Among 118 patients with normal neurologic examinations and normal CT scans, MRI disclosed only one significant lesion, a small meningioma that was not treated surgically. There were no saccular aneurysms detected among the 580 patients who underwent MRI scans, and only one patient had a 5 mm or greater tonsillar descent, a Chiari I malformation that was asymptomatic.

The study by Sempere et al. [8•] provides valuable information about neuroimaging in a large consecutive series of patients referred to a neurology clinic. Questions still remain about the value of MRI versus CT, and MRI without contrast versus with and without contrast, and selection of magnetic resonance angiography (MRA) and magnetic resonance venography (MRV). The low overall detection rate for significant pathology is similar to my experience.

CT versus MRI

If you conclude that CT is as sensitive as MRI for the evaluation of headache, you can miss significant pathology at the patient’s peril and your own medico-legal risk (Table 1). For example, I have reported three types of pathology from my own general neurology practice that were detected on MRI and would have been missed on CT: a hemorrhagic pituitary adenoma mimicking migraine [9], spontaneous low cerebrospinal fluid pressure syndrome mimicking primary cough headache (which would have been missed without the administration of gadolinium) [10], and a pilocytic astrocytoma of the cerebellar hemisphere with mass effect mimicking migraine status [11•]. In addition, I have found occasional incidental saccular aneurysms on MRI scans in my own practice [7], as contrasted to the 0% reported by Sempere et al. [8•]. MRA may detect incidental saccular aneurysms in 2.8% of adults [12]. When available, MRI is the preferred study for the evaluation of headaches, with the exceptions of head trauma, acute headache to rule out subarachnoid hemorrhage, and patients with contraindications to MRI.

Chronic Migraine

The American Academy of Neurology Quality Standards Subcommittee Guidelines state, “Neuroimaging is not usually warranted in patients with migraine and a normal neurologic examination (Grade B)” [13]. Reasons to consider obtaining a scan in cases of suspected CM include an unusual, prolonged, or persistent aura; increasing frequency or severity, or change in clinical features; basilar; confusional; hemiplegic; late-life migraine accompaniments; aura without headache; headaches always on the same side (questionably); post-traumatic; and if requested by the patient or family and friends.

Headache always on the same side is a questionable indication for neuroimaging because 17% of those with migraine without aura and 15% of patients with migraine with aura always have headaches on the same side (side-locked headaches) [14]. However, one potential CM mimic is an arteriovenous malformation, in which side-locked headaches are present in up to 95% of cases [15]. Migraine-like headaches with

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**Table 1. Causes of headache that can be missed on routine CT scan of the head**

<table>
<thead>
<tr>
<th>Vascular disease</th>
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<tr>
<td>Saccular aneurysms</td>
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<tr>
<td>Arteriovenous malformations (especially posterior fossa)</td>
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<td>Subarachnoid hemorrhage</td>
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<td>Carotid or vertebral artery dissections</td>
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<td>Infarcts</td>
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<td>Cerebral venous thrombosis</td>
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<td>Vasculitis (white matter abnormalities)</td>
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<td>Subdural and epidural hematomas</td>
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<td>Neoplastic disease</td>
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<td>Neoplasms (especially in the posterior fossa)</td>
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<td>Meningeal carcinomatosis</td>
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<td>Pituitary tumor and hemorrhage</td>
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<td>Cervicomedullary lesions</td>
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<td>Chiari malformations</td>
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<td>Foramen magnum meningioma</td>
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<td>Infections</td>
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<td>Paranasal sinusitis</td>
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<td>Meningoencephalitis</td>
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<td>Cerebritis and brain abscess</td>
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<td>Low cerebrospinal fluid pressure syndrome</td>
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(Adapted from Evans [42].)
and without visual symptoms can be associated with arteriovenous malformations, especially those in the occipital lobe, which is the predominant location of approximately 20% of parenchymal arteriovenous malformations [16]. However, typical migraine due to an arteriovenous malformation is the exception, as there are usually distinguishing features [11•,17]. Bruyn [15] reported the following features in patients with migraine-like symptoms and arteriovenous malformations: unusual associated signs (papilledema, field cut, bruit; 65%); short duration of headache attacks (20%); brief scintillating scotoma (10%); absent family history (15%); atypical sequence of aura, headache, and vomiting (10%); and seizures (25%).

Frequently, a scan or multiple scans are obtained when patients with CM are concerned about secondary pathologies causing their headaches. Although the yield is very low, as discussed earlier, the scan can be reassuring. In addition, the physician has medico-legal exposure because although rare, the patient may have incidental pathology such as a brain tumor or saccular aneurysm that may later become symptomatic, and the patient may claim that neuroimaging should have been done [11•]. In my practice, I discuss the low yield of imaging with patients and their families, how headaches from brain tumors and aneurysms are usually different from CM, and the approximate 2% prevalence of saccular aneurysms in the general population.

More problematic is whether unruptured saccular aneurysms can cause CM. Qureshi et al. [18] reported on 32 patients with chronic headaches who underwent Gugliemi coil embolization of unruptured aneurysm. Although the authors did not classify patients using IHS criteria, many of the patients clearly had features of migraine with and without aura. After treatment, 59% reported improvement in the severity of their headaches, and the headaches were less frequent. It is possible that there was selection bias—patients with chronic headaches underwent neuroimaging and were found to have incidental aneurysms. Further study would be of interest.

New Daily Headaches
Table 2 lists some primary and secondary causes of new daily headaches present for more than 3 months [19]. According to the IHS classification, second edition, the criteria for NDPH are headache, which within 3 days of onset is daily and unremitting for more than 3 months, with at least two of the following characteristics: bilateral location; pressing/tightening (nonpulsating) quality; mild or moderate intensity; and not aggravated by routine physical activity such as walking or climbing. The criteria require both of the following: no more than one of photophobia, phonophobia, or mild nausea; and neither moderate nor severe nausea and vomiting. In addition, the headache is not attributed to another disorder [1].

Some of these secondary disorders may have a thunderclap or sudden onset of severe headache, whereas others may develop gradually over 1 to 3 days and meet the onset period criteria for NDPH. New-onset daily headaches with a normal neurologic examination also could be due to various other causes, particularly when seen within the first 2 months after onset, including postmeningitis headache, chronic meningitis, hypothryroidism (headache may be a symptom in 30% of cases) [20], brain tumors, leptomeningeal metastasis, temporal arteritis, chronic subdural hematoma, post-traumatic headaches, sphenoid sinusitis, and hypertension. When the headaches have been present for more than 3 months with a normal neurologic examination, the yield of testing is low. A few additional examples will be discussed.

When new-onset tension-type headaches occur, the diagnosis is one of exclusion. Primary and metastatic brain tumors should be considered [21]. Eight percent of patients with headaches and brain tumors have a normal neurologic examination. Papilledema, which is usually associated with headaches, is present in 40% of patients with brain tumors.
The most common location of headaches is bifrontal, although patients may complain of pain in other locations of the head, as well as the neck. Unilateral headaches are usually on the same side as the neoplasm. Although the quality of the headache is usually similar to the tension type, occasional patients have headaches similar to migraine without aura, and rarely migraine with aura and cluster headaches. Most of the headaches are intermittent with moderate to severe intensity, but some patients report only mild headaches relieved by simple analgesics. The “classic” brain tumor headache—severe, worse in the morning, and associated with nausea and vomiting—occurs in a minority of patients with brain tumors.

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 with an orthostatic headache. However, as SIH syndrome persists, a CDH may be present without orthostatic features [22]. SIH syndrome also may present with other types of headaches, including exertional headaches without any orthostatic features, acute thunderclap headaches, paradoxical orthostatic headaches (present in recumbency and relieved when upright), intermittent headaches due to intermittent leaks, and the apecthal form with no headaches at all. Neck or interscapular pain may 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% of cases. 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 [22,23•]. An interesting finding is reversible descent of the cerebellar tonsils below the foramen magnum (acquired Chiari type I malformation), which can be due to SIH syndrome and also to lumbar puncture and overdraining cerebrospinal fluid shunts. The diffuse meningial enhancement on MRI in SIH may be explained by dural vasodilation and a greater concentration of gadolinium in the dural microvasculature and in the interstitial fluid of the dura. (Before the characteristic picture of the postural headache and diffuse pachymeningeal enhancement on MRI was recognized, some patients underwent extensive testing, including meningeal biopsy, to exclude other conditions, such as meningeal carcinomatosis and neurosarcomatosis.) The pleocytosis and increased protein in the cerebrospinal fluid and the subdural fluid collections in SIH are probably due to decreased cerebrospinal volume and hydrostatic pressure changes, resulting in meningial vasodilation and vascular leak.

A lumbar puncture usually demonstrates an opening pressure from 0 to 70 cm H_2O (and can even be negative), although the pressure can be in the normal range, especially if the procedure is performed after a period of bedrest. The cerebrospinal fluid analysis may be normal or can demonstrate a moderate, primarily lymphocytic pleocytosis (50 cells/mm³ are common, and values may be as high as 220 cells/mm³), the presence of red blood cells, and increased protein levels that can rarely be as high as 1000 mg/dL. Cerebrospinal fluid glucose concentration is never low.

CT myelography is more sensitive than other studies for determining the actual site of a cerebrospinal fluid leak because most leaks occur in the spine, especially at the thoracic level. Because the leaks can be high or low flow, early and delayed CT may be helpful. The study may demonstrate extra-arachnoid fluid, meningeal diverticula, and extradural leak of contrast into the paraspinal soft tissues.

Radioisotope cisternography using indium-111 may demonstrate an absence or paucity of activity over the cerebral convexities at 24 or 48 hours. Less commonly, parathecal activity at the approximate level of the leak may be apparent.

Cervical artery dissections, which can present with headache or neck pain alone [24•], can be a rare cause of new daily headaches [25]. Occasionally, the headaches can persist intermittently for months and even years and can lead to a pattern of CDHs, especially after cervical carotid artery dissection [26].

Pseudotumor cerebri (PTC) or idiopathic intracranial hypertension can be a cause of new daily headaches and is easily suspected when papilledema is present. However, PTC without papilledema [27] can rarely occur and should be considered as the cause of NDPH, especially in obese females, who account for 90% of cases of pseudotumor. Conversely, PTC can be present with papilledema and normal cerebrospinal fluid opening pressure [28]. Papilledema initially can be present in PTC and then, rarely, resolve (even though the intracranial pressure is still increased) [29]. Caution is advisable to avoid misdiagnosis, pseudo-PTC [30]. Although the cerebrospinal fluid opening pressure can be up to 25 cm of water in obese patients, the pressure can be falsely increased if the patient is not relaxed, the legs are flexed, and the abdominal muscles are contracted. Cerebral venous thrombosis (CVT) also can be misdiagnosed as PTC when the appropriate MRV study is not obtained [31,32]. In a recent large prospective study, Bono et al. [33•] found that increased cerebrospinal fluid opening pressures without papilledema highly correlated with the presence of bilateral transverse sinus stenosis in obese patients with headaches meeting criteria for episodic migraine and present for a mean duration of 2.4 years.

Headache is present in up to 90% of cases of CVT and is often the initial symptom. The headache can be unilateral or bilateral in any location, mild to severe, and intermittent or constant. The onset is usually subacute but can be sudden or thunderclap. In over 95% of cases, the headache is associated with a variety of neurologic signs, which include papilledema (51%), seizures (42%), focal deficits (39%), encephalopathy (31%), multiple cranial nerve palsies (11%), bilateral cortical signs (4%), and cerebellar signs (3%) [34]. As noted, CVT can be a mimic of PTC.
Neuroimaging studies have variable sensitivities in diagnosing CVT. CT only diagnoses approximately 20% of cases of CVT when demonstrating the hyperdensity of the thrombosed sinus on plain images and the delta sign seen with superior sagittal sinus thrombosis after contrast administration. Helical CT venography is a very sensitive diagnostic method. CVT may be missed on routine MRI of the brain, although echo-planar T2*-weighted MRI may increase the sensitivity [35]. MRV increases the sensitivity of magnetic resonance, especially within the first 5 days of onset or after 6 weeks. CVT also can be demonstrated, of course, on conventional angiography.

Chiari I malformation is a typically congenital malformation of cerebellar tonsillar herniation at least 3 to 5 cm below the foramen magnum, associated with crowding of the cranio cervical junction, obstructive hydrocephalus, and syringomyelia. In an imaging study of patients aged 2 to 18 years with headache [36], Chiari type I malformation was identified in 14 of 241 (5.8%) patients. Five of the 14 (35.7%) patients with Chiari I malformation had headaches secondary to their malformation. Three patients had surgical decompression, with significant headache relief in two patients. Nine patients were diagnosed with migraine (35.7%) and tension-type (28.6%) headaches. Although headache is the common presenting complaint of Chiari I malformation, the malformation is typically an incidental finding on MRI studies done for primary headaches.

Secondary pathology should be considered especially when NDPH occurs in patients aged older than 50 years. In a study of patients aged older than 65 years with new-onset headaches, the prevalence of secondary headaches due to serious pathology was 15% [37]. Temporal arteritis always should be considered, but the diagnosis is often delayed, especially in those aged younger than 70 years [38].

**Hemicrania Continua**

According to the IHS classification, second edition [1], to meet the criteria for HC, the headache should be present for more than 3 months with all of the following characteristics: unilateral without side-shift; daily and continuous, without pain-free periods; moderate intensity, but with exacerbations of severe pain; and with a complete response to indomethacin. During exacerbations, the headache must have one of the following ipsilateral features: conjunctival injection and/or lacrimation, nasal congestion and/or rhinorrhea, and ptosis and/or miosis. The headaches are usually unremitting, but rare cases of remission are reported. HC can be easily confused with CM because approximately 75% of patients with HC have exacerbations of severe throbbing or stabbing pain that can be associated with photophobia (59%), phonophobia (59%), nausea (53%), and vomiting (24%) [39]. The exacerbations can last from 20 minutes to several days, with pain awakening one third of patients. Autonomic features are present in up to 75% of patients, with tearing and then conjunctival injection the most common. Thus, a trial of medication effective for HC, such as indomethacin, should be considered for any patient with chronic unilateral headache that might be HC but can be easily misdiagnosed as migraine.

Rarely, HC many have a secondary etiology, which may include the following [40]: mesenchymal tumor of the sphenoid; lung malignancy; HIV (causal association unclear); C7 root irritation reported to aggravate; left lateral medullary infarction with left vertebral artery occlusion on MRI and MRA (head pain contralateral to infarction); internal carotid artery dissection; unruptured cavernous internal carotid artery aneurysm [41]; prolactinoma (headache exacerbation with dopamine agonists); and venous malformation of the right masseter. Although the yield is probably quite low, MRI of the brain is reasonable when initially evaluating the patient presenting with symptoms consistent with HC.

**Conclusions**

Although the yield is small, judicious use of diagnostic testing for CDH is essential. Serious secondary pathologies may be responsible for headaches similar to those of a primary type, including arteriovenous malformations, SIH, neoplasms, PTC, cervical artery dissections, CVT, Chiari I malformation, and temporal arteritis. Once detected, many of the secondary headaches are eminently treatable as well.

**References and Recommended Reading**

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance


Personal suggestions on the medico-legal implications of headache care.


24. Arnold M, Cumucric R, Stafp C, et al.: Pain as the only symptom of cervical artery dissection. *J Neurol Neurosurg Psychiatry* 2006, 77:1021–1024. There were 20 of 245 patients with spontaneous dissections who had pain as the only symptom—six with headache, two with neck pain, and 12 with both. Pain can be unilateral or bilateral; beware.


