Cluster headache (CH): epidemiology, classification and clinical picture

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INTRODUCTION

Cluster headache - known as trigeminal autonomic cephalalgias

Typified by recurrent attacks of unilateral severe pain

- involve the orbital or periorbital region
- innervated by the first (ophthalmic) division of the trigeminal nerve.

Autonomic symptoms accompany the pain on the same side:

- lacrimation
- conjunctival injection
- nasal congestion or rhinorrhoea (or both)
- ptosis or miosis (or both)
- periorbital oedema

www.clinic-hq.co.uk
CH mostly affects the region of the eye and temple

Most patients first consult a dentist or an ophthalmologist

Arne May, Headache 2013;53:1470-1478
Diagnosis and Clinical Features of Trigemino-Autonomic Headaches

*Misdiagnosis of cluster headache is common in clinical practice and can lead to significant morbidity*
What is cluster headache?

The term cluster headache originates from the tendency of attacks to cluster together into bouts that last several weeks

Episodic form

- the bouts can occur at certain times of year
- often with a seasonal predilection
- they are separated by periods of remission, which last at least a month

Chronic form

- continuous attacks with no respite
Cluster headache

Previously used terms:
Ciliary neuralgia; erythro-melalgia of the head; erythro-prosopalgia of Bing; hemicrania angioparalytica; hemicrania neuralgiformis chronica; histaminic cephalalgia; Horton’s headache; Harris-Horton’s disease; migrainous neuralgia (of Harris); petrosal neuralgia (of Gardner); Sluder’s neuralgia; sphenopalatine neuralgia; vidian neuralgia.
Headache Classification Committee of the International Headache Society (IHS)

The International Classification of Headache Disorders, 3rd edition (beta version)
Diagnostic criteria:

A. At least five attacks fulfilling criteria B–D

B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes (when untreated)\(^1\)

C. Either or both of the following:
   1. at least one of the following symptoms or signs, ipsilateral to the headache:
      a) conjunctival injection and/or lacrimation
      b) nasal congestion and/or rhinorrhoa
      c) eyelid oedema
      d) forehead and facial sweating
      e) forehead and facial flushing
      f) sensation of fullness in the ear
      g) miosis and/or ptosis
   2. a sense of restlessness or agitation

D. Attacks have a frequency between one every other day and eight per day for more than half of the time when the disorder is active

E. Not better accounted for by another ICHD-3 diagnosis.
Who gets it?

Patients typically start to develop the attacks in their 3 to 5 decade

an association with smoking (65%)
- patients are active smokers
- reporting a history of smoking

Alexander D Nesbitt, Peter J Goadssby BMJ 2012;344

A causative link to smoking seems unlikely
Who gets it?
probably affecting about 1 in 1000 people

- A lifetime prevalence of 0.12%
- Data from a door to door study in Norway showing a one year prevalence of 0.3%
  

- A tendency in some families
  
  
  first degree relatives of CH people have an estimated 14-48-fold increased risk of developing CH

The male to female ratio varies between 2.5:1 and 3.5:1.4

Alexander D Nesbitt, Peter J Goadssby BMJ 2012;344:e2407 doi: 10.1136/bmj.e2407
The disorder in women is not exactly the same as in men

- to start earlier in life in women
- women may have two peaks of age of onset compared with only one in men

![Histogram A: Age of onset (y) vs Patients (n)](image1)

- SD = 15.89
- Mean = 29.4

![Histogram B: Age of onset (y) vs Patients (n)](image2)

- SD = 13.47
- Mean = 31.3

Figure 1 Age of onset of cluster headache in (A) women; (B) men.

T D Rozen, R M Niknam, A L Shechter, W B Young, S D Silberstein

*J Neurol Neurosurg Psychiatry* 2001;70:613–617
Cluster headache types

**Episodic CH occurring in bouts (cluster periods)**
*Cluster periods usually last between 2 weeks and 3 months*

- At least two cluster periods lasting
  
  *from 7 days to 1 year (when untreated)*
  
  *and*

- separated by pain-free remission periods of 1 month

**Chronic cluster headache**

CH attacks occurring for more than 1 year without remission or with remission periods lasting less than 1 month

**Probable cluster headache:** Attacks fulfilling all but one of the criteria for cluster headache
• The stereotypical attacks may strike **up to 8 times a day**

• Relatively short-lived

• Strictly unilateral severe head pain

• Accompanied by autonomic phenomena

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*Only in approximately 15% of cases is there a shift from one side of the head to another*

Cluster periods

- circadian and circannual rhythmicity are characteristic of the episodic variant
- little is known in chronic cluster headache
Cluster headache
A prospective clinical study with diagnostic implications

Anish Bahra, MRCP; Arne May, MD; and Peter J. Goadsby, DSc

NEUROLOGY 2002;58:354–361
The pain of cluster headache is unilateral in at least 97%

- mainly focused behind the eye (88-92%)
- over the temple (69-70%)
- over the maxilla (50-53%)

The pain is **sharp, piercing, burning, or pulsating**

- sensation like *“having a red hot poker forced through my eye”*
- intensity is extreme (“11 out of 10”)
- the onset of pain is rapid
- the sensation increases from serious discomfort to pain over the course
- the pain usually stays at maximal intensity for the duration of the attack
- the attack will often end as abruptly as it started
# Site of pain

<table>
<thead>
<tr>
<th>Site</th>
<th>Total</th>
<th>Men</th>
<th>Women</th>
<th>ECH</th>
<th>CCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retro-orbital</td>
<td>92</td>
<td>92</td>
<td>92</td>
<td>92</td>
<td>94</td>
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<tr>
<td>Temporal</td>
<td>70</td>
<td>70</td>
<td>71</td>
<td>68</td>
<td>81</td>
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<tr>
<td>Upper teeth</td>
<td>50</td>
<td>49</td>
<td>51</td>
<td>45*</td>
<td>67*</td>
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<td>Forehead</td>
<td>46</td>
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<td>Jaw</td>
<td>45</td>
<td>44</td>
<td>48</td>
<td>40*</td>
<td>65*</td>
</tr>
<tr>
<td>Cheek</td>
<td>45</td>
<td>44</td>
<td>46</td>
<td>40*</td>
<td>63*</td>
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<tr>
<td>Lower teeth</td>
<td>32</td>
<td>30</td>
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<td>29</td>
<td>44</td>
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<tr>
<td>Neck</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>30</td>
<td>35</td>
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<tr>
<td>Nose</td>
<td>20</td>
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<td>22</td>
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<td>29</td>
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<td>Ear</td>
<td>17</td>
<td>14*</td>
<td>26*</td>
<td>15*</td>
<td>27*</td>
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<td>Shoulder</td>
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<td>14</td>
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<td>25*</td>
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<td>6</td>
<td>7</td>
<td>8</td>
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<td>Parietal</td>
<td>1</td>
<td>0.5</td>
<td>3</td>
<td>2</td>
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</table>

Values are %.

* Indicates a difference for episodic cluster headache (ECH) vs chronic cluster headache (CCH), or for men and women $p \leq 0.05$. 
Laterality and cranial autonomic features in patients with cluster headache

<table>
<thead>
<tr>
<th>Laterality and autonomic features</th>
<th>Total</th>
<th>Men</th>
<th>Women</th>
<th>ECH</th>
<th>CCH</th>
</tr>
</thead>
<tbody>
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<td>Laterality</td>
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<td>Right-sided attacks</td>
<td>60</td>
<td>60</td>
<td>62</td>
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<td>58</td>
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<td>Left-sided attacks</td>
<td>38</td>
<td>38</td>
<td>37</td>
<td>37</td>
<td>42</td>
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<tr>
<td>Right and left equally</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>0</td>
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<tr>
<td>Side change within the bout</td>
<td>18</td>
<td>19</td>
<td>15</td>
<td>14*</td>
<td>33*</td>
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<td>Side change between bouts</td>
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<td>18</td>
<td>18</td>
<td>18</td>
<td>—</td>
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<tr>
<td>Side change within and between bouts</td>
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<td>3</td>
<td>2</td>
<td>3</td>
<td>—</td>
</tr>
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<td>Side change within attack</td>
<td>1</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>1</td>
<td>0</td>
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<td>Autonomic features</td>
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<td></td>
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<td></td>
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<td>Lacrimation</td>
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<td>92</td>
<td>88</td>
<td>92</td>
<td>88</td>
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<td>Conjunctival injection</td>
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<td>71</td>
<td>79</td>
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<td>Nasal congestion</td>
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<td>74</td>
<td>77</td>
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<td>Ptosis/eyelid swelling</td>
<td>74</td>
<td>72</td>
<td>78</td>
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<td>79</td>
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<tr>
<td>Rhinorrhea</td>
<td>72</td>
<td>74</td>
<td>68</td>
<td>76*</td>
<td>56*</td>
</tr>
</tbody>
</table>

Values are %.

* Indicates a difference for episodic cluster headache (ECH) vs chronic cluster headache (CCH) p ≤ 0.05.

How is cluster headache diagnosed?

**Cyclic nature**

**Ipsilateral pain**

- Ipsilateral lacrimation (91%)
- Ipsilateral conjunctival injection (77%)
- Ipsilateral nasal congestion or rhinorrhea (75%/72%)
- Ipsilateral ptosis (74%)
- Ipsilateral oedema of the eyelid or the face (or both) (74%)
- Ipsilateral sweating of the forehead or the face (or both) (38%)
- Ipsilateral miosis (29%)

*About 3% of all patients lack autonomic symptoms*

Which other symptoms occur with the attack?

Each attack is accompanied by one or more cranial autonomic symptom or sign on the same side as the pain

- All of these signs and symptoms are resolve with the cessation of pain
- Between 70% and 93% of patients describe a sense of restlessness and agitation during an attack
  

- Most patients wish to isolate themselves and seek a cold environment

- Between 28% and 50% report nausea

- 23% may vomit during an attack
  

- More than half (54-64%) of patients have photophobia
  
How long does an attack last?

Attacks should last between 15 and 180 minutes

- although on rare occasions they can last longer

*In the British series, a mean untreated minimum duration of 72 minutes and maximum duration of 159 minutes was reported*

How often do individual attacks occur?

PAIN VARIES

• 1 attack every 48 hours to 7 separate attacks in 24 hours

• less frequent attacks may occur

  at the beginning and end of bouts

*The British study found*

• 37% of patients reporting a predictable time of onset during the day

• the mean maximum number of attacks each day to be 4.6

• 72% reporting attacks occurring at predictable times during the night

Does anything trigger the attacks?

53-63% - alcohol
• particularly red wine (70%)
• usually within an 1 hour of ingestion

72% attacks are related to nocturnal sleep

Small cases have reported a raised apnoea-hypopnoea index

Some odours
• volatile organic compounds
• perfume and paint

Nitrates may trigger attacks
glyceryl trinitrate is used to provoke attacks experimentally

Sildenafil has also been reported to induce attacks during a bout
Which conditions resemble cluster headache?

• Cluster headache and the other trigeminal autonomic cephalalgias

• Secondary (or symptomatic) cluster headache may be caused by several structural lesions

• pituitary tumours
• carotid dissections
• cavernous sinus pathology

Conditions associated with cluster headache

- Subclavian steal syndrome [Piovesan et al. 2001]
- Carotid artery thrombosis [Ashkenazi & Brown 2008]
- Cerebral venous thrombosis [Park et al. 2006, Peterlin et al. 2006, Georgiadis et al. 2007, Rodríguez et al. 2008]
- Glioblastoma multiforme [Edvardsson & Persson 2012]
- Hemangiopericytoma [Fontaine et al. 2013]
- Nasopharynx carcinoma [Appelbaum & Noronha 1989]
- Angiomyolipoma [Messina et al. 2013]
- Inflammatory myofibroblastic tumour [Bigal et al. 2003]
- Lipoma [Cologno et al. 2008]
- Arachnoid cyst [Edvardsson & Persson 2013a]
- Sinusitis [Takeshima et al. 1988, Edvardsson & Persson 2013b]
- Aspergilloma [Zanchin et al. 1995]
- Granulomatous pituitary involvement [Favier et al. 2007b]
- Orbital pseudotumour [Harley & Ahmed 2008]
- Cervical spinal epidural abscess [Liu & Su 2009]
- Multiple sclerosis [Gentile et al. 2007]
- Foreign body in the maxillary sinus [Scorticati et al. 2002]
- Cervical syringomyelia and Arnold-Chiari malformation [Seijo-Martinez et al. 2004]
- Sarcoidosis [van der Vliet et al. 2013]
MIGRAINE and CLUSTER HEADACHE
DIFFERENTIAL DIAGNOSIS

Migraine

• Less severe and to last longer

• Cranial autonomic features are less prominent and more likely to be bilateral

• Nausea, vomiting, and bilateral photophobia are common

• Migraine lacks the striking timing

• Agitation and restlessness experienced during a cluster attack

• Alcohol ingestion may also precipitate migraine

**TAKE HOME MESSAGE**

CH treatment is effective

The term “trigeminal autonomic cephalalgia” has been coined by Goadsby and Lipton and is very useful in daily practice


CH is certainly the most prominent and most common of the TACs and is considered one of the most severe pain syndromes in humans

Indeed, female patients have described each attack as being worse than childbirth


CH is still underdiagnosed and suboptimally managed in primary care