

Review

## Acute Headache

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Acute Headache accounts for about 3% of acute medical unit admissions<sup>1</sup> and up to 8% of Emergency Room attendances<sup>2</sup>. What follows is an approach to this problem based on the characteristics of the presenting headache type. For each type of acute headache there is a fairly well defined differential diagnosis. If you appreciate the clinical features that are associated with different headache disorders, then you are more likely to identify the correct cause and manage your patient effectively. You should also appreciate that non-neurological disorders, such as carbon monoxide poisoning<sup>3</sup> can present with acute headache.

Acute Headaches, that present for hospital assessment are usually one of five types:

1. Thunderclap Headache - an abrupt severe headache which is maximal at onset
2. Headache and Fever - a new onset headache with fever
3. Headache with Focal Neurology - a new onset headache with 'soft' focal symptoms such as sensory, visual or motor (weakness) symptoms
4. New Onset Persistent Headache - a person with no prior history of headache who presents with several days or weeks of a new headache
5. Chronic Headache presenting for Pain Relief - a person with a known previous headache diagnosis who is in distress because their treatment is not working.

It goes without saying that the assessment of a patient with an acute headache requires a history, (including past medical history, medication history, social history, family history). The headache history must pay attention to the exact timing and severity of headache ("From the start of the headache, until it reached its worst, how long did it take?"). The recording and reading of vital signs (temperature, pulse rate, blood pressure, respiratory rate and Glasgow Coma Scale), a targeted screening neurological examination and a general medical examination are all essential. Arguably, an ECG could also form part of the initial assessment of acute headache<sup>4</sup>.

### THUNDERCLAP HEADACHE

Thunderclap headache is a headache of abrupt onset which is also maximal at onset. It is still not known how long such a headache has to last to have prognostic significance.

Neuralgic head pains are also sudden, intense and maximal at onset but they would only last for seconds, and are usually repetitive or recurrent. A potentially serious headache would usually cause significant distress and persist. An unproven assumption is that a thunderclap headache should last for at least an hour to be significant, but no single clinical feature is pathognomonic of a serious underlying cause<sup>5</sup>.

The priority in a first presentation of thunderclap headache is to exclude a ruptured intracranial berry aneurysm causing acute subarachnoid haemorrhage<sup>6</sup>. An urgent CT brain performed within 24 hours is the initial investigation of choice for the detection of subarachnoid haemorrhage (Fig. 1). Some recent evidence, which requires further validation in settings other than tertiary referral centres, suggests that a CT within 6 hours of an index thunderclap headache is completely sensitive and specific<sup>7</sup>. If an initial CT Brain is normal, lumbar puncture is required to exclude xanthochromia - which is best performed using CSF spectrophotometry<sup>8</sup>.



Fig 1. A 39 year old man with sudden, severe 'thunderclap' headache and vomiting several times at onset of pain. CT Brain performed on admission to A+E shows subarachnoid blood in left Sylvian Fissure (arrow). Subsequently found to have left middle cerebral artery aneurysm.

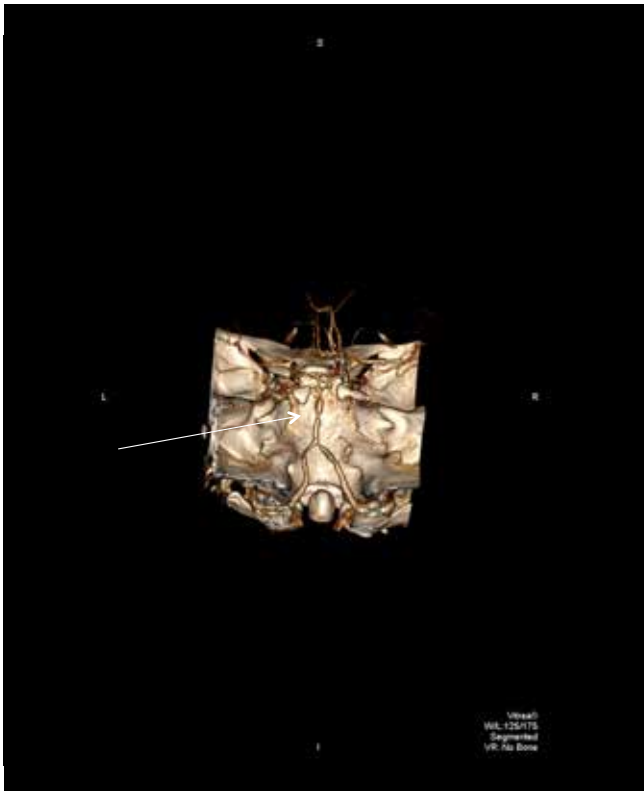
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The role of MRI Brain and MR Cerebral Angiography is still not fully established, but is potentially helpful if arterial dissection, vasoconstriction, venous sinus thrombosis or pituitary apoplexy are suspected<sup>9</sup>. Like all neuro-imaging, you need to know what you are looking for in order to make most use of the test. A normal CT Brain and CSF analysis does not mean that you ‘need an MRI’ – you need to be asking a specific diagnostic question. It is still true that patients who have had thunderclap headache who have a normal CT Brain and normal CSF carry an excellent long term prognosis<sup>10</sup>.

Acute, sudden headache has a large differential diagnosis. The best population-based estimate suggests an incidence of 43 cases per 100,000 adults per year<sup>11</sup>. In prospective cohort studies, which are usually hospital-based, the majority of cases remain unexplained, or are diagnosed as primary headache disorders. In cohort studies, significant neuro-vascular disease is identified in about 17% of cases of sudden and severe headache. The most important cause remains aneurysmal subarachnoid haemorrhage, but arterial dissection<sup>12,13</sup> venous sinus thrombosis<sup>14</sup> and the reversible cerebral vasoconstriction syndrome<sup>15</sup> are important causes to identify and treat.



*Fig 2a.* Man in his 30's with sudden severe headache associated with sexual activity. CT Angiogram reconstruction shows marked basilar artery segmental narrowing (arrow) which subsequently resolved at follow up. Consistent with the Reversible Cerebral vasoconstriction Syndrome.

Rarer clinical associations of thunderclap headache include spontaneous intracranial hypotension<sup>16</sup>, pituitary apoplexy<sup>17</sup>, pheochromocytoma<sup>18</sup> and acute myocardial infarction. There are no published systematic reviews of thunderclap headache

aetiology, but it is likely that there are close to 100 clinical associations of thunderclap headache listed in the medical literature.



*Fig2b.* Resolution of basilar artery segmental narrowing at follow up 8 weeks later (MRA reconstruction)

On an historic note the term ‘Thunderclap Headache’ was first used in 1986 to describe a case where sudden, severe headache was associated with an *unruptured* berry aneurysm<sup>19</sup>. However, in Day and Raskin’s case there was segmental vasoconstriction in the cerebral arteries. It is likely that the aneurysm they identified was an incidental finding, and that this first case of ‘Thunderclap Headache’ was actually the Reversible Cerebral Vasoconstriction Syndrome<sup>20</sup>.

Idiopathic Thunderclap Headache implies that no cause has been identified after appropriate investigation. Idiopathic Thunderclap Headache (Fig 2a and 2b) can be provoked by exertion and sexual activity, and studies of thunderclap headache associated with sexual activity suggest that there is probably a high frequency of reversible cerebral vasoconstriction in people with normal CT Brain and CSF analysis<sup>21</sup>.

### HEADACHE AND FEVER

The great fear amongst patients and their doctor when assessing headache and fever is acute bacterial meningitis, but most people in a community with headache and fever will have a self-limiting systemic illness with headache or a paranasal sinus infection. About 2/3 of people with influenza have a headache as one of their primary symptoms<sup>22</sup>. It is therefore not surprising that in primary care it is very difficult to correctly identify acute bacterial meningitis in children or adolescents at first visit<sup>23</sup>.

The most important diagnosis to consider or exclude is acute bacterial meningitis, although aseptic meningitis is much more common. The causes of bacterial meningitis with the highest incidence are Meningococcal Type b, Tuberculous and Pneumococcal infections. The incidence of Type c Meningococcal Meningitis has fallen by 55% since the introduction of an effective vaccine, and in Northern Ireland

there were no cases of type c meningococcal meningitis in 2009 or 2010<sup>24</sup>. Type b Meningococcal Infection is now the most prevalent cause for which there is no effective vaccine. The Meningitis Research Foundation in association with the British Infection Society publish management guidelines which are summarised in a single page algorithm<sup>25</sup>.

In suspected meningitis, treatment with parenteral antibiotics (Intravenous Cefotaxime) should be commenced as soon as possible. The effectiveness of pre-hospital antibiotic treatment with intramuscular benzylpenicillin remains uncertain as severity of illness confounds the outcome data from prospective studies<sup>26</sup>.

To confirm a diagnosis of meningitis, lumbar puncture should be performed as soon as possible, as delay will reduce the chance of confirming or refuting a diagnosis. It is not essential to perform a CT Brain in suspected meningitis if the patient is fully conscious, has no lateralising signs, has not had seizures and does not have a history of HIV infection<sup>27,28</sup>. If anything in a fully conscious patient, a CT scan could delay treatment and almost certainly delays the timing of LP<sup>29</sup>. The main advantage of early LP is that it will direct appropriate antibiotic treatment. CSF will also permit diagnosis of aseptic meningitis, which will avoid unnecessary antibiotics for your patient.

The vast majority of people who present to hospital with headache and fever of recent onset will have a systemic illness headache. Systemic Illness Headache is a poorly understood and rarely studied condition<sup>30</sup>, as it is self-limiting with good outcome, when the underlying infection resolves. Some people will end up with a non-specific persistent headache that could last for months<sup>31</sup>.

### HEADACHE WITH FOCAL NEUROLOGY

This group of patients have a primary complaint of headache, but alongside the headache they have sensory, visual or motor symptoms. Usually these people turn out to be describing migraine with aura, but if there is no prior history of migraine with aura, brain imaging is required to exclude stroke or cerebral mass lesion for a first presentation with persistent symptoms.

There is now indirect evidence in humans, from functional MRI studies, that migraine aura is a manifestation of Cortical Spreading Depression. Cortical Spreading Depression (CSD) is a physiological response, elicited from mammalian cortex in response to irritant stimuli. The classic studies were performed in the 1940's by the Brazilian Physiologist Leao, while working in Harvard<sup>32</sup>. In CSD, an irritant stimulus will induce a wave of depolarisation which slowly spreads across the cortex, causing sustained depolarisation of neuronal tissue, followed by slow repolarisation. During depolarisation the cortex does not function properly and becomes isoelectric. Functional MRI studies in humans with migraine visual aura have demonstrated that the spread of altered MRI BOLD signal follows the clinical symptom of visual aura at a rate consistent with the rate at which cortical spreading depression

would be expected to occur<sup>33</sup>.

In clinical practice, the key feature of migraine aura is that it is a slowly evolving focal neurological symptom, which will reach its maximum extent within about 5-20 minutes and will persist on average for about 30 minutes<sup>34</sup>, before resolving completely. About 4% of people with migraine with aura will report persistent sensory, visual or motor symptoms lasting beyond 24 hours - 'migraine persistent aura'. There are also people with recurrent migraine aura who get bouts of recurrent one sided weakness, which have been given the acronym MUMS - Migraine with Unilateral Motor Symptoms<sup>35</sup>. Migraineurs are also much more likely to experience vertiginous symptoms or non-specific dizziness<sup>36</sup>. Knowledge of these clinical features of migraine and the underlying mechanism can allow a confident clinical diagnosis in many cases. Incidentally, isolated migraine aura, without ever having had a headache is a potential indication for neuro-imaging<sup>37</sup>.

### NEW ONSET PERSISTENT HEADACHE

This group has the most diverse range of possible diagnoses. They have no past history of significant 'headache' and present for assessment of a new onset headache, which is not sudden in onset, but has persisted and is an unusual symptom for them.

Most ED department staff are aware of Carbon Monoxide Poisoning, in which the vast majority report headache as a presenting feature, although epidemiologic surveys from England imply that the diagnosis is often overlooked<sup>3</sup>. Risk factors for carbon monoxide poisoning include working with internal combustion engines in enclosed spaces e.g. warehouse workers or poorly ventilated home heating systems. The clinical features of the headache are non-specific<sup>38</sup>. Undiagnosed Carbon Monoxide Poisoning can lead to death or permanent neurological disability<sup>39</sup>.

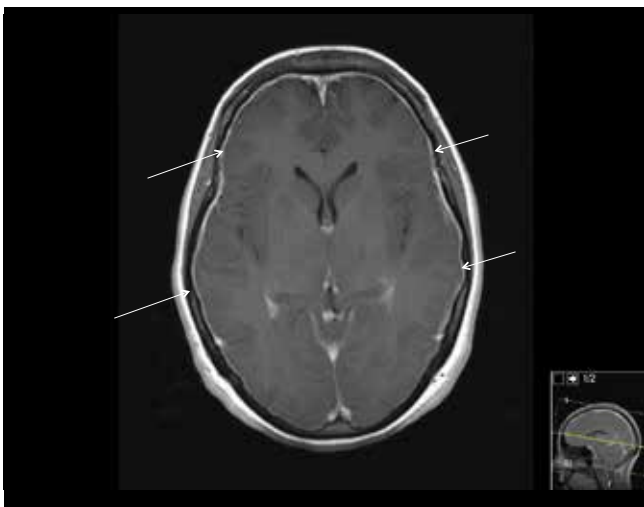
Temporal arteritis should be considered as a potential cause of new onset, persistent headache in someone over 50 years old. An ESR is still a useful test, and if elevated (usually >50mm) should prompt referral for a temporal artery biopsy. National Guidelines on Temporal Arteritis are worth referring to, specifically noting the need to start steroids, and even aspirin prior to temporal artery biopsy, in order to reduce the risk of central retinal artery occlusion<sup>40</sup>. Even today, 25% of people with temporal arteritis will develop visual impairment, which is usually permanent. Stroke, usually in the posterior circulation territory can be due to arteritis, and occipital arteritis can present with all the features of temporal arteritis except that then pain is located in the back of the head. Temporal Biopsy should always be performed as the average duration of steroid treatment is almost two years, and use of steroids for this length of time should be justified using histological means.

Disorders of intracranial pressure - with high or low pressure can present to hospital as persistent severe headache. Idiopathic Intracranial Hypertension (IIH) is typically a

disorder of overweight females, who in addition to persistent headache may report pulse-synchronous tinnitus, or visual symptoms<sup>41</sup>. It is important to rule out venous sinus thrombosis, and CSF constituents should be normal before confirming a diagnosis of idiopathic intracranial hypertension. The main risk to the patient with IIH is visual failure, and prospective studies support dieting and weight loss as a means of preserving vision and improving headache<sup>42</sup>.

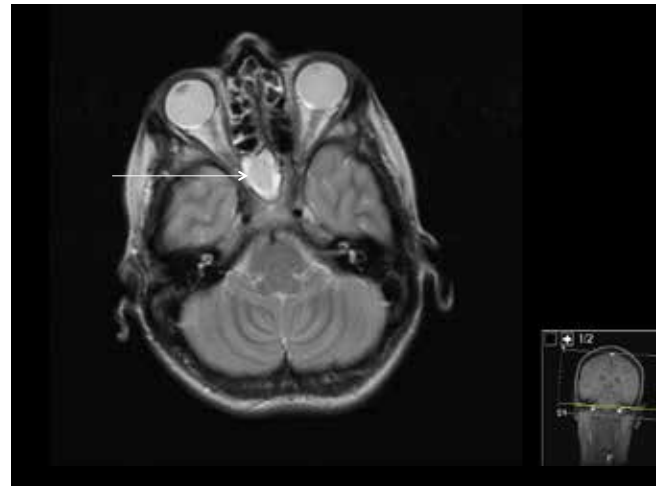


*Fig 3a.* Non contrast Sagittal T1 image. Lady in her 30's with new onset headache, reaching maximum within several hours and with almost complete relief on lying flat. Symptoms persisted for several weeks before MRI Imaging performed. Shows pituitary engorgement (short arrow), sagging of brain stem with loss of normal pontine convexity (long arrow), and cerebellar tonsillar descent (medium arrow).



*Fig3b.* Gadolinium enhanced MRI showing marked dural enhancement (arrows). Symptoms were abolished following 2 epidural blood patch procedures.

If anything, low intracranial pressure has a higher incidence than high intracranial pressure. The most common cause of low intracranial pressure is iatrogenic following lumbar puncture or spinal anaesthetic. Spontaneous intracranial hypotension is usually the result of a spontaneous CSF leak within the spinal canal. The main feature of a low CSF pressure headache is a bitemporal pressure or heaviness that is completely or near-completely relieved by lying flat<sup>43</sup>. Aural symptoms such as muffled hearing or non-pulsatile tinnitus commonly accompany the low pressure states. Standard brain imaging will often overlook this diagnosis. The classic feature on MRI is enhancement of the meninges ( Fig 3a and 3b) - due to venous engorgement of the dura mater. Subtle features such as brainstem sagging or mild degrees of pituitary engorgement are easily missed. Awareness of the features of postural headache and an index of suspicion will lead to the correct imaging study. If low pressure is identified, a series of epidural blood patches are usually effective<sup>44</sup>.



*Fig 4.* A lady in mid-twenties who previously attended neurology with frequent migraine. Presented with new daily persistent headache of several weeks duration like a severe pressure in her head and preventing sleep. Completely unlike previous migraine. MRI Head shows total opacification of right sphenoid sinus (arrow). Her new headache was relieved after surgical treatment, but episodic migraine continued

Paranasal sinusitis is usually suspected on clinical grounds, but often erroneously excluded on the basis that medical treatment has failed. In a new onset of headache without clear sinus symptoms such as nasal congestion or dental tenderness an imaging study may reveal symptomatic congested paranasal sinuses. Symptomatic sinusitis is usually florid on cross-sectional imaging. Isolated Sphenoid Sinusitis is a rare cause of persistent headache, but the reason for considering the diagnosis is that this is a treatable cause of refractory, new onset headache (Fig. 4). In sphenoid sinusitis, the pain can refer to any part of the head, is usually worst at night, and the characteristic features of sinusitis e.g. nasal discharge and facial tenderness are often absent<sup>45,46</sup>.

Cervicogenic headache is pain that originates in the upper cervical spine. It is well established that the muscles, ligaments and facet joints of the upper cervical spine refer

pain to the head<sup>47</sup>. Manual techniques have been validated as means of making a clinical diagnosis of cervicogenic headache<sup>48</sup>, and there is randomised trial evidence that manual treatment and exercise are more effective than control treatment<sup>49</sup>. People who do not respond to manual treatment may be candidates for radiofrequency neurotomy to symptomatic facet joints<sup>50</sup>. Population based estimates imply a cervical-based headache could occur in up to 4% of adults. Often, the headache is unilateral, of recent onset and occurs in the context of prior head or neck injury, or presents with migrainous feature yet has not responded to standard migraine treatment. In older adults with new onset of unilateral headache, with a normal ESR this would be an important, and potentially treatable diagnosis.

Sometimes rarer headache syndromes will present as acute headache. Hypnic Headache is a primary headache disorder of older adults. In Hypnic Headache the patient will retire to bed to sleep completely pain free, but is woken from sleep with an intense diffuse headache that compels them to get up from bed. About 9% of cases of hypnic headache have an underlying structural cause on brain imaging, and the condition is said to respond very well to strong caffeinated drinks (as strong a cup of coffee as you can tolerate) or to low doses of lithium carbonate<sup>51</sup>.

Cluster Headache can often be misdiagnosed as migraine. In cluster headache there is agonising, intense pain - usually over or around the eye that reaches a maximum within no more than a minute or two and is associated with 'autonomic activation'<sup>52</sup>. Autonomic activation is manifest as lacrimation, nasal stuffiness and upper eyelid ptosis. Internal carotid artery dissection and C2 nerve root pain can mimic cluster headache, so care needs to be taken when making this diagnosis. The first line treatments for cluster headache include subcutaneous sumatriptan and high flow oxygen administered via a re-breathable mask at 15 litres per minute - which is effective in over 90% of people with cluster attacks<sup>53</sup>.

The headache of arterial dissection or of venous sinus thrombosis may well present with thunderclap headache, but may also present as a new onset headache. In carotid dissection, a Horner's Sign may be present, and in venous sinus thrombosis the patient's history may reveal an underlying pro-thrombotic risk factor such as recent pregnancy or be associated with transient neurological symptoms.

### CHRONIC HEADACHE PRESENTING IN DISTRESS

The last group of patients are those with a pre-existing chronic headache problem who present in distress. The one group where you need to be vigilant are those with known intracranial hypertension, as their initial headache can be mistaken for migraine, tension headache or medication overuse headache. A patient with previous intracranial hypertension presenting to hospital for pain relief will need to have follow up with their specialist as a repeat lumbar puncture may be required to assess CSF pressure<sup>54</sup>.

Most people with a chronic headache disorder who present for pain relief have Chronic Migraine. A person with Chronic Migraine will have headache on the majority of days in a month (in reality every day), and on at least half of these days will experience a pain that feels like migraine with sensory sensitivity or a partial response to triptan drugs<sup>55</sup>. If someone with migraine presents for pain relief, it is very important to take a wider look at their headache pattern and medication use. The vast majority of people who present for assessment will be over-using medication such as codeine or tramadol. A good rule of thumb is that if pain killers are being used to treat acute headache on more than 10 days per month then the patient has a medication overuse problem. The single most important thing they can do is discontinue pain killers that are being overused<sup>56</sup>.

Achieving pain relief in an acute setting is a challenge as these patients will have been experiencing high levels of pain for years, so adjusting your patient's expectation is very important. There are many different protocols used worldwide to terminate a severe headache attack. Intravenous infusions of neuroleptic<sup>57</sup>, ergot drugs and parenteral NSAIDs can be useful for terminating severe migraine attacks<sup>58</sup>. Patients admitted to hospital for management of migraine should have their lifestyle and use of medication reviewed. If not already on prophylactic medication, this should be considered.

### SUMMARY

Acute headache requiring assessment in hospital is a common scenario. There are five different headache types, each with their own differential diagnosis and investigation plan. The vast majority of people presenting with acute headache have self-limiting complaints, but a significant number will have secondary causes which if untreated may lead to avoidable morbidity.

### DECLARATION

Janssen-Cilag, manufacturers of Topiramate paid for the author to attend the EFNS Meeting in Athens. Allergan, manufacturers of Botox, paid for the author to attend the EHMTIC meeting in London September 2012, and paid an honorarium for speaking on Headache Classification at a Chronic Migraine Masterclass at the Dublin Neurological Institute November 2013.

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