Chronic Paroxysmal Hemicrania (CPH): A Review of the Clinical Manifestations

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SYNOPSIS

On a world-wide basis, 84 cases of CPH were found, 59 females and 25 males: i.e., a F:M ratio of 2.36. Forty-nine cases never exhibited a remitting stage, whereas in 35 cases a history of a remitting stage was obtained, 17 cases still remaining in the remitting stage. In other words, the ratio between the chronic and the remitting stage as of today is 67:17 =3.94. Accordingly, there seems to be a reverse relationship of the chronic versus the remitting stage, when compared to cluster headache. A maximum attack frequency even of 5-6 attacks per 24 hours seems to be consistent with a diagnosis of CPH. Nocturnal attacks occurred in 55 out of 58 cases where such information was available. An unchanging unilaterality was the rule, in that only 3 exceptions have been reported.

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INTRODUCTION

At the time of the first report on CPH (AASH meeting in 1973), only 2 cases were known.[1] By 1976, 3 cases,[2] and by 1979, 8 definite cases were known on a worldwide basis.[3] No *review* of CPH has been conducted by ourselves or by others since then. One cannot expect to have observed all the clinical manifestations, the complete clinical spectrum so to speak, on the basis of the small case material (n=8) reviewed in 1979.

Eighty-four cases have by now been described in the literature[1-38] or reported to us in considerable detail (Table 1), and we have information concerning 10 more cases. If we add all the cases that we have heard about at conferences or more or less from hearsay, the total number by now probably exceeds 150; actually there may, therefore, be several hundred cases. It is, accordingly, high time that the worldwide clinical experience be reviewed (Table 1).

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Table 1
Case Reports of CPH

Published Case Reports	Year	No. of Patients
Sjaastad & Dale	1974	2
Sjaastad & Dale	1976	1
Kayed et al.	1978	1
Price & Posner	1978	1
Christoffersen	1979	1
Manzoni & Terzano	1979	1
Leblanc et al.	1980	1
Sjaastad et al.	1980	2
Stein & Rogado	1980	2
Guerra	1981	2
Hochman	1981	1
Manzoni et al.	1981	1
Rapoport et al.	1981	1
Jensen et al.	1982	1
Kilpatrick & King	1982	2
Pelz & Meskey	1982	1
Geaney	1983	1
Peatty & Clifford Rose	1983	1
Thevenet et al.	1983	3
Bogucki et al.	1984	2
Boulliat	1984	1
Dutta	1984	1
Pfaffenrath et al.	1984	4
Pradalier & Dry	1984	1
Sjaastad et al.	1984	2
Drummond	1985	1
Granella et al.	1985	3
Heckl	1986	2
Pollman & Pfaffenrath	1986	1
Bogucki & Kozubski	1987	1
Centonze et al.	1987	3
Durko & Klimek	1987	1
Hannerz et al.	1987	1
Joubert et al.	1987	1
Kudrow et al.	1987	6
Nebudova	1987	1
Rasmussen	1987	4
Pearce et al.	1987	1
	Sum:	63
Unpublished Case Reports		
Bousser		2
Davalos		1
Graham		1
Greene		1
Jaeger		2
Manzoni		1
Mathew		2
Nappi		2
Sjaastad		8
Wall		1
	Sum:	21
	Total No.:	84

METHODS OF PATIENT SELECTION

The diagnostic criteria employed have *not* been specified in all reports. In trying to establish the diagnosis during the early stages of the CPH story, we have used the diagnostic criteria set forth by Merskey et al.,[39] by Sjaastad et al.[3] and by Sjaastad.[40] These criteria were the only ones available when the present study was started, and they have accordingly also been used in the present context. A positive result of the intraocular pressure (IOP) and corneal indentation pulse (CIP) tests may be *sine qua nons* in CPH. We have carried out such measurements in 7 of our cases with a clearcut result in every case.[41] However, since so few clinicians have the opportunity to carry out this test, it certainly cannot be included among the inclusion criteria in a review article.

The inclusion criteria were: a relatively high maximum frequency of attacks (i.e. > 4/day) during symptomatic periods, and an *absolute* indomethacin effect. It has, furthermore, been deemed highly desirable that the headache be unilateral. Sex preponderance, once considered to be an issue in CPH, has not been made a criterion. Provided the other criteria were in conformity with a diagnosis of CPH, an unusual localization has not been felt to constitute sufficient reason to exclude a case. Other symptoms and signs have been free variables, and this has contributed to the kaleidoscopic appearance of the entire picture.

It goes without saying that a certain amount of personal judgment has been necessary in rejecting/accepting the original diagnoses. Only a few cases with adequate information have been rejected. Even a solitary case presented under another diagnosis has exceptionally been accepted if the original diagnosis has been based on obvious misconceptions.[17]

Most rejections have been based on: incomplete indomethacin effect, either as a solitary factor or combined with other factors such as low frequency of attacks or absence of autonomic involvement. Clinical pictures associated with vascular malformations have also been rejected.[42]

Cases reported to us, just haphazardly, at conferences, meetings, etc. have not been accepted for the present review. Of the cases that, as far as we know, remain unpublished, we have accepted only those on which we have rather complete, type-written reports. We have also accepted cases seen primarily by ourselves during visits to foreign countries, but not reported in the literature so far. Not all the communications give information on all the parameters that we wanted to assess.

OBSERVATIONS

Sex ratio and age of onset. The review includes 84 patients, 25 males (30%) and 59 females (70%), with a F:M sex ratio of 2.36:1.

The mean age of onset was 34.1 ± 16.7 years, and the range 11-81; the mean age at diagnosis was 47.4 ± 14.4 years, varying between a minimum of 22 and a maximum of 82. The mean illness duration was 13.3 ± 12.2 years (Table 2). The distribution of age at onset is shown in Figure 1 and the age at onset by sex in Figure 2. Obviously, the distribution curve is somewhat skewed to the right side; it is significantly different from a gaussian distribution ($p<0.01$). The median age group is 21-30. From 11 to 30 years there are 44 cases, (i.e. 52%).

Family history of headache. A positive family history of cluster headache was found in 1 case (Manzoni unpublished), while a family history of chronic paroxysmal hemicrania was not obtained in any of the cases reported. A family history of migraine was found in 20 patients (23%). This figure is much lower than the one concerning familial occurrence of

Table 2

Timing of the Various Events in Total CPH, Male and Female Patients

	Total CPH	Males	Females	P Values*
Attack duration (min.)	20.9 ± 20.4	21.5 ± 13.3	20.6 ± 23.2	NS
Attack frequency/ 24 hr.	10.8 ± 5.0	11.0 ± 4.1	10.6 ± 5.5	NS
Onset of illness (yrs.)	34.1 ± 16.7	34.9 ± 16.3	32.9 ± 16.2	NS
Duration of illness (yrs.)	13.3 ± 12.2	16.3 ± 14.7	11.8 ± 10.6	NS

*Two-tailed Student's t-test

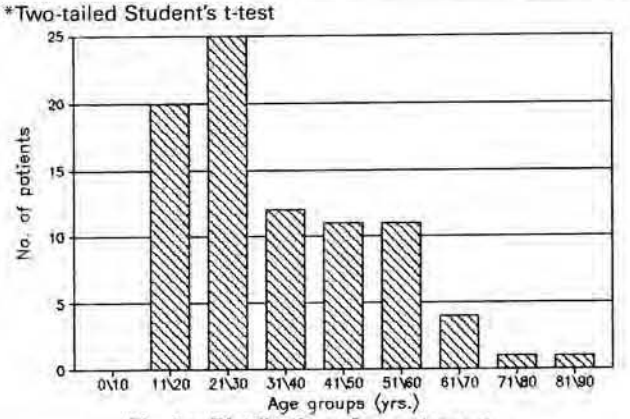

Fig. 1—Distribution of age at onset.

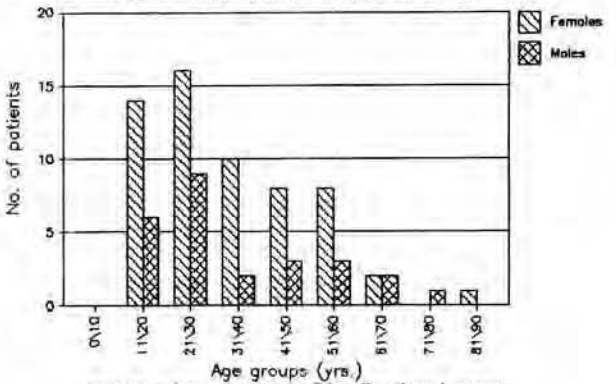

Fig. 2—Age at onset. Distribution by sex.

migraine in migraine patients; it compares, however, rather well with the figures for familial occurrence of migraine in cluster headache patients (i.e. 15-35%).

Past personal history. A previous head trauma was reported by 12 patients (14%), a neck trauma by 7 (8%), and migraine by 4 (5%). A history of cluster headache was reported by 1 patient.[38] The interpretation of such an apparent coexistence is not easy. A chance co-existence must be a rare phenomenon. It should in this context be mentioned that no *absolute* criteria exist as far as cluster headache is concerned.

A past history of other disease was reported in some cases: diabetes,[14] malignant melanoma,[5] urticaria,[2,19] hyperthyroidism,[12] goitre (Sjaastad unpublished), eosinophilic granuloma,[16] a bilateral Holmes-Adie's syndrome,[17] a homolateral skull osteoma,[20] skull fracture,[11] exophthalmos,[34] ankylosing spondylitis,[33] epilepsy,[5,11] cyclic idiopathic thrombocytopenia,[2] and rheumatoid arthritis (Sjaastad unpublished). Moreover, onset after flu-like disease,[21] after surgical intervention for uterine polyps[19] or fibroma (Bousser unpublished), and maxillary sinusitis[43] have been described. No history of psychological disturbances, antedating the onset, has been reported. The two first patients were explored psychologically and psychiatrically and were found to be normal.[2]

Relationship to female sex cycle. Since there is a rather clear female preponderence in CPH, the relationship to the life cycle in the female becomes important.

CPH started immediately post-partum in 5/10 cases. Attacks disappeared during pregnancy in 9/10 cases. Birth control pills had no influence on headache tendency. Benefit from menstruation was reported in 4 cases, while worsening occurred in 11 (Table 3). There is not sufficient information available as to the influence of menopause.

Table 3

Relationship between Pregnancy, Menstruation and Headache

	No.	No. of cases with information	%
No headache during pregnancy	9	10	90
Onset of headache upon delivery	5	10	50
Benefit from menstruation	4	15	27
Impairment during menstruation	11	15	73
Fluctuation with menstruation	3	6	50
Influence of birth control pills	0	4	0

Localization of pain. The pain was strictly unilateral in all of the patients with the exception of 1 case in whom bilateral pain has been described.[29] The site of maximal pain is evident from Figure 3. A spreading of the pain during the solitary attack, mostly backwards, was reported in 43 cases (51%). Nine patients noted a neck soreness and 2 a sort of "stiffness" in the neck during the attack.

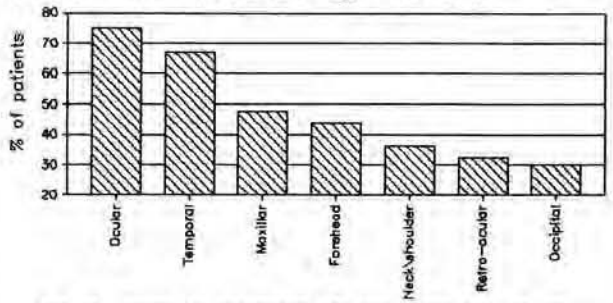

Fig. 3—Areas indicated as the site of maximal pain.

The pain distribution was equally frequently present in each hemicranium. At pain maximum, 2 patients felt the pain even slightly beyond the midline. In 3 patients, there may have been a shift of the pain side from the non-chronic ("remitting") stage to the continuous ("non-remitting") stage.[16,20,24]

During the attack, three patients had observed hypersensitivity of the hair and five hypersensitivity of the skin corresponding to the first trigeminal division on the symptomatic side.

Character of pain. The pain intensity was excruciating at the peak of attack in 67 of the reports, where such information was available, while in 3 it was moderately severe. The character of the pain is evident from Figure 4.

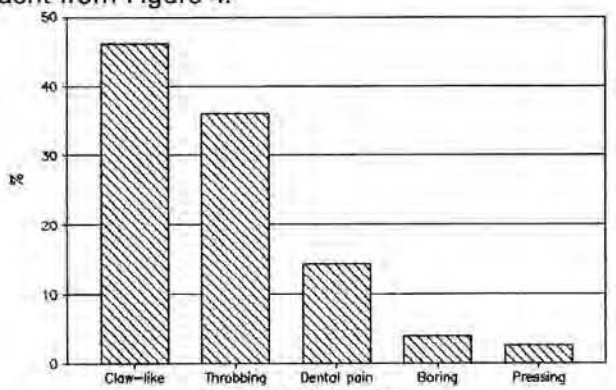

Fig. 4—Pain Quality.

The pain was accentuated by coughing in 3 cases, by bending forwards in 2 cases, and by the Valsalva manoeuvre in 2 cases. Interparoxysmal pain or discomfort in the painful area was described in 28 patients.

The headache tended to improve with the menses in 4 cases, with stress in 7 cases, with joy in 5, and with happy expectations in 3. Weather conditions have not been observed to cause any fluctuations. Fifteen patients had had pain free episodes lasting from 1 to 6 months, during the chronic stage, the freedom from pain occurring during periods of stress, pregnancy, etc.

During attacks, the patients tried to sit quietly, holding the head in the hands or curled up in bed, and/or paced the floor (Table 4). Four subjects had experienced suicidal thoughts during the worst periods.

Table 4
Patients Behaviour During the Attack (n = 33)

— Sitting quietly or curling up in the bed	15
— Pacing the floor	18
— Both	7

Duration and frequency of attacks. The duration of the single headache attack varied from a minimum of 13 ± 10 minutes, in the mild period to a maximum of 29 ± 26 minutes (range 2-120), with a mean value of 20.9 ± 20.4 minutes (Table 2; Figure 5). One out of nine patients with a maximum attack duration exceeding 45 minutes, experienced attacks lasting up to 2 hours.

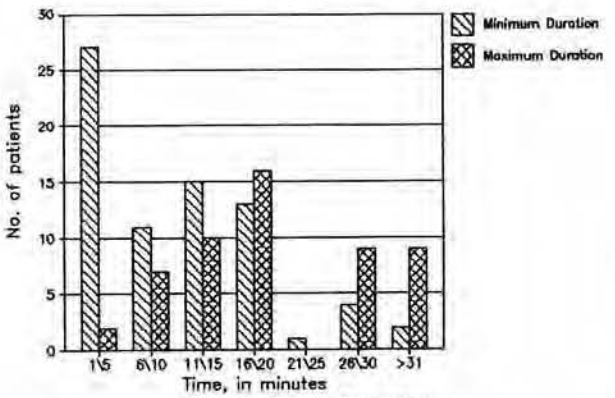

Fig. 5—Attack Duration.

There was a considerable fluctuation in attack frequency (i.e. 1-40). The mean minimum attack frequency was 8 ± 4 (range 2-14) and the maximum 15 ± 7 (range 6-40), with a mean of 10.8 ± 5.0 (Table 2; Figure 6). In one case (Manzoni unpublished), attacks occurred only in the morning hours in some periods and in the afternoon hours in other periods.

In Russell's study[43] the attack frequency ranged from 4 to 38 per 24 hours, with a mean of 13.6. The mean duration with mild attacks was 6.5 minutes, vs 21.8 with severe attacks. The mean duration of attacks was 13.3 ± 7.6 minutes (range 3-46). In our material, some relationships were detected: a) the higher the attack frequency, the shorter the attack duration, and b) the earlier the onset of illness, the lower the attack frequency (Table 5). In connection with a) we would like to state: the information given in the case reports is obtained on a retrospective basis. Russell's study was prospective, and the attack duration was measured, two factors that make the information obtained definite.

Highly varying attack frequency and duration have been reported in 37 patients ("modified cluster pattern"). In some patients, there are only reminiscences of attacks in the best periods.[2]

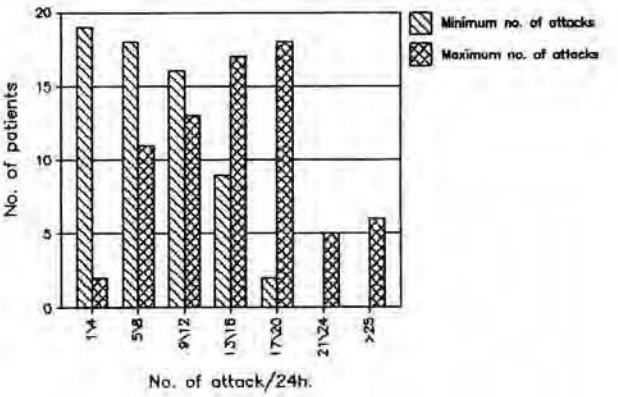

Fig. 6—Attack Frequency

Table 5
Correlation Matrix of Demographic Variables with Duration and Frequency of Attacks (Pearson r)

	Attack Duration	Attack Frequency	Illness Duration	Onset of Illness	Age
Attack duration:					
Males	-	-0.42*	-0.28	0.09	-0.20
Females	-	-0.25	-0.10	0.27	0.21
Total CPH	-	-0.28**	-0.14	0.22	0.13
Attack frequency					
Males		-	0.05	-0.18	-0.17
Females		-	0.17	-0.26	-0.16
Total CPH		-	0.13	-0.24*	-0.16

*$p < 0.03$ **$p < 0.01$

Accompanying phenomena. Lacrimation, nasal stuffing, conjunctival injection, and rhinorrhea, all on the symptomatic side, were the most frequent symptoms and signs accompanying the attack (Table 6). In one patient, bilateral tearing has been described.[19] It should be emphasized in this connection that, if quantified, there is also an increased nasal and tear gland secretion even on the non-symptomatic side.[44]

Nocturnal attacks. Fifty-five patients experienced nocturnal attacks; usually, there was no nocturnal preponderance of attacks. Three cases without nocturnal awakenings have been described. For the remainder, no definite information is available.

Remitting stage[45] (non-chronic, non-continuous stage, "Pre-CPH stage"). CPH is characterized by various stages, the chronic stage either being primary or representing a transition from a non-chronic stage. Since no definition of the length of the unremitting course in CPH has been stipulated, as of today, the chronic cluster headache criteria (> 12

Table 6
Accompanying Phenomena in CPH

Symptoms and Signs	No.
Lacrimation	52
Nasal stenosis	35
Conjunctival injection	30
Rhinorrhea	30
Ptosis	28
Photophobia	18
Miosis	15
Nausea	12
Generalized sweating	8
V1 hypersensitivity	7
Phonophobia	6
Temporal artery pulsation	5
Visual phenomena	4
Temporal artery dilatation	4
Tinnitus	3
Vomiting	2
V2 hypersensitivity	2
Exophthalmus	1

months) were employed. In a number of cases, the headache seems to stop at the non-chronic stage.

Thirty-five patients had experienced a remitting stage (42%). In 17 cases, this non-chronic stage still persisted, whereas, in 18 cases, the chronic stage had evolved (Table 7). The mean duration of the non-chronic stage was 18.2 years (range 1-35 years). In the group of patients still in the remitting stage, the mean duration of headache had been 19.6 years; in the group with CPH, after transition to the chronic stage, the mean duration of headache had been 16.9 years. In 16 of the cases, there had been a crescendo curve as far as the duration of the symptomatic period and the number of attacks per day in the "pre-CPH stage" are concerned; this steady deterioration could be traced in 6 cases still in the non-chronic stage and in 9 whose headache had already made a transition into the CPH stage.

No significant differences were found between the total group of CPH patients, patients still in pre-CPH stage, and those who already had entered into an overt CPH stage, in terms of: female:male ratio, present age, age at onset of illness, the duration of the non-chronic CPH, the number of patients with and without worsening of headache periods, duration and frequency of attacks (Table 7). On the other hand, in patients with a history of unremitting CPH, the onset of headache was later, and there was a longer mean duration of attacks (Table 7). It should be noted that the information in the literature is obtained only retrospectively, and no *exact* data are given.

It is worthy of note that the number of patients with a chronic course (i.e. 67) is much higher than those with a remitting course at the present time (i.e. 17, a ratio of 3.94).

Difference between the clinical pictures in the two sex groups. Onset of illness, duration of illness, attack frequency, and duration were found not to differ significantly between male and female subgroups (Table 2).

A negative correlation of attack duration with attack frequency was found in males (Table 5), the longer the attack duration, the lower the attack frequency.

Precipitation of attacks. In nine reports (10%), it was specifically mentioned that the patients were able to precipitate attacks by head flexion (n=5) or rotation (n=4) to the symptomatic side. In 5 patients, it was possible to precipitate headache, during neck examination while the patient bent the head forward and/or by exerting an external pressure over the C2 root and/or the transverse processes of C4-C5 on the symptomatic side. The attack pattern (5/9 cases) and/or the severity of pain (6/9 cases) seem to be similar to those during the spontaneous attacks. In two of these patients the headache started a few seconds after beginning of head flexion, during the worst period these attacks being associated with unilateral tearing, conjunctival injection, slight miosis, and ptosis.

Alcohol-induced attacks were experienced in 5 patients (7%) and an histamine-induced attack (his-

Table 7
Demographic Data of Patients with a History of "Remitting-Unremitting" Course (Mean ± SD)

	Remitting Stage by History	Still in Remitting Stage	Transition to CPH	Unremitting from Onset	p* Values
F:M ratio	1.7:1	1.42:1	1.57:1	3.1:1	
N. of patients	35 (42%)	17 (20%)	18 (22%)	49 (58%)	
Present age	45.1 ± 14.4	45.5 ± 16.8	44.8 ± 12.2	48.8 ± 13.2	NS
Onset of illness	26.9 ± 13.2	25.8 ± 14.2	27.8 ± 12.5	36.8 ± 11.9	NS
Remitting stage duration (years)	18.2 ± 12.2	19.6 ± 13.5	16.9 ± 11.1		NS
Worsening of periods	15	6	9**		NS
Mean duration of attacks (min.)	16.1 ± 9.7	15.1 ± 5.9	17.0 ± 12.5	21.1 ± 8.5	NS
Mean frequency of attacks	10.7 ± 4.2	10.0 ± 4.7	11.4 ± 3.6	10.5 ± 3.9	NS

*Two-tailed Student's t-test
**by history, prior to unremitting stage clear deterioration as evidenced by long lasting bouts etc.

tamine injection) in one patient (Nappi, unpublished case). There is a paucity of reports concerning nitroglycerine precipitation of attacks. Due to the high frequency of attacks, the spontaneously occurring and possibly precipitated ones may be confounded.

Physical examination and laboratory data. The general physical examination was normal in all patients. In 7 patients, however, a certain tenderness was observed in the neck on the symptomatic side, and in three patients a neck hypomobility towards the symptomatic side was observed.

Eyelid edema, facial erythema, and telangiectases, all on the symptomatic side, have been reported in some cases.[6,46]

The neurological examination was normal in all but one patient (signs of diffuse, peripheral, sensory neuropathy.)[13]

Twenty-eight patients underwent a CAT scan of the brain, and 31 had an EEG recording; all of these investigations were normal. In 2 out of 16 angiographies carried out, the angiograms revealed a small anterior communicating artery aneurysm.[2,17] In one case, a narrowing of the ophthalmic vein and a poor contrast filling of the cavernous sinus, on the symptomatic side, were demonstrated on orbital phlebography.[33]

Two patients underwent a NMR scanning of the brain that was found to be within normal limits (Sjaastad, unpublished cases).

Drug treatment. Indomethacin abolished the tendency to attacks completely in all the reported cases, provided the drug was given in adequate dosage (inclusion criterion). This seems to be a *sine qua non* for the CPH diagnosis at the present time. There is a considerable intraindividual variation in attack intensity and frequency, and the indomethacin requirement fluctuates accordingly (mean dosage: 100 mg; usual range 25-300 mg/24 h). Some patients, however, needed only 12.5 mg. per day or even only every alternate day during periods with the most lenient symptoms.

Indomethacin had been administered between 0.4 and 16 years (mean 6.2 years). The beneficial effect usually appears within 2 days (range 1-5 days) and may appear within a few hours. On discontinuation, headache re-appears within an average of 2.8 days (range 1-14 days). Long-lasting remissions have, however, been observed after indomethacin discontinuation[7,14,16] (Russell and Sjaastad, unpublished data). This possibly indicates a "pre-CPH stage." In one case,[47] a long-lasting remission occurred even in the chronic stage. A reduction in indomethacin requirement over time has been found in 20 patients. Signs of tolerance development (tachyphylaxis) have not been observed.

During treatment, purpura was observed in 1 patient,[24] abdominal pain in 2,[19,32] peptic ulcer in 1 (Sjaastad, unpublished) and nausea, vomiting, vertigo in one (Manzoni, unpublished).

Salicylates brought about a partial relief of pain in a large number of patients (25 out of 37 reports) (Table 8). A partial and transitory beneficial effect has been obtained with naproxen in 4 cases, with prednisone in 2 cases (in one of these two cases,[33] an optimal effect was produced with prednisone), with ergotamine in 2 cases, and with butazolidine, diclofenac, and ketoprofen in 1 case each. Lithium treatment has led to a considerable deterioration of the situation. Blind studies with placebo (7 cases) have been carried out: this led to no modification of their pain attack (Table 8).

Table 8
Drug Treatment Other than Indomethacin in CPH

Drug	Partial Efficacy Reports	Total Number of Reports
Salicylates	25	37
Ergotamine	3	36
Prednisone	2	18
Betareceptor blocking agents	0	13
Pizotifen	0	11
Carbamazepine	0	11
Lithium	1	11
Amitriptyline	0	8
Ketoprofen	1	7
Methysergide	0	7
Butazolidin	1	6
Naproxen	4	5
Phenobarbital	0	5
Oxygen	0	4
Tiapride	0	3
Ibuprofen	0	3
Diclofenac	2	2
Valproate	0	1
Verapamil	0	1
Clonazepam	0	1
Nimodipine	0	1
Histamine	0	1
Placebo	0	7

Surgical and non-pharmacological treatment. Ten patients had undergone different procedures/operations (tooth extractions, stellate ganglion blocks, cervical sympathetic blocks, trigeminal sensory root section, infraorbital nerve section, sphenopalatine anaesthetic injection and gangliectomy, infiltration of the point of Arnold, and ethmoidosphenectomy) with little or no success. Various other procedures, like chiropractic manipulation of the neck (n = 4), hypnotism, and biofeedback (n = 4) had also been carried out in some of the cases, but with no or borderline response. Acupuncture (n = 5) seems to be of little or no benefit in the bad periods; during the periods of moderate attacks, there may seem to be some effect in the occasional case. On the whole, attempts at such surgical and para-medical procedures for the relief of this type of pain at present seem unwarranted.

The follow-up of CPH patients ranges from 0.3 to 16 years (mean 2.3 years).

COMMENTS

It is, admittedly, a considerable drawback not to have been able to observe personally all the cases included. This is an inherent weakness of a patient review, based on retrospectively obtained information. Moreover, not all the reports reviewed contained complete and extensive clinical histories. Nevertheless, some unknown aspects of this headache seem to emanate from this study, only some of which will be commented upon.

The prevalence of CPH. The prevalence of cluster headache patients consulting physicians seems to be around 7 per 10,000.[48] The still more rarely occurring headache, CPH, seems to be much more frequently occurring than originally observed. Headache specialists particularly interested in cluster headache and seeing many such cases, would be likely to see CPH cases as well. The relative frequency of CPH (total number, including the subgroups) and cluster headache (inclusive of subgroups) in some relatively large materials is recorded in Table 9. The mean CPH:cluster headache ratio is approximately 1.9% (Table 9). By extrapolation, on the assumption that the approximate gross prevalence of cluster headache is known, one might get some hints as to CPH prevalence.

Admittedly, the knowledge concerning CPH as a headache entity is still too limited among the medical profession to secure a reasonable level of diagnostically verified cases at the present time. This ratio may change considerably in the foreseeable future.

Table 9

The Relative Frequency of CPH and Cluster Headache (CH) in Various Relatively Large Materials

	CPH Cases (Total)	Cluster Headache Cases (Total)	CPH in per cent of CH
Own material[2,4,46,49]	9	280	3
Manzoni et al.[50]	4	176	2
Kudrow[51]	9	960	0.9
		mean ratio:	1.9

The female preponderance. There was originally a clear preponderance of female cases in clinical materials; thus, in 1979, the status was as follows: a ratio F:M = 7:1.[46] In the pure Norwegian material, the sex-ratio is still 4.5:1.

The first male was reported in 1978[5] and as suspected later, the number of male cases is still increasing. Since in the beginning it was believed that CPH, at least to a large extent, was a female disease, male cases may partly not have been reported for that very reason. The original figures for males say, therefore, have been too low. For the same reason, the presently found ratio of 2.36:1, may not be the end of this story. In the end, there may be only a slight female preponderance or a rather *even* sex distribution in CPH. The present authors believe, however, that there will remain a rather clear female preponderance in CPH. The sex ratios in cluster headache and CPH obviously differ markedly.

The various forms of CPH. The 2 original cases were in the chronic stage and, as we see it now, both were primary chronic cases.[2] In 1980,[3] when scrutinizing the chronic cases (n = 8), it was discovered that in 4 of them the chronic stage was antedated by a "non-chronic" stage. There thus clearly seemed to be a secondary chronic stage in CPH, like in cluster headache. The term "non-chronic" was used at the time on the supposition that since in these cases the headache eventually had become chronic, it would become chronic in most (all?) similar cases. Since no cases had been followed from the pre-chronic to the chronic period, we did not have any *proof* that the disorder in the "non-chronic stage" was identical with that in the chronic stage, e.g. with a *complete* indomethacin effect. Theoretically, however, the chances that there really were two sides of the same story seemed overwhelming.

At approximately the same time however, the first cases remaining in the non-chronic stage were observed.[9] After that, many similar cases have been reported, e.g. by Jensen et al.,[14] Pelz and Merskey,[16] Geaney,[17] and, later, also by Kudrow et al.[35] These cases partly had a long-lasting story of headache, and during the years since they were diagnosed none of them are known to have made the transition to the chronic stage. Thus, even today there are no cases that have been followed from the pre-chronic period to the chronic stage. Although it is *not known* or proven, it is highly likely, based on present information, that there will be cases of cyclic CPH that never will reach the chronic stage, just like in the ordinary episodic cluster headache. We saw our first such case in 1979; this patient may seem to be approaching the chronic stage at the present time, with steadily shorter remissions.

The relative importance of the various stages can only be guessed upon at the present time. However, the present figures indicate that the non-chronic stage is increasing in importance numerically speaking, irrespective of the question whether or not the cases discovered in this stage are going to reach the chronic stage. Whether one in CPH at any time will reach the distribution of stages typical of cluster headache i.e. with a clear preponderance of the non-chronic stage, can only be speculated upon.[47] The distribution of CPH cases in the various stages recorded in Table 7 does not, so far, indicate that it will.

New aspects. It is rather evident that some softening of the original, rather rigid criteria has taken place over the years.

This goes for the number of attacks at the maximum (it presently seems to be acceptable with a maximum of around 4-5 attacks/24 hours), the mean

frequency of attacks in the clinical material being 10.8 ± 5.0 (Figure 6). Furthermore, the *presence of nocturnal attacks* does not seem to be a *sine qua non*; this has actually been known for some time. In the vast majority of cases, there are nocturnal attacks, but the night preponderance of attacks does not seem to be as characteristic of CPH as it is of cluster headache.

As suspected during the early phase, the pain of the attacks, in the chronic stage, is *usually* excruciating at its maximum. There does, however, not invariably have to be very severe or excruciatingly severe attacks to justify the diagnosis. The notion of *unilaterality of the headache* seems to have stood the test of time. An unchanging unilaterality may even be more frequently occurring in CPH (3 exceptions out of 84 cases = 3.5%) than in cluster headache (approximately 15% side shift) significant at $p < 0.025$ (Chi^2 Yates = 5.52). It is noteworthy that the female preponderance seems to be confirmed (F:M ratio of 2.36); this is equivalent to a p-value well below 0.001 regarding the difference versus normal population (99.9% confidence limits: 14-47%). Moreover, so is the fact that the chronic stage seems to prevail over the remitting stage (by a factor of 3.94), while in cluster headache the chronic course is rarely seen[50] (ratio chronic: episodic = 0.12). There is a statistically significant difference between the two headaches in these respects ($p < 0.001$; Chi^2 Yates = 28.7).

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