Cluster headache is a relatively uncommon disorder. It is more common in men than women, it can start at any age and most sufferers are or have been smokers (1). It is rare to see this condition occurring with familial tendency (i.e. repeated in different family members as an inherited disorder).

**Duration, frequency and time course of attacks**

The condition derives its name from the fact that patients typically experience “clusters” of pain, whereby they have a few weeks of severe intermittent episodes of pain recurring throughout this period. Between clusters they are entirely free of pain. Typically each episode of pain lasts somewhere between 20 minutes and 4 hours, but some patients may rarely have a background mild discomfort or longer attacks (2). Patients most commonly have 1 – 3 attacks per day but it may be more or less frequent. Such episodic clusters may repeat over the years, and in some cases the condition may change from intermittent clusters into a chronic form of continued attacks (chronic cluster headache). Some patients may start off with the chronic form and revert to episodic or vice versa. Although cluster headache is often a lifelong affliction, it may disappear in some patients.

**Typical and diagnostic features of pain**

The pain is typically extremely severe and usually recalled as the most severe ever experienced (e.g. far worse than childbirth in women who have had children). One of the most useful diagnostic features of the pain in cluster headache is that patients describe a sense of *intense restless agitation* whereby they can not stay still in just one position; instead, it is usual that patients hold their head or press in very tight, bang their head against things, rock, pace about, etc. This is different from migraine, where patients almost always want to stay very still and find that even small movements of the head or relatively minor exertion exacerbates the pain.

Another very useful diagnostic feature of cluster headache is that pain may, in some, be precipitated within a short time of consuming even small amounts of alcohol (e.g. within an hour or so, unlike with migraine where pain typically occurs the day after). Other trigger factors include volatile smells and warm environments. However, when out of the acute cluster, patients will be able to drink alcohol without triggering an attack.

---

(1) Unfortunately, stopping smoking does not seem to turn off cluster headache.
(2) If attacks are briefer and/or more frequent, then it may be that this is not cluster headache but another one of the disorders in this “family” of disorders otherwise known as *trigeminal autonomic cephalgias* (TACs). Other TACs include:

- **a)** paroxysmal hemicrania (usually 5-40 attacks of severe unilateral pain per day lasting typically 10-20 minutes each)
- **b)** SUNCT (typically 40-200 or more unilateral severe attacks of pain per day, often triggered by facial stimuli (e.g. touch, talking, cold winds, eating, shaving etc.), lasting up to about 2 minutes, with or without background pain.
- **c)** Hemicrania continua (a constant one-sided headache with days where the pain may be worse, often with prominent red eye, runny eye, droopy eye, blocked nose or runny nose at that time and a tendency to want to stay still, often with superimposed jabbing pains on the one side of the head.

All 3 of these disorders have attacks of pain there are typically accompanied by significant facial “autonomic” symptoms on the *same side* as the pain (e.g. involuntary drooping of the eyelid, tearing, bloodshot eye, nasal running/congestion, flushing etc).

Hemicrania continua is typically diagnosed by its complete response to a drug called indometacin (which is also used to treat the condition).
Location of pain

The disorder is characterised by extremely severe pain that is almost always limited to one half of the head / face (less than 1% of patients have pain on both sides of the head). As a clinician, we are normally highly reluctant to diagnose cluster headache in patients who have experienced bilateral pain in any of their attacks or who have pain on different sides during the same cluster; all such patients should have detailed MRI brain and pituitary scans and pituitary function blood tests. That said, patients may have clusters which occur on different sides (e.g. remains right-sided throughout the cluster, then occurs on the left time in the next cluster a year or two later). It is most typical to see the pain centred around one eye, but it may occur anywhere in the head, neck or face.

Associated features of an attack

The pain is typically associated with autonomic symptoms and these may be quite dramatic. They are on the same side of the face as the pain and may include conjunctival injection (a bloodshot eye), ptosis (droopy or swollen eyelid), tearing from one eye, or nasal congestion or stuffiness, distended blood vessels, flushing, sweating or a sense of fullness in one ear. Attacks may be accompanied by other symptoms that are seen in different conditions such as migraine and these may include aura (e.g. visual disturbance with zig-zags, loss of vision, or shimmering), nausea, photophobia (sensitivity to light, usually just in the eye on the side of the pain), or even more rarely sensitivity to noise (phonophobia) or smell (osmophobia).

Investigations

Sometimes if there is doubt about the diagnosis, diagnostic tests may be used. These may include a GTN stimulation test, whereby 3 sprays of glyceryl trinitrate (a spray more commonly used to alleviate pain in angina) will usually trigger a “typical” acute attack within 90 minutes; such response is not seen with other headache conditions, although a bilateral mild headache occurs in most people. The other test is a trial of indometacin (either as tablet form, increasing to 250mg over about a week and staying at this dose for 2 weeks, or as a double-blinded test using an intramuscular injection and comparing with a dummy or placebo injection to see if there is response); conditions such as paroxysmal hemicrania should be completely controlled by this intervention, whereas there should be no difference if this is truly cluster headache, where the attacks will continue unabated.

Most patients who have cluster headache have this as a “primary” headache disorder, i.e. it is a condition in its own right. A very small number of patients develop cluster headache because of other pathology, i.e. as a secondary headache disorder. For this reason, it is usual to investigate for an underlying cause once cluster headache has been diagnosed, although investigations most often are normal. Typical investigation may include a magnetic resonance (MRI) scan of the brain and pituitary gland as well as a scan of the blood vessels (e.g. MR angiogram). These tests are “non-invasive”, i.e. painless and essentially risk-free. A blood test for testing pituitary function is also normally considered.

Treatment

There is no treatment that will “cure” the condition and permanently stop it recurring. Treatment is either aimed at individual attacks of pain (acute attack medication) or at preventing attacks recurring (preventative treatment). As cluster headache is relatively rare, most of the preventative treatments outlined below have not been subjected to rigorous scientific testing. First line preventative drugs have been associated with greater positive experience.

Acute attack strategies

The pain of cluster headache is usually too severe to be helped by conventional painkillers. Treatments need to work fast and be effective. The most helpful treatments are usually inhaled high flow 100% oxygen or drugs called Triptans.
1. **High flow 100% oxygen**

A significant percentage of cluster headache sufferers derive considerable benefit from oxygen. In some patients, oxygen may work for some attacks only and it is worth trying this on more than one occasion if it fails to help the first time.

To work, the oxygen must be provided in pure 100% form from an oxygen cylinder. Oxygen concentrators do not work. The oxygen should be delivered by a sealed mask (preferably a non-breathing mask that has a bag attached to it). This comes from an oxygen cylinder at high flow (e.g. 12-15 litres per minute).

Oxygen can not be used near naked flames and we would not prescribe it to people that smoke in their house.

Oxygen may be prescribed as a large fixed cylinder or as a portable cylinder. On the NHS, oxygen can be arranged in the workplace should it be required, or even set up in a UK holiday destination if given enough warning. Oxygen is prescribed on the NHS by your consultant or GP filling in a home oxygen order form (HOOF). If it is not helpful or is no longer needed it is very important to let the supplier know, as charges are incurred to the NHS by the day, not by the amount actually used, regardless of consumption.

If oxygen is prescribed on a HOOF form, it is extremely important that the prescription of oxygen is cancelled as soon as patients no longer require it and are out of cluster. It would be normal practice for a treating clinician to agree to cancel this on the patient’s behalf (patients are not allowed to cancel their own supply with Air Products or other providers) on the understanding that oxygen will be provided urgently in the patient goes back into cluster (oxygen can be set up within hours of filling in a HOOF form, so that a supply is at the patient’s house on the same day).

Some patients use oxygen to treat their cluster headache and find it initially beneficial but then the cluster headaches become longer and stop responding. If that occurs, patients should limit their use to 15 minutes at any one time and perhaps avoid using oxygen on every single attack. This may bring back responsiveness to this treatment.

2. **Triptans**

These drugs are also used for treatment of migraine. However, as cluster headache attacks are short it is important to deliver the drug to the bloodstream quickly.

a. **Sumatriptan injection**

   The method which allows fastest relief of pain is to inject as a subcutaneous (s/c) injection under the skin using an autoinjector pen device. It usually works within a few minutes. This is pre-filled and easy to use. The drug is sumatriptan (Imigran) and comes in 6mg injections that can be used up to twice a day. It is important that GP’s allow use of this drug on a frequent basis for cluster headache if control has not been achieved using preventative strategies given the usual dramatic efficacy of this drug for such a devastatingly painful condition. It is true that frequent use of triptan medication may lead some to develop mild medication overuse headaches similar to migraine between attacks of cluster headache but this is normally seen by patients as a small price to pay if it helps them control their severe attacks.

   The pen is held against the thigh and the trigger should be pressed and held for 10 seconds before withdrawing.

   It is difficult to know what to do if attacks are more frequent than twice per day and not controlled by preventative strategies. Recent reports have shown that just a third of the injector pen (2mg) is all that is typically required to abort an attack. Although not endorsed by the manufacturers of this device, some patients disassemble their injector cartridges (this can only be done with branded imigran cartridges, as opposed to the newer generic injectors (Sunn) and use a small stick (e.g. cocktail stick) to manually inject just a third or half of the injector at a time (e.g. if they have frequent daily attacks). The risk of skin infections usually is seen as a small price to pay if they get relief from their pain.
b. Sumatriptan 20mg (Imigran) or Zolmitriptan 5mg (Zomig) nasal spray

These spray devices are nearly as fast acting as the injectable sumatriptan (Imigran) autoninjector device.

As such, it is better to tip the head forward, spray and then keep the head forward for 3-4 minutes afterwards. Zolmitriptan has the advantages of three times per day use and it is generally reported to have a less unpleasant taste than sumatriptan.

Other acute attack treatments used less commonly include intranasal Lidocaine, intranasal capsaicin or octreotide injection.

Preventative strategies:

The choice of preventative depends on whether a patient has episodic or chronic cluster headache and, if episodic, how long the cluster typically lasts. The most useful “first line” regimen is a combination of a brief reducing course of steroids and introduction and upwards titration of verapamil with careful ECG monitoring (see below). Verapamil is probably also the treatment of choice for long term control of chronic cluster headache. For brief clusters, methysergide may alternatively be used.

First line preventatives

a. Steroids:

Steroids are often used as they typically turn the pain off as soon as they are started. We have to be cautious with steroid use as frequent and prolonged use may cause osteoporosis (thinning of the bones). They may possibly also cause gastric irritation and possible peptic ulceration. Extremely rarely they have been implicated in cases where the hip joint has disintegrated (avascular necrosis of the hip) leading to a need for hip replacement. However, avascular necrosis has not been reported following short courses of steroids.

If steroids are to be used, it is generally recommended that they are used for as short a period of time as possible and at the lowest dose needed.

In cluster headache, they are most usefully used when waiting for the effect of other preventatives to take effect. Typical courses would be 60 mg each morning for 3 days, reducing each 3 days by 10mg until stopped. It would also be typical to receive bone protection (e.g. a biphosphonate such as weekly alendronate (fosamax) tablets with calcium supplementation (e.g. 2 calcichew daily). In addition, it is often sensible to give a stomach protector such as a proton pump inhibitor (e.g. omeprazole 20mg or lansoprazole 30mg daily). These additional drugs are only required during the period of steroid use.

As the drug dose is tapered the pain generally returns. Hopefully by the time this happens, the main preventative drug will already be starting to work.

b. Verapamil:

The recognition that a calcium channel antagonist drug called verapamil works to turn off cluster headache in the vast majority of patients has dramatically changed the successful practical management and outlook of this condition.

Verapamil is a drug that has traditionally been used to treat heart conditions. It is used commonly in headache clinics in the UK and USA in unlicensed format to a much higher dose than used for heart complaints. It is generally regarded as a safe and well tolerated treatment for cluster headache, as long as it is closely supervised. As the drug may slow conduction of electric impulses in the heart, an ECG is performed before it is started and before every dose increment (4). A typical regime would be to start at a dose of 120mg twice daily and increase every week by 120mg, with an ECG before each dose. The maximum dose we may need to reach is 960-1080mg per day and it is often necessary to use such high doses to achieve
If someone taking verapamil develops dizziness, blackouts, shortness of breath, or chest pain, they are advised to attend their local casualty department that day for an ECG, to consider dose reduction if necessary.

The most common side effects are mild and include ankle swelling or constipation (typically helped by a laxative such as movicol or docusate sodium). More rarely people may experience agitation or irritability.

The majority of patients tolerate this drug well.

Good practice should include regular ECG’s at 2-3 monthly intervals where used on a long term basis. If high doses are required (e.g. more than 720mg per day, it is often sensible to perform 24 hour ECG recordings even if the ECG is normal and the patient reports no cardiac side effects.

Where the cluster has been well controlled, then the patient may reduce the dose every 4-8 weeks to see if pain recurs (i.e. indicating ongoing need for the previous higher dose).

If the drug has been used for past episodes of cluster headache and a high and safe dose has been achieved at that time, then recurrence of a bout of cluster headache can be treated with rapid escalation over about a week to a dose 120mg below that previously required; at that point an ECG is recommended and the dose can be titrated more slowly up in deemed safe by repeat ECG monitoring.

**Second line** drugs used most commonly where there is intolerance to verapamil include:

a. **Methysergide:** this is a very effective drug but long term use may rarely result in complications and is to be avoided unless strict monitoring is in place. The drug is best avoided in those with circulatory problems (e.g. narrowing in the blood vessels of the legs, angina, or Raynauds disease. The benefit of methysergide is that response is seen quickly. The dose is titrated up to one that stops bouts of pain. If needed long term it may be necessary to have a “drug holiday”, whereby the drug is stopped temporarily for 2 months after 6 months of use. If required for more than a few months, it is good practice to monitor for any early problems as this drug may occasionally cause thickening of some tissues within the body (e.g. fibrosis if the tissues around the lungs or kidneys or damage to the heart valves); monitoring is with blood tests (inflammatory markers, kidney function tests), chest x-ray, and heart scans (echocardiogram).

b. **Lithium:** a drug that was the most commonly used before verapamil was shown to be effective. The drug requires close monitoring of blood levels to avoid problems with the thyroid gland or kidneys and high levels may cause patients to develop toxic symptoms including tremor and feeling unwell.

c. **Sodium Valproate:** a useful second line drug where verapamil has been poorly tolerated or unhelpful. Side effects may include increase in appetite or minor temporary hair loss whilst on the drug (e.g. seeing more hairs on the bathroom floor; it does not cause patches of baldness and in most patients this is not seen as a significant problem. Although appetite is increased on this drug, weight gain is not seen if patients are careful with their diet. More rarely a mild tremor is seen. All of these side effects disappear when the drug is stopped. Blood tests are usually performed if patients feel unwell on the drug as is may extremely rarely affect the liver. The drug is started at small doses of 200mg per day (preferably the long acting epilim chrono version of the drug) and increased every 5-7 days by 200mg in twice daily dosage until pain disappears. Maximum dose is 100mg twice daily. It is important that women of childbearing age do not get pregnant whilst taking this drug as it may increase the risk of damage to an unborn baby (including the risk of significant learning disability); contraceptive precautions are essential and it is advisable to also take folic acid 5mg whilst on this medication as folic acid may reduce the risk of spina bifida in the unlikely case of unplanned pregnancy.
d. **Topiramate;** another useful and generally well tolerated second line preventative. It is important that women of childbearing age do not get pregnant whilst taking this drug as it may increase the risk of damage to an unborn baby; contraceptive precautions are essential and it is probably advisable to also take folic acid 5mg whilst on this medication as folic acid may reduce the risk of spina bifida in the unlikely case of unplanned pregnancy.

Approximately one out of five patients can not tolerate the drug because of side effects that may appear quite dramatic but typically reverses within 3 days of stopping the drug (severe difficulties with memory or speech, or aggressive change in personality / severe mood change). Such side effects are often seen at the initial low doses. In patients that tolerate the drug when first started, it is usually remains well tolerated. It usually causes some degree of weight loss (about 10% of body mass), it may cause change in appetite or taste perversion (loss of or change of taste, with some things tasting different), and most patients develop reversible tingling in their hands and feet. Tingling is usually seen at higher doses when the drug starts taking effect on the condition and may be alleviated by use of potassium citrate if troublesome; most patients do not find these side effects too troublesome if the drug is working well to turn off or reduce the severity of their pain.

There are extremely rare reports of acute glaucoma and if there is a history of glaucoma it is important to check first with an eye specialist that this drug is safe to use. The main advice is to seek urgent attention from an optician or casualty department if a patient develops a painful red eye with loss of vision; the pressure in the eye can be checked to see if it is safe to continue the drug. Dosing is usually 25mg once a day, increased every 1-2 weeks to an initial dose of between 50 and 75mg twice daily, although doses up to 200-250mg twice daily may sometimes be needed if tolerated and still in pain.

e. **Pizotifen:** this is a drug that is commonly used in migraine but may be successful in some patients with cluster headache. Its side effects may include weight gain and drowsiness. The dose is initially 0.5mg at night but may be increased slowly to a maximum tolerated dose or as high as 3-4.5mg daily each night.

f. **Gabapentin;** gabapentin has been anecdotally reported to help some patients with cluster headache but would normally be used if more conventional drugs have failed. It is generally well tolerated and safe and starts with a dose of 300mg per day, increasing by 300mg every 5 days to a dose that controls pain or a maximum of 900-1200mg three times daily.

g. **Melatonin;** this drug is not licensed in the UK but is freely available over the counter in the USA and easily available via the internet. It is more commonly used to aid sleep and is generally regarded as a safe drug. There have only been anecdotal reports of its efficacy in cluster headache and it is not certain how useful this drug may be. The dose is 10mg half an hour before bed.

h. **Greater occipital nerve block;** this involves an injection of local anaesthetic and steroid under the skin at the back of the head, around the greater occipital nerve. If ineffective, it may be worth considering injecting both sides. It is generally regarded a safe procedure although it may cause a little dimple under the skin that is permanent, due to the local effect on steroids on the fat under the scalp. This is not normally a problem as the injection is under the hair above the hairline. Typically, patients will experience local pain at the site of the injection, typically for a day or two. The nerve block has been reported anecdotally to help up to 50% of patients with cluster headache. It may turn off the headache disorder or may temporarily alleviate pain for a month or two. If helpful, the procedure can be repeated at intervals.

i. **Greater occipital nerve stimulation;** this is an experimental technique that involves the implantation of a wire over the greater occipital nerves on both sides, under the skin at the back of the head. This is then attached to a pacemaker device that is sited under the skin over the anterior chest wall.
There have been initial encouraging reports from a very limited number of patients who have had this procedure after being resistant to other therapies; some have found their pain abolished and others noticed helpful reductions in the severity or frequency of attacks. It only works while the device is switched on. It takes a few weeks after implantation to take effect. Some patients will experience complications, for instance need to replace a lead (wire) or change the battery, necessitating further minor operation. This is currently available to a very limited extent, usually as part of a study. It is only considered when all other treatments have been exhausted and found to be unhelpful.

j. Deep brain (hypothalamic) stimulation; the implantation of a wire within the brain in a region called the hypothalamus (connected to a pacemaker box implanted under the skin over the chest wall) has been shown to successfully turn off cluster headache pain in a limited number of patients who have had this procedure. As the procedure involves major brain surgery with its inherent risks, and greater occipital nerve stimulation only require a local and relatively minor procedure, this is not advocated at the present time except in exceptional circumstances.

k. Intravenous dihydroergotamine (IV DHE) this treatment entails a 3-4 day inpatient stay for an intravenous drip of DHE. It is generally well tolerated but is to be avoided in patients with severe hypertension or certain circulatory disorders. Anecdotally it has been shown to terminate a cluster bout in some patients.

Further information on cluster headache

Further information is available via the cluster headache society, the UK Organisation for the Understanding of Cluster Headache (OUCH). This society operates very useful patient support and has advisors available on the telephone, as well as a useful patient website with patient chat group. The Walton Centre have also printed a version of the advise given on the OUCH website for those without internet access. This is available as a separate information sheet. Please see enclosed appendix for a copy of the information provided by OUCH on cluster headache and other headache disorders. The details of OUCH are:

http://www.ouchuk.org/
tell: 01646 651 979

For practical advice our Customer Care Team provide a (PALS) service. Contact Customer Care Team on 0151 529 6100,

email: customer.careteam@thewaltoncentre.nhs.uk or visit www.thewaltoncentre.nhs.uk

Alternatively, log on to: www.neurosupport.org.uk or call 0151 298 2999 for advice and information for people with

Produced by: Dr Nicholas Silver, October 2008
Version: 2
Reviewed: December 2012
Date of Review: December 2013

©The Walton Centre NHS Foundation Trust. All rights reserved. No reproduction by or for commercial organisations is allowed without the express written permission of The Walton Centre.