Chapter 85

Cluster Headaches: Introduction and Epidemiology

Peter J. Goadsby and Peer Tfelt-Hansen

CLASSIFICATION AND SHORT DESCRIPTION

Cluster headache (CH) falls into group 3 of the International Headache Society (IHS) classification, the trigeminal autonomic cephalalgias, and is coded 3.1 (6) (Table 85-1). In the tenth revision of the International Classification of Diseases (ICD-10) of the World Health Organization (WHO), it is coded G44.0 (episodic CH-G44.01, chronic CH-G44.02) (21).

Cluster headache is characterized by attacks of strictly unilateral severe pain with orbital, supraorbital, or temporal location. Attacks typically last 15 to 180 minutes and usually occur one or several times per day, especially at night. They are accompanied by ipsilateral conjunctival injection, lacrimation, rhinorrhea or nasal congestion, eyelid edema, miosis, and low-grade ptosis. There is a clear male preponderance.

Two main clinical forms of CH may be identified: *episodic* and *chronic*. The most common form is the episodic form, which affects 80% to 90% of patients. It is characterized by periods of attacks (bouts, cluster) and periods of remission. In the cluster period, the patient experiences from one to eight attacks per day (days without headache may occur); this period may last from 7 days to 1 year. Between cluster periods, patients are usually completely pain free, but short-lasting pain periods with isolated short attacks may occur.

The chronic form lacks the remissions and is diagnosed after 1 year without remission or if remissions have lasted less than one month. The patient may suffer from the chronic form from the beginning of the disease (chronic CH unremitting from onset), or it may develop from the episodic form (chronic CH evolved from episodic). In clinical practice, the essential differentiation between episodic and chronic cluster headache, in terms of how they are managed, is whether there are sufficiently long breaks to allow preventive treatment to be discontinued. Apart from these main clinical forms of CH, which affect the vast majority of patients, there are atypical cases, coded 3.4 in the IHS classification. These patients present some CH symptoms but differ in clinical course, additional signs, or both. These forms constitute the borderland of CH (also called *variants*).

Other Terms

Previously used terms include erythroprosopalgia of Bing (7), ciliary or migrainous neuralgia (Harris), erythromelalgia of the head, Horton's headache, histaminic cephalgia, petrosal neuralgia (Gardner), sphenopalatine, Vidian and Sluder's neuralgia, and hemicrania periodica neuralgiformis. The term "cluster headache" was introduced relatively recently, in 1952, by Kunkle and colleagues (11,12). By then, CH certainly had been known for a long time under other names (10), as demonstrated by the striking similarities between this condition and most other syndromes listed in Table 85-2. The abundance of eponyms and synonyms used in the past to describe the same form may have been indirectly responsible for the late recognition of CH as such. In fact, according to Koehler (9), the first report on CH dates to 1641, when Nicolaas Tulp, a famous Dutch physician, published his *Observationes Medicae*, in which he describes the case of Isaak van Halmaal, who "in the beginning of the summer season, was afflicted with a very severe headache, occurring and disappearing daily on fixed hours. For rarely it lasted longer than two hours. This recurring pain lasted until the fourteenth day. . . ." Another probable case from the 17th century was described by Thomas Willis, who, in *De Anima Brutorum*, mentioned a headache whose attacks tended to recur more severely at the time of the sun's solstice and equinox, although in most cases it struck people in between, at preferred hours during the 24-hour day (16). Nappi and Manzoni (16) also argued

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-85 Olesen- 2057G GRBT050-Olesen-v6.cls August 18, 2005 0:43

TABLE 85-1 International Headache Society Classification of Cluster Headache (6a)

3.1 Diagnostic criteria:
- A. At least five attacks fulfilling B through D
- B. Severe or very severe unilateral orbital, supraorbital, and/or temporal pain lasting 15 to 180 minutes if 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. Forehead and facial sweating
  4. Ipsilateral eyelid edema
  5. Ipsilateral forehead and facial sweating
  6. Ipsilateral miosis and/or ptosis
  7. A sense of restlessness or agitation
- D. Attacks have a frequency from one every other day to eight per day
- E. Not attributed to another disorder

3.1.1 Episodic cluster headache
Description: occurs in periods lasting 7 days to 1 year separated by pain-free periods lasting ≥month or more
Diagnostic criteria:
- A. All fulfilling criteria A through E of 3.1
- B. At least two cluster periods lasting from 7 to 365 days and separated by pain-free remissions of ≥1 month

3.1.2 Chronic cluster headache
Description: Attacks occur for >1 year without remission or with remissions lasting <1 month.
Diagnostic criteria:
- A. All alphabetical headings of 3.1
- B. Attacks recur for >1 year without remission periods or with remission periods <1 month

TABLE 85-2 Cluster Headache Synonyms and Related Syndromes

Previous Terms	*Authors*	*Year*
Red migraine	Moellendorf	1867
Angioparalytic hemicrania	Eulenburg	1883
Sphenopalatine ganglion neuralgia	Sluder	1910
Erythrosopalgia	Bing	1913
Syndrome de vasodilatation hemicéphalique d'origine sympathique	Vallery-Radot and Blamoutier	1925
Ciliary neuralgia	Harris	1926
Syndrome du nerf nasal	Charlin	1931
Vidian neuralgia	Vail	1932
Autonomic faciocephalalgia	Brickner and Riley	1935
Migrainous neuralgia	Harris	1936
Erythromelalgia	Horton et al.	1939
Greater superficial petrosal neuralgia	Gardner et al.	1947
Histaminic cephalgia	Horton	1952

that CH and chronic paroxysmal hemicrania were both described in 1747 when Oppermann, in his doctoral dissertation on "hemicrania horologica," described the case of a 35-year-old woman who, since the age of 29 years, had been suffering from daily 15-minute attacks every hour of the day and night with such regularity as to tell the hour more accurately than the clock in the city square.

In 1822, Hutchinson, in his book *Cases of Neuralgia Spasmodica*, edited in London, described a hemicrania that, after recurring for several hours daily for long periods, departs suddenly. Also, Hall (*Principles of the Theory and Practice of Medicine*, 1834) saw similar cases, calling them *hemicrania intermittens* or *brow ague* (17).

Most of the definitions listed in Table 85-2 are of merely historical interest, because they were commonly used for only brief periods. Among them, however, are some worthy of mention, namely Harris's *migrainous neuralgia* (4,5), a term that is still quite popular. Thus, Ekbom (2) used *chronic migrainous neuralgia* as the title for his chapter on chronic CH, and *Horton's headache* (8) was used for many years and still is considered of great interest in that the name is from the author who, more than any other, played a prominent role in investigating CH in the 1940s and 1950s. As for Sluder's *sphenopalatine ganglion neuralgia* (19), also listed in Table 85-2, it is still an open question whether it should be considered an equivalent form of CH or an autonomous clinical syndrome, as suggested by Sjaastad (18).

EPIDEMIOLOGY

The prevalence of cluster headache has been studied in six population-based surveys; see Table 85-3 (17a). The Swedish study was in 18-year-old men (3) and resulted probably in a minimum estimate because onset of cluster headache is generally after the age of 20 years. In both San Marino surveys (1,20b), an extensive data search was done, the medical records of neurologic, otorhinolaryngologic, and ophthalmologic services from the past 15 years were examined, general practitioners were contacted, and a letter was sent to all households in San Marino. In the U.S. study (20) with the highest prevalence, 401 per 100,000, the diagnosis was based on case records and was not confirmed by a clinical interview. In addition, people were included with only one attack and with attacks not clearly of 15- to 180-minutes' duration (17a,20). In the Norwegian study all inhabitants in a community were interviewed by an experienced neurologist according to the criteria of the IHS (18a). This study also had a high prevalence, 381 per 100,000, and three of the seven affected participants did not fill the strict criteria for cluster headache (18a). In the Italian survey all participants were interviewed by an experienced neurologist (17a).

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-85 Olesen- 2057G GRBT050-Olesen-v6.cls August 18, 2005 0:43

TABLE 85-3 Epidemiologic Surveys of Cluster Headache

Country (Ref.)	*Diagnosis Clinically Confirmed?*	*Age*	*Sex*	*Population Sample*	*Affected*	*Prevalence per 100,000 (95% CI)*
Sweden (3)	Yes	18 years	Men	9803	9	92 (42–174)
San Marino (1)	Yes	All ages	Both	21,792	14	69 (39–114)
USA (20)	No	All ages	Both	6476	26	401 (262–588)
San Marino (20b)	Yes	All ages	Both	26,628	15	56 (31–92)
Norway (18a)	Yes	18–65 years	Both	1838	7	381 (153–783)
Italy (13–15)	Yes	18–65 years	Both	6500	13	200 (146–254)

CI, confidence interval. From Russell 2004 (17a).

If averaging, taking the number of subjects into account, the four other studies (1,3,17a,20b), one comes up with a prevalence of 87 per 100,000. If the two studies (18a,20) with the highest prevalence are included, the prevalence is 138 per 100,000.

CH cases have been reported by authors from various continents (1a,17a,20a), and it is therefore reasonable to assume that this type of headache occurs everywhere in the world. An epidemiologic study carried out in the People's Republic of China (22) reported only 14 CH cases of 246,812 inhabitants (0.006%). In this study, however, the prevalence of migraine (0.7%) also was found to be markedly lower than commonly reported in the literature for the general population. It is likely, therefore, that these findings were influenced by methodologic factors as well as a possibly lower prevalence of all primary headaches in the Chinese population.

A nationwide mailing to all Dutch family practitioners with an invitation to refer diagnosed or suspected CH resulted in only 1429 patients being identified, a prevalence of 9 per 100,000 inhabitants, and the authors concluded that the diagnosis is often not made or is delayed in many patients (20c).

REFERENCES

1. D'Alessandro R, Gamberini G, Benassi G, et al. Cluster headache in the Republic of San Marino. *Cephalalgia* 1986;6:159–162.
1a. Dousset V, Henry P, Michel P. Epidemiology of headache. *Rev Neurol (Paris)* 2000;156[Suppl 4]:24–29.
2. Ekbom K. Chronic migrainous neuralgia. In: Rose CF, ed. *Handbook of clinical neurology*, vol 48, *Headache*. Amsterdam: Elsevier Science Publishers, 1986:247–255.
3. Ekbom K, Ahlborg B, Schele R. Prevalence of migraine and cluster headache in Swedish men of 18. *Headache* 1978;18:9–19.
4. Hardman RA, Hopkins EJ. A survey of migrainous neuralgia. *J College General Practitioners* 1966;11:195–200.
5. Harris W. Ciliary (migrainous) neuralgia and its treatment. *BMJ* 1936;1:457–460.
6. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia* 1988;8[Suppl 7]: 1–96.
6a. Headache Classification Committee of the International Headache Society. The international classification of headache disorders. *Cephalalgia* 2004;24[Suppl 1]:1–160.
7. Heyck H. Cluster Kopfschmerz (Bing-Horton syndrome?). *Fortschr Neurol Psychiatr* 1976;44:37–50.
8. Horton BT. Histaminic cephalgia. *Lancet* 1952;2:92–98.
9. Koehler PJ. Prevalence of headache in Tulp's *Observationes Medicae* (1641) with a description of cluster headache. *Cephalalgia* 1993;13:318–320.
10. Kudrow L. *Cluster headache: mechanisms and management*. New York: Oxford University Press, 1980.
11. Kunkel RS, Frame JR. Chronic cluster headache: long-term follow-up. In: Olesen J, ed. *Headache classification and epidemiology*. New York: Raven Press, 1994:113–116.
12. Kunkle EC, Pfeiffer JR, Wilhoit WM, et al. Recurrent brief headaches in cluster pattern. *Trans Amer Neurological Assoc* 1952;77:240–243.
13. Manzoni GC. Male preponderance of cluster headache is progressively decreasing over the years. *Headache* 1997;37:588–589.
14. Manzoni GC. Gender ratio of cluster headache over the years: a possible role of changes in lifestyle. *Cephalalgia* 1998;18:138–142.
15. Manzoni GC, Micieli G, Granella F, et al. Cluster headache: course over ten years in 189 patients. *Cephalalgia* 1991;11:169–174.
16. Nappi G, Manzoni GC. *Primary headaches: clinical approach and management*. London: Smith-Gordon and Company Limited, 1996.
17. Olivarius de Fine B. Migraine variants [Letter]. *BMJ* 1971;2:49–50.
17a. Russell MB. Epidemiology and genetics of cluster headache. *Lancet Neurol* 2004;3:279–283.
18. Sjaastad O. *Cluster headache syndrome: major problems in neurology*, vol 23. London: WB Saunders, 1992.
18a. Sjaastad O, Bekketeig LS. Cluster headache. Vågå study of headache epidemiology. *Cephalalgia* 2003;23:528–533.
19. Sluder G. The syndrome of sphenopalatine ganglion neuralgia. *Am J Med Sci* 1910;140:868–878.
20. Swanson JW, Yanagihara T, Stang PE, et al. Incidence of cluster headaches: a population-based study in Olmsted County, Minnesota. *Neurology* 1994;44:433–437.
20a. Tekle Haimanot R, Seraw B, Forsgren L, et al. Migraine, chronic tension-type headache, and cluster headache in an Ethiopian rural community. *Cephalalgia* 1995;15:449–450.
20b. Tonon C, Guttman S, Volpini M, et al. Prevalence and incidence of cluster headache in the republic of San Marino. *Neurology* 2002;58:1407–1409.
20c. van Vliet JA, Ecketrs PJE, Haan J, et al. Features involved in the diagnostic delay of cluster headache. *J Neurol Neurosurg Psychiatr* 2003;74:1123–1125.
21. World Health Organization by the International Headache Society. ICD-10 guide for headaches: guide to the classification, diagnosis and assessment of headaches in accordance with the tenth revision of the international classification of diseases and related health problems and its application to neurology. *Cephalalgia* 1997;17[Suppl 19]:1–82.
22. Zhao F, Tsay JY, Cheng X, et al. Epidemiology of migraine: a survey in 21 provinces of the Peoples Republic of China, 1985. *Headache* 1988;28:558–565.