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## Disclaimer
◆ Attack of severe pain localised to the unilateral orbital, supra-orbital, and/or temporal areas; lasts from 15 minutes to 3 hours. Occurs from once every other day to 8 times per day.

◆ Attacks occur at the same time period for several weeks (the cluster period); accompanied by ipsilateral autonomic signs. Most patients are restless or agitated during attacks compared to people with migraine who often report motion sensitivity during attacks.

◆ Pathophysiology is thought to result from hypothalamic activation with secondary trigeminal and autonomic activation. Cluster period attacks can be precipitated by alcohol, volatile smells, warm temperatures, and sleep.

◆ Diagnosis is based on International Headache Society 3-beta (IHS-3b) criteria.

◆ Medications for acute treatment should be used in combination with prophylactic medications.

◆ Greater occipital nerve blockade often provides relief until preventative medications take effect. Neurostimulation techniques have provided dramatic response in patients with chronic cluster headaches that are refractory to medical treatments. Invasive neurostimulation techniques employed in cluster headache include occipital nerve stimulation and posterior hypothalamic region deep brain stimulation. Emerging techniques include invasive sphenopalatine ganglion stimulation and non-invasive vagal nerve stimulation.
### Definition

Cluster headache is considered one of the most painful conditions known to humanity. The clinical picture consists of unilateral headache attacks lasting 15 to 180 minutes, associated with autonomic symptoms secondary to parasympathetic hyperactivity and sympathetic hypo-activity. Some patients will develop chronic cluster headache and experience daily attacks without periods of remission. Pain is often localised to the unilateral orbital, supra-orbital, and/or temporal areas and can occur from once every other day to 8 times per day.

During an attack the pain is strictly unilateral, although some patients report the pain shifting sides between or during bouts but not during the attack itself. Both cluster bouts and attacks during a cluster period can show cyclical periodicity occurring at the same time of year or the same time of day. Autonomic features accompanying pain include ptosis, conjunctival injection, lacrimation, rhinorrhoea, nasal stuffiness, eyelid and facial swelling, aural fullness, facial sweating, and redness. Most patients become very restless or agitated during an acute attack, unlike people with migraine who often report motion sensitivity during attacks.

Ninety percent of patients will have episodic cluster headache,[1] which consists of attacks lasting from 7 days to 1 year (averaging from 2 weeks to 3 months), separated by remission periods lasting at least 1 month. The chronic form of cluster headache is seen in approximately 10%[1] and consists of attacks that occur for more than 1 year, with less than 1 month's remission.[2] The condition may be chronic from onset or may evolve over time from the episodic form.

### Epidemiology

This is one of the few primary headaches that affect men predominantly (male-to-female ratio varies between 2.5:1 and 3.5:1).[1] [6] [7] Studies suggest the prevalence of cluster headache is likely to be at least one person per 500,[8] and between 8% and 10% in a headache clinic population.[9] The age of onset is usually between 20 and 40 years. Although extremely rare, it has been reported in children as young as 6 years of age. Approximately 90% of affected people have the episodic form; 10% have the unremitting form from onset (primary chronic cluster headache).[10]

### Aetiology

The aetiology is not known. A history of head trauma, heavy cigarette smoking, and heavy alcohol intake are all associated with the disease,[1] [11] although no causal relationship has been found. Smoking cessation has no effect on the disease.[12] Some studies have reported an association between cluster headache and sleep apnoea, with some patients having improved headache control with treatment of their sleep apnoea.[13] The condition does appear to have a heritable tendency in some families, with first-degree relatives of affected people having an estimated 14- to 48-fold increased risk of developing it.[8]

### Pathophysiology

The pathogenesis is complex and not understood completely. The 3 cardinal features of the disorder are:

- Trigeminal distribution of the pain
- Ipsilateral cranial autonomic symptoms
Cluster headache

- Circadian/circannual pattern of attacks.

There is now a well-described physiologic reflex arc, the trigemino-parasympathetic reflex, that is thought to potentiate the trigeminal pain and cranial autonomic features of cluster headache.[14] Nociceptive information from pain-sensitive structures in the face, and particularly the dura mater and cerebral blood vessels, is carried to the brainstem via the trigeminal nerve. Within the brainstem, these trigeminal fibres synapse in the area known as the trigeminocervical complex (TCC). Information is then sent to the hypothalamus, thalamus, and cortex via the pain-processing pathways. Afferent trigeminal signals arriving at the TCC activate the cranial parasympathetic system. This results in increased firing of the parasympathetic fibres innervating facial structures, and causes the autonomic features seen in an attack. Neurotransmitters released at these parasympathetic nerve endings cause further irritation of the trigeminal sensory nerve endings, and this potentiates the reflex arc further. The timing of cluster headaches and the agitation associated with attacks have led to the belief that the hypothalamus must play a role in the pathophysiology of cluster headache.

This theory has been supported by functional neuro-imaging studies that have detected activation of the posterior hypothalamic region ipsilateral to the pain during a cluster attack.[15]

Classification

International classification of headache disorders-3 beta (ICHD-3b)[2]

Cluster headache and other trigeminal autonomic cephalalgias:

Cluster headache

- Episodic cluster headache
- Chronic cluster headache.

Paroxysmal hemicrania

- Episodic paroxysmal hemicrania
- Chronic paroxysmal hemicrania.

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), and short-lasting unilateral neuralgiform headache attacks with autonomic features (SUNA):

Probable trigeminal autonomic cephalalgia

- Probable cluster headache
- Probable paroxysmal hemicrania
- Probable SUNCT.
Secondary prevention
Patients are advised to contact their physician as soon as possible following the start of another episode so that appropriate therapy can be initiated.
Case history

Case history #1

A 44-year-old male smoker presents with a 9-year history of recurrent headaches. Headaches occurred twice-monthly initially, always in the early hours of the morning (2 a.m. to 3 a.m.). The headaches have increased to an average of 2 episodes per day. The acute episodes can occur at any time, and last between 2 and 4 hours. He always has a nocturnal event. Attacks are triggered immediately after drinking alcohol or with the smell of strong aftershave or petrol. The pain is excruciating and focused around his right eye. The right eye reddens and tears, the right eyelid droops, and the right nostril runs. He becomes severely agitated during attacks, often pacing the room or rocking back and forth. Physical examinations, lumbar puncture, brain magnetic resonance imaging (including pituitary views), and pituitary function blood tests are normal.

Other presentations

Migrainous features can be seen in cluster headache, including aura symptoms (14% of patients[1]), ipsilateral photophobia and/or phonophobia (61.2%), and nausea and vomiting (27.8%).[3] During remission periods, patients may report mild pre-headache sensations or shadows in the same location as the cluster headaches. Three percent of patients fail to report autonomic features and agitation during attacks. Continuous background pain has been reported in nearly one third of patients with chronic cluster headache.[4] [5]

Step-by-step diagnostic approach

The diagnosis of cluster headache, as with all primary headache syndromes, is purely clinical. It is important to elicit a good history for the condition.

History

There is no standard test, and diagnosis is based on clinical history eliciting the features of severe unilateral pain with agitation and cranial autonomic features. Patient symptoms should fulfil International Headache Society (IHS) diagnostic criteria with any atypical features raising suspicion of a secondary cause.[2]

- Cluster headache

  A. At least 5 headaches fulfilling criteria B to D.

  B. Severe or very severe unilateral orbital, supra-orbital, and/or temporal pain lasting 15 to 180 minutes if left untreated.

  C. Headache is accompanied by at least one of the following:

    1. Ipsilateral conjunctival injection and/or lacrimation
    2. Ipsilateral nasal congestion and/or rhinorrhea
    3. Ipsilateral eyelid oedema
4. Ipsilateral facial and forehead oedema
5. Ipsilateral miosis and/or ptosis
6. A sense of restlessness or agitation.

D. Attacks have a frequency from 1 every other day to 8 per day.

E. Not attributed to another disorder.
• Episodic cluster headache
  A. Attacks fulfilling criteria A to E for cluster headache
  B. At least 2 cluster periods lasting 7 to 365 days and separated by pain-free remission periods lasting at least 1 month.
• Chronic cluster headache
  A. Attacks fulfilling criteria A to E for cluster headache.
  B. Attacks occur over more than 1 year without remission periods or with remission periods lasting less than 1 month.

Pain is unilateral, typically of rapid onset and felt in the orbital, retro-orbital, or temporal regions. It is excruciating, peaks within minutes, and lasts for approximately 15 to 180 minutes before rapidly subsiding. Patients are often agitated and cannot lie still. Associated autonomic symptoms ipsilateral to the pain include: lacrimation, conjunctival injection or reddening, nasal congestion, rhinorrhea, eyelid and/or facial swelling, ptosis, miosis, and facial and forehead sweating.

The average number of attacks is 4 per day.[1] The maximum number of attacks, by IHS criteria, is 8. Higher numbers of attacks should raise suspicion of paroxysmal hemicrania and should prompt an indometacin trial. Thirty-seven percent of patients report a predictable time of onset during the day, and 72% report predictable nocturnal attacks, which often waken them from sleep. Patients might complain of associated symptoms, such as nausea and vomiting (up to 50%), ipsilateral photophobia (54% to 64%), phonophobia (43%), or osmophobia (26%) during attacks. Approximately 14% of patients have an aura before the attack, most often with visual or sensory symptoms.[1] [7] [16]

Triggers for attacks include: alcohol (50%-60%), sleep (72%, including daytime naps), volatile smells (such as perfume or paint), and warm temperatures. Note that in the case of alcohol, cluster attacks will be triggered within one hour of ingestion, in contrast to migraine, where attacks are triggered several hours later.

**Examination**

Neurological examination may reveal a persistent partial Horner’s syndrome or isolated ptosis, even between bouts. However, in most cases the examination will be normal, and any abnormal findings should prompt investigation of a secondary cause.

**Laboratory tests**

Erythrocyte sedimentation rate is checked to exclude giant cell arteritis in all headache patients over 50 years of age. Some centres will also check pituitary function with blood tests, including thyroid function tests, luteinising hormone, follicle-stimulating hormone, insulin-like growth factor 1, cortisol, prolactin, testosterone, estradiol, progesterone, glucose, and growth hormone.
Cluster headache

**Imaging**
There is no imaging test to diagnose cluster headache, but a brain computed tomographic scan or magnetic resonance imaging (MRI) is a reasonable screening test to rule out secondary causes. In the UK, National Institute for Health and Care Excellence guidelines indicate that patients should be reviewed or discussed with a neurologist or headache specialist before imaging is carried out. Due to a number of reports of pituitary tumours presenting with cluster-like symptoms, some centres recommend MRI of the pituitary but this should be at the discretion of the reviewing specialist. Other tests include polysomnography (which can be used for patients with a history that suggests sleep apnoea) and ECG (which can be used to exclude conduction abnormalities resulting from drug choices).

**Risk factors**

### Strong

**male sex**
- Ratio of men to women is between 2.5:1 and 3.5:1.[1]

**family history**
- Twin and family studies show a 14-fold increase in risk in first-degree relatives of patients with the disease and a 2-fold increase in second-degree relatives.[8] However, in most cases there is no FHx of cluster headache.

**head injury**
- A high proportion of patients have a history of head trauma with concussion, but causative links are not established.[11][12]

**cigarette smoking**
- Up to 85% of patients are heavy smokers, but stopping smoking does not reduce the frequency of cluster headaches.[1][11][12] However, smoking does increase the risk of coronary artery disease, which can influence treatment.

**heavy drinking**
- Alcohol consumption is often an immediate trigger for headache during a cluster period.[12][13]

**History & examination factors**

### Key diagnostic factors

#### presence of risk factors (common)
- Key risk factors include FHx, male sex, head injury, heavy smoking, and heavy drinking.

#### repeated attacks of unilateral pain (common)
- Rapid onset of unilateral orbital, retro-orbital, or temporal pain, or maxillary region, which peaks within minutes and lasts for approximately 15 to 180 minutes. The average number of attacks is 4 per day,[1] with a maximum of 8. Higher numbers of attacks should raise suspicion of paroxysmal hemicrania.
Cluster headache

Diagnosis

excruciating pain (common)

- Pain is excruciating. It is described as the worst pain ever experienced, with women comparing it to childbirth. Often the pain is described as boring, sharp, piercing, burning, or pulsating. A number of patients will complain of a constant pressing or burning background pain or ‘shadows’ between acute attacks. Suicidal thoughts are common as a result of the pain.

lacrimation, rhinorrhoea, and partial Horner's syndrome (common)

- International Headache Society criteria require at least one autonomic feature for diagnosis, although autonomic features are absent in 3% of patients.[2] Lacrimation is the most frequent symptom, followed by conjunctival injection, nasal congestion, rhinorrhoea, and partial Horner’s syndrome (ptosis and miosis).

agitation (common)

- Most patients are agitated and restless. They might pace, rock back and forth, bang their head against the wall, or lie on a cool tile floor. Only 7% of patients can lie still during an attack.[1]

nausea, vomiting (common)

- Common associated symptoms.

photophobia, phonophobia (common)

- Common associated symptoms.

migrainous aura (common)

- Typical migraine aura has been reported by approximately 14% of patients.[1] [7] [16]

Diagnostic tests

1st test to order

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>brain CT scan or MRI</td>
<td>normal in primary cluster headache; abnormal results might indicate secondary causes (e.g., tumour, cavernous sinus pathology)</td>
</tr>
<tr>
<td>eythrocyte sedimentation rate</td>
<td>normal in primary cluster headache</td>
</tr>
<tr>
<td>pituitary function tests</td>
<td>normal in primary cluster headache; abnormalities may suggest secondary causes resulting from a pituitary adenoma</td>
</tr>
</tbody>
</table>
Other tests to consider

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>polysomnogram</td>
<td>• Useful for patients with a history that suggests sleep apnoea (which has been suggested as being over-represented in patients with cluster headache) and on patients with medically intractable chronic cluster headaches. Can also be performed on those with chronic cluster headaches, although evidence to support this is lacking.</td>
</tr>
<tr>
<td></td>
<td>abnormal in patients with sleep apnoea</td>
</tr>
<tr>
<td>ECG</td>
<td>• Used to exclude conduction abnormalities before starting treatment with calcium-channel blocker (i.e., verapamil) or increasing verapamil dose.</td>
</tr>
<tr>
<td></td>
<td>often normal; conduction abnormalities or evidence of ischaemic changes may alter drug choices</td>
</tr>
</tbody>
</table>

Differential diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine</td>
<td>• Repeated attacks of severe unilateral or bilateral throbbing or pressure pain, which is often severe. Pain lasts at least 4 hours without treatment. Prominent associated features of migraine include nausea and vomiting, photophobia (often bilateral), phonophobia, and motion sensitivity. Approximately 1 in 3 patients will have an aura with their headache and these can consist of visual, sensory, motor, or speech disturbance. Autonomic features can be seen but tend to be bilateral and less prominent than in cluster headache. Triggers may include alcohol (delayed response of several hours), sleep deprivation or excess, hunger, dehydration, bright lights, atmospheric pressure changes, and some foodstuffs. Oxygen does not have a dramatic effect on the pain, and it often responds well to oral triptans. A family history is seen in the majority of patients.</td>
<td>• There are no distinguishing diagnostic tests, although a complete response to high-flow oxygen is unusual.</td>
</tr>
<tr>
<td>Condition</td>
<td>Differentiating signs / symptoms</td>
<td>Differentiating tests</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Paroxysmal hemicrania</strong></td>
<td>• Signs and symptoms are similar to those of cluster headache, with severe unilateral orbital, supra-orbital, or temporal pain, and ipsilateral autonomic symptoms of the eye and nose. Attacks are 3 times more common in women than in men; shorter (2 minutes to 30 minutes) and more frequent (between 1-40/day) than cluster headache; and respond to indometacin. Attacks can be episodic or chronic.[2]</td>
<td>• Completely responds to indometacin.</td>
</tr>
<tr>
<td><strong>Short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)</strong></td>
<td>• At least 20 attacks of severe unilateral orbital, supra-orbital, or temporal stabbing or pulsating pain lasting 5 seconds to 4 minutes, accompanied by ipsilateral lacrimation and/or conjunctival injection. Attacks occur from 3 to 200 times daily.[2]</td>
<td>• There are no distinguishing diagnostic tests.</td>
</tr>
<tr>
<td><strong>Trigeminal neuralgia</strong></td>
<td>• Paroxysmal attacks of brief, unilateral, electric-shock-like pains, lasting from a fraction of a second to 2 minutes, usually affecting the second and third divisions of the trigeminal nerve. Trigger factors for pain may include shaving, smoking, talking, and brushing teeth. Attacks are stereotyped in the individual patient. No clinically evident neurological lesion. Pain often evokes spasms of facial muscles on the affected side (tic douloureux).[2]</td>
<td>• There are no distinguishing diagnostic tests.</td>
</tr>
<tr>
<td><strong>Hemicrania continua</strong></td>
<td>• Continuous unilateral headache that lasts for at least 3 months and responds to indometacin. Headache is of moderate intensity with exacerbations of severe pain. One ipsilateral autonomic feature is usually included.[2]</td>
<td>• Complete response to indometacin.</td>
</tr>
<tr>
<td>Condition</td>
<td>Differentiating signs / symptoms</td>
<td>Differentiating tests</td>
</tr>
<tr>
<td>---------------------------------------</td>
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</tr>
<tr>
<td>Angle-closure glaucoma</td>
<td>• Severe pain in the region of the eye due to raised intraocular pressure. Other symptoms include nausea, blurred vision, corneal oedema, and redness of the eye.[2]</td>
<td>• Tonometry shows raised intra-ocular pressure. • Gonioscopy shows narrow angles. • Eye examination shows reduced visual acuity; a semi-dilated, fixed pupil; a cloudy cornea; and optic disc changes.</td>
</tr>
<tr>
<td>Cluster-tic syndrome</td>
<td>• Symptoms of both cluster headache and trigeminal neuralgia. Both conditions need to be treated.[2]</td>
<td>• There are no distinguishing diagnostic tests.</td>
</tr>
<tr>
<td>Primary stabbing headache</td>
<td>• Single or repeated transient stabs of pain felt mainly in the orbit, temple, and parietal area, lasting up to a few seconds and recurring up to many times per day. Location of pain can move around and change sides. More common in people with migraine or cluster headache.[2]</td>
<td>• There are no distinguishing diagnostic tests.</td>
</tr>
<tr>
<td>Idiopathic or primary cough headache</td>
<td>• Sudden onset of headache caused only by coughing or straining, lasts from 1 second to 30 minutes. Usually bilateral. Indometacin is often effective treatment. Secondary causes of cough headache, such as posterior fossa lesions, should be considered.[2]</td>
<td>• There are no distinguishing diagnostic tests for primary cough headache. MRI of posterior fossa should be considered to exclude secondary causes of cough headache.</td>
</tr>
<tr>
<td>Primary exertional headache</td>
<td>• Pulsating headache lasts from 5 minutes to 48 hours; brought on only by physical exertion, especially at high altitude or in hot weather. Indometacin is usually effective.[2]</td>
<td>• There are no distinguishing diagnostic tests.</td>
</tr>
<tr>
<td>Headache associated with sexual activity</td>
<td>• Dull ache in head or neck occurring during sexual activity and intensifying at orgasm, or a sudden, explosive headache occurring at orgasm, lasting up to 3 hours.[2]</td>
<td>• There are no distinguishing diagnostic tests.</td>
</tr>
</tbody>
</table>
### Condition | Differentiating signs / symptoms | Differentiating tests
--- | --- | ---
Hypnic headache | • Dull headache occurs only during sleep and wakes the patient. Headache occurs >15 times per month, lasts ≥15 minutes, with no autonomic phenomena. Pain is usually bilateral, is mild to moderate, and can be treated with caffeine or lithium.[2] Onset is after age 50 years. | • There are no distinguishing diagnostic tests.
Primary thunderclap headache | • Sudden onset of severe headache lasting 1 hour to 10 days and not recurring regularly over the subsequent weeks or months. Often associated with vascular disorders, which must be excluded (particularly subarachnoid haemorrhage).[2] | • There are no distinguishing diagnostic tests.
Subarachnoid haemorrhage | • Sudden onset of intense and incapacitating headache, often unilateral at onset and accompanied by nausea, vomiting, altered consciousness, and nuchal rigidity.[2] | • MRI or CT scan without contrast has >90% sensitivity in the first 24 hours. Lumbar puncture should be performed if neuroimaging has not provided the diagnosis.
Giant cell arteritis | • Pain and tenderness over temporal artery, which might occur with loss of vision. Pain resolves within 3 days of high-dose corticosteroid treatment.[2] | • Duplex scanning of temporal arteries might reveal thickening of the arterial wall. ESR >50 mm/hour and elevated CRP seen in majority of patients. Biopsy shows giant cell arteritis.

### Diagnostic criteria

**International classification of headache disorders-3 beta (ICHD-3b)**[2]

- Cluster headache
  
  A. At least 5 headaches fulfilling criteria B to D.
  
  B. Severe or very severe unilateral orbital, supra-orbital, and/or temporal pain lasting 15-180 minutes if left untreated.
  
  C. Headache is accompanied by at least 1 of the following:
1. Ipsilateral conjunctival injection and/or lacrimation
2. Ipsilateral nasal congestion and/or rhinorrhoea
3. Ipsilateral eyelid oedema
4. Ipsilateral facial and forehead oedema
5. Ipsilateral miosis and/or ptosis
6. A sense of restlessness or agitation.

D. Attacks have a frequency from 1 every other day to 8 per day.

E. Not attributed to another disorder.

- Episodic cluster headache

A. Attacks fulfilling criteria A to E for cluster headache.

B. At least 2 cluster periods lasting 7-365 days and separated by pain-free remission periods lasting at least 1 month.

- Chronic cluster headache

A. Attacks fulfilling criteria A to E for cluster headache.

B. Attacks occur over a period of >1 year without remission periods or with remission periods lasting <1 month.
Step-by-step treatment approach

The aim of treatment is to provide prompt relief from acute attacks while using preventative therapy to suppress attacks for the duration of the bout, or over longer periods in chronic cluster headache.

Treatment of cluster headache can be separated into acute treatments, transitional treatments, and preventative treatments. Lifestyle advice should also be given where appropriate; for example, avoiding alcohol and other triggers.

Acute attack therapy

Acute therapy is used to abort an individual attack. Standard painkillers are ineffective and there is no evidence to support the use of non-steroidal anti-inflammatory drugs, opioids, or paracetamol in these patients. Prescription of these agents should be avoided. Abortive treatment is focused on parenteral triptans and inhaled oxygen. As stated in guidelines from the UK’s National Institute for Health and Care Excellence, all patients with cluster headache should be offered oxygen or subcutaneous or nasal triptans in the absence of contra-indications.[17]

Triptans:

- Oral medications are of little or no benefit because symptoms begin with little or no warning and peak rapidly.[18]
- Subcutaneous sumatriptan has been shown to be effective in acute treatment.[18] One study found that patients were free of pain or had only mild pain within 15 minutes of administration of subcutaneous sumatriptan.[19] There is also good evidence that nasal sumatriptan and zolmitriptan are effective, with nearly 50% of patients given either drug reporting freedom from pain.[20] [21] [22] [23]
- Cardiovascular risk factors (e.g., coronary artery disease [CAD], cerebrovascular disease, or uncontrolled hypertension) can preclude the use of triptans. A maximum of 2 doses of subcutaneous sumatriptan can be used in a 24-hour period without the risk of tachyphylaxis.

Oxygen:

- Oxygen given at a rate of at least 12 L/minute for at least 15 minutes through a non-rebreathing face mask[17] has shown efficacy in aborting cluster attacks.[20] [21] [24] One double-blind randomised placebo-controlled crossover study found that 78% of patients were pain-free after inhalation of 100% oxygen at 12 L/minute for 15 minutes.[21]

Transitional therapy

Preventative medicine may take at least 2 weeks at the maximum dose to exert their full effect. Drugs or interventions that act more quickly (but are not appropriate for long-term use) are often started concurrently with standard preventative agents to suppress attacks rapidly. These interventions are referred to as transitional or bridge therapy. A short tapering course of prednisolone is used most commonly. However, corticosteroids must not be used on a regular basis (more than 2-3 times a year), however, due to the risk of side effects.

Other options include intravenous dihydroergotamine, or greater occipital nerve block. Greater occipital nerve block has been found to render nearly two-thirds of patients pain-free at 4 weeks.[25] A nerve block is often performed once at the start of a bout but can be repeated on a regular basis (once every 3-4
Cluster headache months) in patients with chronic cluster headache. Dihydroergotamine is contraindicated in patients with cardiovascular risk factors (e.g., CAD, hypertension) and should not be used in these patients.

**Preventative therapy**

The main goal is rapidly suppressing individual attacks and maintaining remission for the duration of the patient's typical cluster period. In the episodic form, once the patient has been headache-free for at least 2 weeks, the preventative therapy is gradually tapered off. In the chronic form, preventative therapy is continued indefinitely. However, if the patient remains headache-free, reducing the dose is periodically attempted.

Verapamil is considered the first-line preventative therapy for both episodic and chronic forms,[17] although some other medicines are also used, alone or in combination.[20] [26] An ECG must be performed before verapamil is prescribed to exclude bradycardia and other conduction abnormalities. ECGs are then repeated before each dose increase to check for signs of developing heart block.[27] Side effects include constipation, dizziness, and ankle-swelling. Once the bout is over, verapamil should be slowly withdrawn. On entering the next bout, the patient should be started at the previous maximum efficacious dose, as long as the baseline ECG is normal.

Second-line preventative therapies include topiramate (may be effective in up to 50% of patients),[28] [29] [30] [31] [32] lithium,[33] [34] gabapentin,[35] [36] [37] [38] and melatonin.[39] Valproate semisodium may be considered as a third-line option. In 2018 the European Medicines Agency finalised a review of valproate and its analogues, recommending that these medicines are contraindicated for migraine prophylaxis during pregnancy due to the risk of congenital malformations and developmental problems in the infant/child.[40] In the US, valproate and its analogues are contraindicated for migraine prophylaxis in pregnant women. In both Europe and the US, valproate and its analogues must not be used in female patients of childbearing potential unless there is a pregnancy prevention programme in place and certain conditions are met.[40]

**Neuromodulation**

Surgery should be considered once all other options have been tried. Patients can be considered for neuromodulation with methods such as occipital nerve stimulation (ONS) or deep brain stimulation (DBS) of the posterior hypothalamic region.[41] The mechanisms by which neuromodulation works in cluster headache remain unknown, but they are thought to involve a neuroplastic response of the brain's pain matrix.

The rationale for ONS lies in the important role the trigeminocervical complex has in cluster headache. ONS has been shown in 4 cohort studies to be a promising therapeutic option in intractable chronic cluster headache, with over two-thirds of patients showing a good response.[42] [43] [44] [45] There is now evidence that ONS is effective even in the longer-term treatment of chronic cluster headache.[46] [47]

The rationale for DBS in chronic cluster headache stems from the imaging findings of activation of the ipsilateral posterior hypothalamic region in cluster attacks.[15] There are now over 80 published cases, with two-thirds of patients achieving a 50% or more improvement in their headache frequency over a mean follow-up of 2.2 years.[48] [49] [50] [51] One prospective open-label study of 21 patients has shown sustained efficacy over a median of 18 months.[52] One randomised, double-blind placebo-controlled trial of DBS in cluster headache, involving only a 2-month study period, failed to show a difference between sham and active stimulation.[53] However, it has since become clear that it takes at least 3 months to see
a benefit with this procedure, and so the negative outcome of this trial is thought to be due to the short study period. The potential side-effect profile of DBS includes intracerebral bleed, stroke, death, infection, and seizure (although all are very rare), and so should only be offered to those who have failed all options including peripheral neurostimulation with ONS.

Decompression or destruction of the trigeminal nerve is no longer routine surgical treatment for cluster headache. These therapies were previously used for refractory cluster headache, but morbidity is significant for a low rate of pain cessation. Given the promising results of neuromodulation, these surgical techniques should not be considered in the treatment options for cluster headache.[54]

**Treatment details overview**

Consult your local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing. (see Disclaimer)

### Acute

**acute attack: without CVD or uncontrolled hypertension**

<table>
<thead>
<tr>
<th>Step</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>subcutaneous sumatriptan</td>
</tr>
<tr>
<td>1st</td>
<td>oxygen</td>
</tr>
<tr>
<td>2nd</td>
<td>intranasal zolmitriptan</td>
</tr>
<tr>
<td>3rd</td>
<td>intranasal sumatriptan or oral zolmitriptan</td>
</tr>
<tr>
<td>3rd</td>
<td>intranasal lidocaine</td>
</tr>
<tr>
<td>plus</td>
<td>transitional therapy</td>
</tr>
<tr>
<td>adjunct</td>
<td>greater occipital nerve block</td>
</tr>
</tbody>
</table>

**acute attack: with CVD or uncontrolled hypertension**

<table>
<thead>
<tr>
<th>Step</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>oxygen</td>
</tr>
<tr>
<td>2nd</td>
<td>intranasal lidocaine</td>
</tr>
<tr>
<td>adjunct</td>
<td>transitional therapy</td>
</tr>
<tr>
<td>adjunct</td>
<td>greater occipital nerve block</td>
</tr>
</tbody>
</table>

### Ongoing

**episodic/chronic cluster headache**

<table>
<thead>
<tr>
<th>Step</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>verapamil</td>
</tr>
<tr>
<td>2nd</td>
<td>lithium</td>
</tr>
<tr>
<td>2nd</td>
<td>topiramate</td>
</tr>
<tr>
<td></td>
<td>Ongoing</td>
</tr>
<tr>
<td>----</td>
<td>----------------------</td>
</tr>
<tr>
<td>2nd</td>
<td>gabapentin</td>
</tr>
<tr>
<td>2nd</td>
<td>melatonin</td>
</tr>
<tr>
<td>3rd</td>
<td>valproate semisodium</td>
</tr>
<tr>
<td>4th</td>
<td>surgery</td>
</tr>
</tbody>
</table>
**Treatment options**

<table>
<thead>
<tr>
<th>Acute</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute attack: without CVD or uncontrolled hypertension</td>
</tr>
<tr>
<td>1st subcutaneous sumatriptan</td>
</tr>
<tr>
<td>Primary options</td>
</tr>
<tr>
<td>- sumatriptan: 6 mg subcutaneously as a single dose, may repeat at least one hour after initial dose if required, maximum 12 mg/day</td>
</tr>
<tr>
<td>- Triptans are contraindicated in patients with coronary artery disease, peripheral vascular disease, or cerebrovascular disease, and should not be used in patients with uncontrolled hypertension or severe hepatic impairment or within 24 hours of any other 5HT1 agonist or ergotamine-type medication.</td>
</tr>
<tr>
<td>- Subcutaneous sumatriptan is the most effective treatment for symptomatic relief. [19] [20] It is the only medicine approved for this purpose.</td>
</tr>
<tr>
<td>- A systematic review has found that 74% to 75% of sumatriptan-treated patients obtained relief within 15 minutes compared with 26% of patients in the placebo group, and determined that the number needed to treat is 2.4 for 15-minute pain relief. [18]</td>
</tr>
<tr>
<td>1st oxygen</td>
</tr>
<tr>
<td>- High-dose and high-flow-rate oxygen has been shown to be effective in the acute treatment of cluster attacks, and it decreases both the intensity and duration of an attack. [20] [21] [24] although it is less convenient than sumatriptan.</td>
</tr>
<tr>
<td>- It is safe, can be used multiple times a day, and is not contraindicated in patients with hypertension or vascular disease.</td>
</tr>
<tr>
<td>- When oxygen is used properly, approximately 70% of patients obtain relief within 15 minutes. [12] [20] [21] Some patients find oxygen more effective if used when pain is at maximum intensity; others find that it merely delays the attack for minutes to hours.</td>
</tr>
<tr>
<td>- Oxygen should be given at 100% with a flow rate of at least 12 L/minute through a non-rebreathing face mask for at least 15 minutes or until the attack is terminated.</td>
</tr>
</tbody>
</table>
### Acute

<table>
<thead>
<tr>
<th>2nd</th>
<th>intranasal zolmitriptan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» zolmitriptan nasal: 5 mg (one spray) in one nostril as a single dose, may repeat at least 2 hours after initial dose if required, maximum 10 mg/day</td>
<td></td>
</tr>
<tr>
<td>» Triptans are contraindicated in patients with coronary artery disease, peripheral vascular disease, or cerebrovascular disease, and should not be used in patients with uncontrolled hypertension or severe hepatic impairment or within 24 hours of any other 5HT1 agonist or ergotamine-type medication.</td>
<td></td>
</tr>
<tr>
<td>» Zolmitriptan nasal spray is well tolerated and effective within 30 minutes in episodic disease, with a number needed to treat of 2.8.[20] [21] [22]</td>
<td></td>
</tr>
<tr>
<td>» Used in patients who do not respond to subcutaneous sumatriptan or those who are phobic of needles.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3rd</th>
<th>intranasal sumatriptan or oral zolmitriptan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» sumatriptan nasal: 5-20 mg in one nostril as a single dose, may repeat at least 2 hours after initial dose if required, maximum 40 mg/day</td>
<td></td>
</tr>
<tr>
<td><strong>OR</strong></td>
<td></td>
</tr>
<tr>
<td>» zolmitriptan: 2.5 to 5 mg orally as a single dose, may repeat at least 2 hours after initial dose if required, maximum 10 mg/day</td>
<td></td>
</tr>
<tr>
<td>» Triptans are contraindicated in patients with coronary artery disease, peripheral vascular disease, or cerebrovascular disease, and should not be used in patients with uncontrolled hypertension or severe hepatic impairment or within 24 hours of any other 5HT1 agonist or ergotamine-type medication.</td>
<td></td>
</tr>
<tr>
<td>» Sumatriptan nasal spray is less effective than subcutaneous injection but appears effective compared with placebo.</td>
<td></td>
</tr>
<tr>
<td>» Oral zolmitriptan is less effective than nasal zolmitriptan at 30 minutes (47% versus placebo 29%).[7]</td>
<td></td>
</tr>
</tbody>
</table>

| 3rd | intranasal lidocaine |
### Cluster headache

#### Treatment

**Acute**

*requiring attack suppression*  

**Primary options**

- **lidocaine**: 1 mL of a 10% lidocaine solution placed with a cotton swab intranasally (ipsilaterally/bilaterally) for 5 minutes. Can bring about rapid relief of cluster headache in at least one third of patients. Application should be as close as possible to the sphenopalatine fossa.\(^{[12]}\) \(^{[13]}\)

- **During administration**, patient should recline the head back and towards the affected side.\(^{[12]}\)

*plus*  

**transitional therapy**

**Primary options**

- **prednisolone**: 60 mg orally once daily for 5 days, then reduce dose by 10 mg/day every 3 days

OR

- **dihydroergotamine**: 1 mg intravenously as a single dose, may repeat after 60 minutes if required, maximum 2 mg/day or 6 mg/week

**Preventative medicine** may take at least 2 weeks at the maximum dose to exert their full effect. Drugs or interventions that act more quickly (but are not appropriate for long-term use) are often started concurrently with standard preventative agents to suppress attacks rapidly. These interventions are referred to as transitional or bridge therapy. Options include corticosteroids, dihydroergotamine, and nerve blocks.

- **Corticosteroids** are the fastest-acting agents for inducing remission and are effective as transitional therapy.

- **Approximately 70% to 80%** of patients respond and might become headache-free within 24 hours to 48 hours of the initial dose. There is inadequate evidence regarding which corticosteroid regimen is superior.\(^{[12]}\) \(^{[55]}\)

Patients should be screened for potential contraindications (e.g. coronary artery disease, hypertension, diabetes) prior to treatment with corticosteroids. In these patients, greater occipital nerve blocks should be considered if they are available.

- **Intravenous dihydroergotamine** can work well as transitional therapy and is effective when
### Acute

<table>
<thead>
<tr>
<th>Adjunct</th>
<th>Greater Occipital Nerve Block</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Greater occipital nerve (GON) block has been found to render nearly two-thirds of patients pain-free at 4 weeks.[25]</td>
</tr>
<tr>
<td></td>
<td>Should be considered before any other surgical procedure, when other medical treatments have failed.[12]</td>
</tr>
<tr>
<td></td>
<td>A mixture of corticosteroid and local anaesthetic, or local anaesthetic alone, is injected into the GON on the symptomatic side. The injection point lies two-thirds of the distance on a line drawn from the centre of the mastoid to the external occipital protuberance. If the process is successful and needs to be repeated, then at least 3 months should be left between blocks.</td>
</tr>
</tbody>
</table>

### Acute Attack: With CVD or Uncontrolled Hypertension

<table>
<thead>
<tr>
<th>1st</th>
<th>Oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Triptans are contraindicated in patients with coronary artery disease, peripheral vascular disease, or cerebrovascular disease, and should not be used in patients with uncontrolled hypertension or severe hepatic impairment or within 24 hours of any other 5HT1 agonist or ergotamine-type medication.</td>
</tr>
<tr>
<td></td>
<td>Oxygen is the preferred treatment in patients with these contra-indications.</td>
</tr>
<tr>
<td></td>
<td>Although less convenient than sumatriptan, it tends to be effective in decreasing the intensity and the duration of an attack.[20][24] It is safe, can be used multiple times a day, and is not contraindicated in patients with hypertension or vascular disease.</td>
</tr>
<tr>
<td></td>
<td>When oxygen is used properly, approximately 70% of patients obtain relief within 15 minutes.[12][20][21] Some patients find oxygen more effective if used when pain is at maximum intensity; others find that it merely delays the attack for minutes to hours.</td>
</tr>
<tr>
<td></td>
<td>Oxygen should be given at 100% with a flow rate of at least 12 L/minute through a non-rebreathing face mask for at least 15 minutes or until the attack is terminated.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2nd</th>
<th>Intranasal Lidocaine</th>
</tr>
</thead>
</table>
### Acute

<table>
<thead>
<tr>
<th>Primary options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>lidocaine</strong>: 1 mL of a 10% lidocaine solution placed with a cotton swab intranasally (ipsilaterally/bilaterally) for 5 minutes</td>
</tr>
<tr>
<td>Can bring about rapid relief of disease in at least one third of patients. Application should be as close as possible to the sphenopalatine fossa.</td>
</tr>
<tr>
<td>During administration, patient should recline their head back and towards the affected side.</td>
</tr>
</tbody>
</table>

| Prednisolone: 60 mg orally once daily for 5 days, then reduce dose by 10 mg/day every 3 days |
| Corticosteroids are the fastest-acting agents for inducing remission and are effective as transitional therapy. |
| Approximately 70% to 80% of patients respond and might become headache-free within 24 hours to 48 hours of the initial dose. There is inadequate evidence regarding which corticosteroid regimen is superior. |
| Patients should be screened for potential contraindications (e.g. coronary artery disease [CAD], hypertension [HTN], diabetes) prior to treatment with corticosteroids. In these patients, greater occipital nerve blocks should be considered if they are available. |
| Dihydroergotamine is contraindicated in patients with cardiovascular risk factors and/or established cardiovascular disease (e.g., CAD, HTN) and should not be used in these patients. |

### Ongoing

<table>
<thead>
<tr>
<th>greater occipital nerve block</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients who do not respond to other transitional suppressive therapy, or for whom typical transitional suppressive drugs are contraindicated, nerve block can be considered as short-term suppression. It induces short-term remission in most patients.</td>
</tr>
<tr>
<td>Should be considered before any other surgical procedure, when other medical treatments have failed.</td>
</tr>
</tbody>
</table>

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### Ongoing episodic/chronic cluster headache

<table>
<thead>
<tr>
<th>1st</th>
<th>verapamil</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» verapamil: 80 mg orally (immediate-release) three times daily initially, increase gradually according to response, maximum 480 mg/day (although some specialists recommend higher maximum doses)</td>
<td></td>
</tr>
<tr>
<td>» Highly effective as a long-term prophylaxis. Established treatment of choice for prevention, although evidence is sparse.</td>
<td>[12] [20] [26]</td>
</tr>
<tr>
<td>» Preventative therapy should be started as soon as possible at the onset of a cluster episode.</td>
<td></td>
</tr>
<tr>
<td>» Regular preparation appears to be more effective than the long-acting formations.</td>
<td></td>
</tr>
<tr>
<td>» ECG is done to check for conduction delays before starting treatment and before each dose increase but should not be used if the patient has heart block or arrhythmias.</td>
<td>[27]</td>
</tr>
<tr>
<td>» In the episodic form, once the patient has been headache-free for at least 2 weeks, the preventative therapy is gradually tapered off.</td>
<td></td>
</tr>
<tr>
<td>» In the chronic form, preventative therapy is continued indefinitely. However, if the patient remains headache-free, reducing the dose is periodically attempted.</td>
<td></td>
</tr>
<tr>
<td>» When restarting medication if it has already been successful in previous bouts, patients can be immediately started on the highest dose they last tolerated without the need for a gradual increase, as long as their baseline ECG is normal.</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>2nd</th>
<th>lithium</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» lithium: consult specialist for guidance on dose</td>
<td></td>
</tr>
<tr>
<td>» Effective as prophylaxis, with improvement in as many as 63% of patients with episodic form of disease, although evidence has been contradictory.</td>
<td>[12] [20] [33]</td>
</tr>
</tbody>
</table>
| » Lithium levels should be monitored to prevent toxicity. | [12] Although no therapeutic level for lithium has been established for cluster headache, clinical experience suggests that patients respond best when at the higher end of
<table>
<thead>
<tr>
<th>2nd</th>
<th>topiramate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» <strong>topiramate</strong>: 25 mg orally once daily for 7 days, increase by 25 mg/day increments once weekly to 100-200 mg/day given in 2 divided doses</td>
<td></td>
</tr>
<tr>
<td>» Appears to be relatively effective in clinical practice in the treatment of chronic cluster headache, with up to 50% of patients responding. [28] [29] [30] [31] [32]</td>
<td></td>
</tr>
<tr>
<td>» In the episodic form, once the patient has been headache-free for at least 2 weeks, the preventative therapy is gradually tapered off.</td>
<td></td>
</tr>
<tr>
<td>» In the chronic form, preventative therapy is continued indefinitely. However, if the patient remains headache-free, reducing the dose is periodically attempted.</td>
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<table>
<thead>
<tr>
<th>2nd</th>
<th>gabapentin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
</tr>
<tr>
<td>» <strong>gabapentin</strong>: consult specialist for guidance on dose</td>
<td></td>
</tr>
<tr>
<td>» Gabapentin is an appropriate second-line treatment for cluster headache, although evidence is scarce and clinical experience is not always as dramatic as that reported in the literature. [35] [36] [37] [38] In the episodic form, once the patient has been headache-free for at least 2 weeks, the preventative therapy is gradually tapered off.</td>
<td></td>
</tr>
<tr>
<td>» In the chronic form, preventative therapy is continued indefinitely. However, if the patient remains headache-free, reducing the dose is periodically attempted.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2nd</th>
<th>melatonin</th>
</tr>
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<tbody>
<tr>
<td><strong>Primary options</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Ongoing

- **melatonin:** consult specialist for guidance on dose

  Melatonin might be effective at causing remission within 3 to 5 days but evidence is largely anecdotal.[20] [39]

  Given its safety profile, some have suggested it as first-line therapy in all patients requiring short-term prevention.[13] [56] However, better-quality evidence is available for other therapies.

  - In the episodic form, once the patient has been headache-free for at least 2 weeks, the preventative therapy is gradually tapered off.

  - In the chronic form, preventative therapy is continued indefinitely. However, if the patient remains headache-free, reducing the dose is periodically attempted.

### 3rd

**valproate semisodium**

**Primary options**

- **valproate semisodium:** 200 mg orally twice daily initially, increase gradually according to response, maximum 1500 mg/day (some specialists recommend higher doses)

  Valproate semisodium (equimolar amounts of valproic acid and sodium valproate) may be considered as a third-line option.

  In 2018 the European Medicines Agency finalised a review of valproate and its analogues, recommending that these medicines are contraindicated for migraine prophylaxis during pregnancy due to the risk of congenital malformations and developmental problems in the infant/child.[40] In the US, valproate and its analogues are contraindicated for migraine prophylaxis in pregnant women. In both Europe and the US, valproate and its analogues must not be used in female patients of childbearing potential unless there is a pregnancy prevention programme in place and certain conditions are met.[40]

  - For patients receiving this drug in the episodic form, preventative therapy is gradually tapered off once the patient has been headache-free for at least 2 weeks.

  - In the chronic form, preventative therapy is continued indefinitely. However, if the patient remains headache-free, reducing the dose is periodically attempted.

### 4th

**surgery**
### Ongoing

- Occipital nerve stimulation may have a role in the preventative treatment of medically-refractory chronic cluster headaches. It appears to be well tolerated and safe, and presents an alternative to deep brain stimulation.[41] [42] [43] [44] [45]

- Deep brain stimulation of the posterior hypothalamic region can relieve intractable cluster headaches, with over two-thirds of patients reporting over a 50% improvement in attacks,[48] [49] [50] [51] but it carries greater risk than peripheral neurostimulation. Guidelines should be followed, and surgery should only be considered in chronic patients intractable to all other treatment options.[41] [48]
Emerging

Novel neuromodulation techniques

Novel neuromodulation techniques include invasive sphenopalatine ganglion stimulation and non-invasive vagal nerve stimulation. The sphenopalatine ganglion is a key component of the trigemino-autonomic loop that is responsible for the production of the autonomic features in cluster attacks. An implantable miniaturised device has been developed specifically to treat cluster headache. Evidence shows that the device is useful both in the treatment of acute attacks and potentially as a preventative agent.[57] [58] There is no evidence available on its long-term effectiveness. One device for the non-invasive stimulation of the vagal nerve has been trialled in the treatment of chronic cluster headache. Open-label evidence suggests that the adjunctive prophylactic use is potentially effective, well tolerated, and cost-effective in the preventative treatment of cluster headache.

Botulinum toxin type A

Botulinum toxin type A has been found to be an effective preventative treatment in migraine.[59] There are a number of reports in the literature of botulinum toxin type A being useful in chronic cluster headache, although no randomised placebo-controlled studies have yet taken place.[60] [61] [62] [63]

Psychological treatments

Relaxation training, thermal biofeedback, and cognitive behavioural therapy might help patients to cope with the disease.[13]


**Recommendations**

**Monitoring**

All patients with suspected cluster headache should be seen by a neurologist, and all patients with atypical attacks or who fail first-line treatment should be referred to a headache specialist.

Evidence of gingival hyperplasia should be watched for in patients taking verapamil. ECG is checked after every dose increase to look for abnormal conduction. Thyroid function, renal function, and electrolytes are monitored periodically in patients taking lithium. The objective of follow-up visits is to monitor response of headaches to current therapy and adjust as necessary to achieve complete relief, as well as to monitor for adverse effects.

**Patient instructions**

Patients who smoke are advised to stop. Patients should be advised to follow their clinician’s recommendations on how to gradually increase the dose of their preventative drugs to their maximum. They must also be made aware that it can take several weeks to see the full effect of a drug. Patients are directed to taper slowly off preventative medications once they are completely headache-free for 2 weeks and/or once they have moved beyond their usual cluster period duration. In chronic disease, patients are advised to continue preventative medications for 6 months to 12 months before considering taper. Thereafter, the patient can periodically attempt to reduce or eliminate medication as long as headaches do not recur.

Patients who develop chest pain on triptans must inform the prescribing doctor as soon as possible and not re-use the triptans until reviewed.

Patients should be advised to avoid alcohol and other triggers where appropriate. [NHS Choices: cluster headaches] [Organisation for the Understanding of Cluster Headache (OUCH UK)]

Females of childbearing potential must follow a pregnancy prevention programme while on treatment with valproate medicines. For EU countries, the European Medicines Agency states that this programme should include:[40]

- an assessment of patient’s potential for becoming pregnant;
- pregnancy tests before starting and during treatment as needed;
- counselling about the risks of valproate treatment and the need for effective contraception throughout treatment;
- a review of ongoing treatment by a specialist at least annually; and
- a risk acknowledgement form that patients and prescribers will go through at each such annual review to confirm that appropriate advice has been given and understood.
Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>depression</td>
<td>short term</td>
<td>medium</td>
</tr>
</tbody>
</table>

Patients can become depressed and anxious about their condition. Usually improves with effective treatment of the disease. The possibility of suicide must be kept in mind, although this is seen rarely.

Prognosis

Long-term prognosis is unclear. However, epidemiological studies have suggested that symptoms tend to improve with increasing age.[12] Although the disease is excruciating and incapacitating, there are no real long-term complications.
## Diagnostic guidelines

### Europe

**Headaches in over 12s: diagnosis and management**

*Published by:* National Institute for Health and Care Excellence  
*Last published:* 2015

**Guidelines for all healthcare professionals in the diagnosis and management of migraine, tension-type, cluster and medication-overuse headache**

*Published by:* British Association for the Study of Headache  
*Last published:* 2010

### International

**International classification of headache disorders-3 beta (ICHD-3b)**

*Published by:* Headache Classification Committee of the International Headache Society  
*Last published:* 2013

### North America

**Diagnosis and treatment of headache**

*Published by:* Institute for Clinical Systems Improvement  
*Last published:* 2013

## Treatment guidelines

### Europe

**Headaches in over 12s: diagnosis and management**

*Published by:* National Institute for Health and Care Excellence  
*Last published:* 2015

**Cluster headache and other trigemino-autonomic cephalalgias**

*Published by:* European Academy of Neurology (European Federation of Neurological Societies)  
*Last published:* 2011

**Guidelines for all healthcare professionals in the diagnosis and management of migraine, tension-type, cluster and medication-overuse headache**

*Published by:* British Association for the Study of Headache  
*Last published:* 2010

### North America

**Treatment of cluster headache: The American Headache Society evidence-based guidelines**

*Published by:* The American Headache Society  
*Last published:* 2016
Online resources

1. NHS Choices: cluster headaches (external link)

2. Organisation for the Understanding of Cluster Headache (OUCH UK) (external link)
Key articles

- Law S, Derry S, Moore RA. Triptans for acute cluster headache. Cochrane Database Syst Rev. 2013: (7);CD008042. Full text  Abstract

References


18. Law S, Derry S, Moore RA. Triptans for acute cluster headache. Cochrane Database Syst Rev. 2013: (7);CD008042. Full text   Abstract


41. European Academy of Neurology (European Federation of Neurological Societies). Cluster headache and other trigemino-autonomic cephalgias. 2011 [internet publication]. Full text


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