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## Headache and migraine

Nearly everyone gets a headache occasionally, whereas about one in five women and one in fifteen men suffer from migraines.<sup>1</sup> Migraine treatment which works for one person often fails for another, so patient and practitioner should evaluate the options together. Preventive measures are indicated for frequent headache, and in all cases there is a place for non-drug approaches.

### Diagnosing headaches

Identifying secondary headaches due to serious causes, such as meningitis, subarachnoid haemorrhage, or intracranial tumours, is a major concern in headache diagnosis. Signs of serious secondary headache are listed on page 2. In the context of the patient history and physical examination, these may require further investigation, including neuro-imaging.

Medicine use, including over-the-counter (OTC) preparations, should be taken into account when forming a diagnosis. For recurrent headache, investigate the possibility of medication-overuse headache (see page 3), as the prevalence is about 1% in the adult population.<sup>2</sup>

Headache is an adverse effect of numerous drugs, typically oestrogen (including combined oral contraceptives), calcium-channel blockers, nitrates, NSAIDs (particularly indomethacin),

and some erectile dysfunction drugs (sildenafil, tadalafil and vardenafil).<sup>3,4</sup> Caffeine withdrawal can also cause headache.

Table 1 may assist in the differential diagnosis of migraine, tension-type headache, and medication-overuse headache. However, it is quite common for an individual to suffer from episodes of both migraine and tension-type headache. Rarer headaches (such as cluster headache) are not discussed in this *News*.

About a third of migraine sufferers experience an aura in association with other symptoms.<sup>1</sup> The aura is characterised by focal neurological symptoms that may precede or accompany the headache. The symptoms last for up to an hour, reverse fully between episodes, and can include lights, spots, loss of vision, pins and needles, numbness and speech disturbances.<sup>4</sup>

**Table 1: Diagnostic criteria for some common headache types in adults**

Migraine	Tension-type headache	Medication-overuse headache (probable)
<p>Headache lasting 4–72 hours</p> <p>At least two of the following:</p> <ul style="list-style-type: none"> <li>— unilateral location</li> <li>— throbbing character</li> <li>— worsening pain with routine activity</li> <li>— moderate to severe intensity</li> </ul> <p>and at least one of the following:</p> <ul style="list-style-type: none"> <li>— nausea and/or vomiting</li> <li>— photophobia and phonophobia</li> </ul> <p><i>Without aura:</i> at least five attacks</p> <p><i>With aura:</i> at least two attacks</p>	<p>Headache lasting 30 min to 7 days</p> <p>At least two of the following:</p> <ul style="list-style-type: none"> <li>— bilateral location</li> <li>— non-pulsatile character</li> <li>— no aggravation with routine activity</li> <li>— mild to moderate intensity</li> </ul> <p>and neither of the following:</p> <ul style="list-style-type: none"> <li>— nausea and/or vomiting</li> <li>— photophobia and phonophobia (but may have one or the other)</li> </ul>	<p>Headache on &gt; 15 days/month</p> <p>Regular medication use for &gt; 3 months, with intake on <i>either</i></p> <ul style="list-style-type: none"> <li>— ≥ 15 days/month of simple analgesics</li> </ul> <p>or</p> <ul style="list-style-type: none"> <li>— ≥ 10 days/month of ergotamine</li> <li>— 5HT<sub>1</sub> agonist ('triptan')</li> <li>— opioid</li> <li>— combination analgesic</li> </ul>

Adapted from the *International Classification of Headache Disorders*, 2nd ed.<sup>4</sup>

### Secondary headache: red flags<sup>3,5</sup>

Any of the following may warn of serious secondary headache

- confusion
- drowsiness
- vomiting
- neurological signs that persist between headaches
- fever
- new headache in patient > 50 years of age
- sudden onset
- headache that wakes patient
- head injury
- severe and debilitating pain

## Treating tension-type headache

Episodic tension-type headache is generally non-disabling and self-limiting. Occasional headache can be treated symptomatically with simple analgesics or physical therapy such as massage or stretching of the neck and scalp muscles. There is some evidence that spinal manipulation by a physiotherapist or other practitioner can reduce pain.<sup>6</sup> Many behavioural interventions useful in migraine, such as stress reduction, relaxation and cognitive behavioural therapy, may help to prevent tension-type headache.

## Managing acute migraine

The choice of drug for acute migraine typically needs to be refined over a series of attacks (see Table 2). Often therapy is initiated with a simple analgesic. If this fails consistently, the treatment is escalated to a migraine-specific drug (such as a 5HT<sub>1</sub> agonist or ergotamine) for subsequent attacks, and further alternative agents trialled as necessary. Whichever agent that is found to be most effective is then used at the onset of each new attack. A more cautious approach, where initial therapy for each migraine attack is always a simple analgesic and a migraine-specific drug is only added if the headache persists, has been shown to result in significantly more disability.<sup>7</sup>

### Advice for patients

Migraine sufferers need to know what to do when they experience an attack. When acute medication fails to abort the migraine symptoms, resting in a quiet, darkened room and avoiding all activity is advisable.<sup>3</sup> With experience, patients can identify which drugs are most effective for managing their attacks and respond accordingly. Using the appropriate agent promptly, when the attack is mild, will give the best results.<sup>8</sup>

## Mild-to-moderate migraine

For individuals suffering from mild-to-moderate migraine attacks, trial a simple analgesic.<sup>8</sup> Aspirin and other NSAIDs reduce migraine headache severity to mild or no pain in a large proportion of cases.<sup>9</sup> Paracetamol has also been shown to be efficacious in mild-to-moderate migraine<sup>10</sup>, and can be used where aspirin or NSAIDs are not tolerated or are contra-indicated. A soluble analgesic formulation may be preferable, particularly with nausea or vomiting. If simple analgesics fail repeatedly, escalate to treatment with a migraine-specific agent.

## Severe migraine

Where migraine is severe or disabling (i.e. in a third or more of sufferers<sup>1</sup>), or if simple analgesics have been tried unsuccessfully, use migraine-specific agents such as the 5HT<sub>1</sub> agonists ('triptans'), ergotamine or dihydroergotamine.<sup>8</sup> Compared to other migraine drugs, the triptans give the highest proportion of individuals pain-free at 2 hours post-dose.<sup>11</sup> One trial showed ergotamine to be less efficacious than oral sumatriptan and more likely to cause nausea and vomiting, though with a significantly lower rate of migraine recurrence within 48 hours.<sup>12</sup>

Good self-management is required to optimise triptan use. Triptans appear to work best when used as soon as possible after the headache of migraine begins to develop<sup>13</sup>; earlier dosing (when only the aura or prodrome is present) or later dosing (when pain is more severe) is less effective.

Experience with the different triptans is that individual responses vary unpredictably, and patients may need to try more than one of them over time.<sup>8</sup> A problem with the triptans is that headache returns within 24 hours in around 30% of cases, although an additional dose may deal with this recurrence.<sup>14</sup>



**Table 2: Recommended options for acute drug treatment of migraine<sup>3,8</sup>**

<b>Mild-to-moderate migraine</b>	<ul style="list-style-type: none"> <li>● aspirin 600–900 mg, followed by 600 mg every 4 hours</li> <li>● NSAID</li> <li>● paracetamol 1000 mg every 4 hours (max 4 g/day)</li> </ul>
	<p><i>With nausea and vomiting</i></p> <ul style="list-style-type: none"> <li>● paracetamol and some NSAIDs are available as suppositories</li> <li>● add an anti-emetic (domperidone, metoclopramide, or prochlorperazine); use a non-oral route if necessary</li> </ul>
<b>Severe migraine or no response to simple analgesics</b>	<ul style="list-style-type: none"> <li>● 5HT<sub>1</sub> agonist (naratriptan, sumatriptan, or zolmitriptan)</li> <li>● ergotamine 1–2 mg as initial dose (max 6 mg/day; 10 mg/week)</li> </ul>
	<p><i>With nausea and vomiting</i></p> <ul style="list-style-type: none"> <li>● sumatriptan, by nasal spray or subcutaneous injection</li> <li>● dihydroergotamine, by intramuscular or subcutaneous injection</li> <li>● ergotamine/caffeine suppository</li> <li>● add an anti-emetic (domperidone, metoclopramide, or prochlorperazine); use a non-oral route if necessary</li> </ul>
<p><b>Note:</b></p> <ul style="list-style-type: none"> <li>● If there is no response to the initial dose of 5HT<sub>1</sub> agonist, do not repeat.</li> <li>● Do not give a 5HT<sub>1</sub> agonist within 24 hours of ergotamine or dihydroergotamine.</li> <li>● Do not give ergotamine or dihydroergotamine within 6 hours of a 5HT<sub>1</sub> agonist.</li> <li>● Ergotamine, dihydroergotamine and 5HT<sub>1</sub> agonists should not be given to patients with vascular disease or poorly controlled hypertension.</li> </ul>	

## Medication-overuse headache

Headache and migraine sufferers may fall into a pattern of escalating medication use, coupled with increasing frequency and intensity of headaches, culminating in chronic daily headache or chronic migraine (sometimes known as 'transformed migraine'). The term 'medication-overuse headache' is now used for this condition, in preference to rebound headache, drug-induced headache, or medication-abuse headache. Medication-overuse headache has been associated with almost all drugs used for acute migraine treatment.<sup>2</sup>

The *International Classification of Headache Disorders* states that medication-overuse headache should be suspected when any acute migraine drugs, including combination analgesics (e.g. Mersyndol or Panadeine), are used 10 or more days per month.<sup>4</sup> A diagnosis of probable medication-overuse headache is also specified if simple analgesics are used 15 or more days per month.<sup>4</sup> About 1% of adults are estimated to suffer from medication-overuse headache.<sup>2</sup>

Treatment for medication-overuse headache should include withdrawal of the overused agent<sup>2</sup>; this often needs specialist management from a pain or headache clinic. Depending on the severity of the syndrome, and the type of drugs overused, resolution may take weeks or even months.<sup>15</sup>

## Codeine not recommended

Combination analgesics, particularly OTC preparations containing aspirin or paracetamol with codeine, are widely used in pain, headache and migraine. Survey data from the US indicate that the majority of people with migraine self-medicate with OTC drugs, and that about half have never received a formal diagnosis of migraine.<sup>16</sup>

Codeine should be avoided in headache and migraine, even though the addition of codeine  $\geq$  30 mg/dose may provide marginally better pain relief than aspirin or paracetamol alone.<sup>17</sup> Codeine, as with other opioids, can worsen symptoms of nausea and vomiting and impede the absorption of other medications.<sup>8</sup> Additionally, codeine is likely to fail in up to 10% of the population who do not metabolise codeine into its active form, morphine.<sup>18</sup>

Combination analgesic preparations, but also more generally, codeine and other opioids, are associated with the development of medication-overuse headache, and for this additional reason are not recommended.<sup>19</sup> **Pethidine should not be used** to treat migraine (see *NPS News* 22).<sup>20</sup>

## Preventing migraine

When migraines are frequent and cause regular disability, consider preventive measures including prophylactic drug treatment, and behavioural or complementary approaches. Reducing migraine frequency may also help avoid medication-overuse headache.

### Lifestyle changes

Non-drug interventions to prevent migraine are worth considering, whether or not drug prophylaxis is warranted, as the risk of adverse effects from these is low. As most migraine sufferers are aware, avoiding trigger factors (such as stress, irregular sleep, skipping meals, or eating particular foods) is broadly recommended. Smoking is sometimes mentioned as precipitating migraine, and chocolate, cheese, citrus fruit and wine are often-reported dietary triggers.<sup>21,22</sup> A headache diary may be useful in establishing the importance of trigger factors, as well as for monitoring the success of treatment (see 'Resources for patients', below).

Stress is one of the most commonly named trigger factors for migraine<sup>22</sup>; massage, yoga and exercise may be useful in reducing stress. There is a consistent body of evidence showing the efficacy of relaxation training (such as progressive muscle relaxation or meditation), relaxation training combined with biofeedback, and cognitive behavioural therapy.<sup>23</sup> Non-drug measures may have an added benefit when combined with drug prophylaxis.<sup>23</sup>

### Prophylactic drug therapy

Along with non-drug approaches, consider prophylactic drug therapy for those who suffer from **three or more severe migraines per month**.<sup>19</sup> The goal of prophylactic drug therapy is to reduce headache frequency by more than half; unfortunately this is often unachievable. All prophylactic drugs may cause significant adverse effects, and choice of therapy involves balancing tolerability with individual response.

To minimise adverse effects, prophylactic drugs typically require dose titration. However, after the desired dose has been achieved, it may take an additional 1–3 months before the full effect is seen. The medication should be withdrawn or changed if there is insufficient response. When prophylaxis is effective, withdraw therapy after 4–6 months to assess continuing need.<sup>19</sup> Patients may find that a headache diary is helpful in monitoring the effect of prophylactic therapy.

In the absence of adequate head-to-head trials, the recommended prophylactic drugs appear to be equal in efficacy.<sup>24</sup> The beta-blockers, propranolol and metoprolol, are first-line. Pizotifen is registered as a migraine prophylaxis drug, but has not been studied as extensively as the beta-blockers. The available evidence indicates pizotifen is effective<sup>25</sup>; drowsiness and weight gain are the most frequently reported adverse effects.<sup>25</sup> Methysergide is also effective but carries a number of serious risks (e.g. retroperitoneal or pulmonary fibrosis) and is considered second-line.<sup>25</sup>

Amitriptyline has no indication for migraine in Australia, but has been shown to be an effective prophylactic, and may have a place in migraine with frequent tension-type headache, or in migraine with concurrent sleep disturbance or depression.<sup>19</sup> While the anti-epileptics valproate and topiramate have demonstrated efficacy<sup>26</sup>, valproate is not approved for migraine prophylaxis and topiramate is not available through the PBS for its migraine prevention indication.

There are two listed prophylactic drugs which have been superseded and which should be avoided: clonidine, as there is no evidence of efficacy, and cyproheptadine, due to inconclusive evidence of efficacy.<sup>25</sup>

## Resources for patients

Self-management is an important aspect of headache treatment. Using a diary, migraine sufferers can monitor the frequency and severity of attacks, note potential triggers, and keep track of successful therapies. Information for consumers on the actions and adverse effects of prescription and OTC medication can assist in choosing the right treatment at the right time and avoiding medication overuse.

- The NSW Therapeutic Advisory Group migraine patient information brochure includes a pain diary for monitoring migraine triggers, frequency and severity. Go to: [www.clininfo.health.nsw.gov.au/nswtag/publications/guidelines/migraine\\_patient.pdf](http://www.clininfo.health.nsw.gov.au/nswtag/publications/guidelines/migraine_patient.pdf)
- The Better Health Channel web site gives background information about migraine. Elsewhere on the site is an explanation of the different types of headaches, and information on treatment. Go to: [www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/Headache\\_migraines?OpenDocument](http://www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/Headache_migraines?OpenDocument)
- The article 'Taking the pain out of choosing a painkiller' (NPS *MedicinesTalk*, Winter 2004) explains the safe and effective use of OTC analgesics, including paracetamol. Go to: [www.nps.org.au/resources/content/cons\\_mt\\_winter\\_04.pdf](http://www.nps.org.au/resources/content/cons_mt_winter_04.pdf)

## Children and migraine

Five to ten percent of children suffer from migraine and, until puberty, equal numbers of boys and girls are affected.<sup>27</sup> Some children initially present with recurrent abdominal pain and minimal symptoms of headache.<sup>28</sup> Migraines in children peak in intensity more quickly than in adults, and can be as short as one hour; the headache may be bilateral. Initial consultation for severe headache in children should include a full neurological examination to rule out serious causes.<sup>28</sup>

Treatment of migraine in children should follow the same general approach as with adults, although drug options for children are more limited. Behavioural interventions (such as relaxation training) may be helpful for recurrent migraine, as there is specific evidence they work in children.<sup>28</sup> These should be trialled before or concurrently with the introduction of pharmacotherapy.

Prompt use of paracetamol or an NSAID is often the only treatment required (aspirin should not be used in children under 18 years). A randomised controlled trial of paracetamol, ibuprofen or placebo in childhood migraine demonstrated that both active treatments relieved pain significantly, with no clear difference in efficacy between the two.<sup>29</sup> As in adults, the risks of medication overuse should be kept in mind. Anti-emetics such as prochlorperazine, or the antihistamines dimenhydrinate or promethazine, may have value in reducing nausea and vomiting, although this is unvalidated.<sup>28</sup>

Childhood migraine which cannot be managed using simple analgesics probably requires the attention of a paediatrician.



## Complementary update

### Acupuncture

Acupuncture is used as both an acute and a preventive therapy for migraine, but an effect has not been demonstrated in a randomised controlled trial with adequate blinding. There are a few rigorous unblinded trials showing those receiving acupuncture benefit over those receiving no treatment.<sup>30</sup> In a three-way trial in 179 subjects comparing sumatriptan injection, placebo injection or acupuncture in the acute treatment of migraine, acupuncture was significantly better than placebo and not significantly less effective than sumatriptan.<sup>31</sup>

### Physical therapies

Spinal manipulation, including osteopathic and chiropractic treatment, is often used by migraine and tension-type headache sufferers. There is moderately good evidence that regular spinal manipulation can prevent migraine as effectively as drug prophylaxis.<sup>6</sup> Adverse effects seen in these small-scale trials were minor<sup>6</sup>, but there are long-standing concerns that cervical spinal manipulation may be rarely associated with stroke.<sup>32</sup>

### Herbal/complementary therapies

The evidence for the benefit of herbal medicines and dietary supplements in migraine is very limited. A small number of randomised controlled trials have demonstrated a benefit of riboflavin (vitamin B<sub>2</sub>) or magnesium in preventing migraine.<sup>25</sup> Feverfew is the best-studied herb, but effects in trials have been mild and transient at best, and there is insufficient evidence to recommend its use.<sup>33</sup> There appears to be little concern regarding serious adverse effects or interactions with any of these agents.

Recently, unblinded studies of both co-enzyme Q<sub>10</sub><sup>34</sup> and melatonin<sup>35</sup> suggest that these agents may prevent migraines, though there are yet to be placebo-controlled trials confirming this. Both melatonin and co-enzyme Q<sub>10</sub> may interact significantly with warfarin.<sup>36,37</sup> Melatonin is not sold in Australia, and there are a few reports of serious CNS adverse effects associated with its use.<sup>36</sup>

# What's what

<b>Combination analgesics</b>	aspirin/codeine	Aspalgin, Codiphen, Codis, Codral Forte, Disprin Forte, Veganin
	ibuprofen/codeine	Nurofen Plus
	paracetamol/codeine	Codalgin, Codapane, Codral Pain Relief, Dolaforte, Dymadon, Febricod, Hexal Comfarol Plus, Mersyndol Day Strength, Painstop, Panadeine, Panamax Co, Prodeine
	paracetamol/codeine/doxylamine	Codalgin Plus, Fiorinal, Mersyndol, Panalgesic
<b>5HT<sub>1</sub> agonists ('triptans')</b>	naratriptan	Naramig
	sumatriptan	Imigran, Suvalan
	zolmitriptan	Zomig
<b>Ergot alkaloids</b>	dihydroergotamine	Dihyergot
	ergotamine/cafeine	Cafergot
<b>Anti-emetics</b>	domperidone	Motilium
	metoclopramide	Maxolon, Pramin
	prochlorperazine	Stemetil, Stemizine
<b>Antihistamines</b>	dimenhydrinate	Dramamine
	promethazine	Avomine, Phenergan
<b>Beta-blockers</b>	metoprolol	Betaloc, Lopresor, Metohexal, Metolol, Metrol, Minax
	propranolol	Deralin, Inderal
<b>Anti-epileptics</b>	topiramate	Topamax
	valproate	Epilim, Valpro
<b>Other drugs used for migraine prophylaxis</b>	amitriptyline	Endep, Tryptanol
	clonidine	Catapres
	cyproheptadine	Periactin
	methysergide	Deseril
	pizotifen	Sandomigran

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*The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the clinical circumstances of each patient.*



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