

# Chronic Daily Headache in Children and Adolescents: A Multi-Faceted Syndrome

*Shashi S. Seshia, Shuu-Jiun Wang, Ishaq Abu-Arafeh, Andrew D. Hershey, Vincenzo Guidetti, Paul Winner, Çiçek Wöber-Bingöl*

**ABSTRACT:** Chronic daily headache (CDH) is a multi-faceted, often complex pain syndrome in children and adolescents. Chronic daily headache may be primary or secondary. Chronic migraine and chronic tension-type are the most frequent subtypes. Chronic daily headache is co-morbid with adverse life events, anxiety and depressive disorders, possibly with other psychiatric disorders, other pain syndromes and sleep disorders; these conditions contribute to initiating and maintaining CDH. Hence, early management of episodic headache and treatment of associated conditions are crucial to prevention. There is evidence for the benefit of psychological therapies, principally relaxation and cognitive behavioral, and promising information on acupuncture for CDH. Data on drug treatment are based primarily on open label studies. The controversies surrounding CDH are discussed and proposals for improvement presented. The multi-faceted nature of CDH makes it a good candidate for a multi-axial classification system. Such an approach should facilitate biopsychosocial management and enhance consistency in clinical research.

**RÉSUMÉ:** La céphalée quotidienne chronique chez les enfants et les adolescents, un syndrome à multiples facettes. La céphalée quotidienne chronique (CQC) est un syndrome douloureux à multiples facettes qui est souvent complexe chez les enfants et les adolescents. La céphalée quotidienne chronique peut être primaire ou secondaire. La migraine chronique et la céphalée de tension chronique sont les sous-types les plus fréquents. La CQC est une comorbidité des incidents fâcheux de la vie, de l'anxiété et des troubles dépressifs, possiblement liée à d'autres troubles psychiatriques, syndromes douloureux et troubles du sommeil. Ces états contribuent à amorcer et à maintenir la CQC. Le traitement précoce de la céphalée épisodique et le traitement des comorbidités est donc crucial pour la prévention. Certaines données démontrent un bénéfice des psychothérapies, principalement de la relaxation et de la thérapie cognitivo-comportementale, et l'acupuncture pour le traitement de la CQC semble prometteuse. Les données sur le traitement médicamenteux sont basées principalement sur des études ouvertes. Nous discutons des controverses entourant la CQC et des moyens proposés pour améliorer son traitement. Le fait que la CQC possède de multiples facettes fait d'elle un bon candidat à un système de classification à plusieurs axes. Une telle approche devrait faciliter la prise en charge biopsychosociale et rehausser la cohérence dans le domaine de la recherche clinique.

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In 1982, Mathew et al first used the term "chronic daily headache" (CDH) to describe headaches that occurred almost daily in adults.<sup>1</sup> Twelve years later, Holden et al published the first report on children with CDH.<sup>2</sup> Since then, there have been at least 21 reports globally.<sup>3-23</sup> Cumulative knowledge suggests that CDH is not only a common chronic pain syndrome in children (the term will be used to include adolescents), but also a multi-faceted, and often complex one. The appreciation of the many aspects of CDH is pivotal to clinical research and management, and is the thrust of our review.

## DEFINITIONS AND CLASSIFICATION: THE CONTINUING CONTROVERSY

### Background

In the almost 30 years since the original description, CDH continues to evoke passionate debate. Globally accepted criteria

are still lacking.<sup>24-26</sup> As a consequence, it is difficult to compare studies, undertake meta-analysis or assess epidemiological data.

Chronic daily headache was not addressed in the first International Classification of Headache Disorders [ICHD-I] developed by the International Headache Society [IHS].<sup>27</sup> Therefore, Silberstein et al proposed a classification scheme for "daily and near-daily headaches."<sup>28</sup> Wöber-Bingöl et al and Nappi et al supported the need to improve the classification for CDH.<sup>9,29</sup> These views were countered with the argument that virtually all chronic headache (CH) patients could be classified using ICHD-I.<sup>30</sup> Welch and Goadsby emphasized that CDH encompassed a group of headache disorders, either primary or secondary, characterized by a "high frequency of headache"; they felt that the term CDH had clinical utility, and that a classification of CDH could be accommodated in the appendix of the main ICHD.<sup>31</sup> Chronic daily headache was not considered

From the Department of Pediatrics, Division of Pediatric Neurology (SSS), University of Saskatchewan, Saskatoon, Saskatchewan, Canada; Department of Neurology (SJJ), National Yang-Ming University School of Medicine; Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan; Paediatric Neurology (IAA), Stirling Royal Infirmary, Stirling; Royal Hospital for Sick Children, Glasgow; University of Dundee, UK; Pediatrics and Neurology (ADH), University of Cincinnati, College of Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; Palm Beach Headache Center (PW), Premiere Research Institute, Palm Beach Neurology, Nova Southeastern University, West Palm Beach, Florida, USA; Italian Headache Society, Department of Child and Adolescent Neurology (VG), Psychiatry and Rehabilitation, University of Rome "La Sapienza," Roma, Italy; Department of Child and Adolescent Neuropsychiatry (CWB), University of Vienna, Wien-Vienna, Austria.

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Correspondence to: Shashi S. Seshia, Department of Pediatrics (Division of Pediatric Neurology), University of Saskatchewan, Saskatoon, Saskatchewan, S7N 0W8, Canada.

in ICHD-II.<sup>32</sup> However, CDH was discussed subsequently by the Headache Classification Committee; they advised that CDH should not be used as a diagnostic entity, chronic headache (CH) being preferred as the umbrella designation,<sup>33</sup> an opinion challenged by Solomon.<sup>34</sup> Despite the recommendation of the Headache Classification Committee, CDH is more widely used than CH and entrenched globally in the pediatric and adult literature, strengthening the argument for its formal adoption.

### Definitions and criteria

'Chronic' has been defined inconsistently in ICHD-II.<sup>32</sup> We suggest that all subtypes of CDH be defined unambiguously as headache occurring  $\geq 15$  days a month for  $\geq 3$  months.<sup>20,26,34</sup>

Silberstein et al required that the average duration of headache be  $> 4$  hours/day untreated, while acknowledging that this criterion was arbitrary.<sup>28</sup> Headache duration in CDH forms of the trigeminal autonomic cephalalgias (TACs) may be  $< 4$  hours/day.<sup>31</sup> Hence, the suggestion that the duration criterion be reassessed has merit and needs to be explored further,<sup>26</sup> especially since duration may influence diagnosis and management.

### Classification of CDH

Chronic daily headache in children can be sub classified, using the ICHD frame-work [Table; appendix table] into primary (Codes 1-4) and secondary (Codes 5-12) types.<sup>11,14,15,17, 19,20,27,32</sup> The provisos for the diagnosis of any of the primary headache disorders include the caveat: "History and physical and neurological examinations do not suggest any of the disorders listed in groups 5-12...or (such disorders are) ruled out by appropriate investigations..."<sup>32</sup>

Four issues that are the subject of continuing debate will be discussed.

#### *Transformed migraine*

Transformed migraine was proposed as a CDH subtype by Silberstein et al.<sup>28</sup> As Mathew et al initially pointed out, transformed and transformation reflect change or evolution over a period of time from intermittent or episodic headache to CDH.<sup>1,35</sup> We suggest that transformed not be used to describe type; rather, a particular CDH subtype, such as chronic migraine (CM), could be transformed or new-onset.

#### *Chronic migraine (Appendix code 1.5.1)*

The revised criteria for CM are currently as follows:<sup>33</sup>

- A. Headache (tension-type and/or migraine) on  $\geq 15$  days per month for at least three months,
- B. Occurring in a patient who has had at least five attacks fulfilling ICHD-II criteria for (code 1.1) migraine without aura,
- C. On  $\geq 8$  days per month for at least three months headache has fulfilled C1 and /or C2 below,
  - (1) Has met criteria for migraine without aura as outlined in ICHD-II, and (2) Treated and relieved by triptan(s) or ergot before the development of C1.
- D. No medication-overuse (as defined under code 8.2) and not attributed to another causative disorder.

The revised (ICHD-IIR) criteria for CM have been reviewed critically, and the requirement for a response to triptans or ergot

(C1) and the absence of medication-overuse for diagnosis (D) questioned.<sup>24</sup> The assimilation of tension-type headache (TTH) within CM (Criterion A above) has also been challenged.<sup>20,25,26,34</sup> Some of us favor the ICHD-IIR criteria for CM; others feel that until there is definite evidence to support that position, CDH with features of both migraine and TT should be classified as 'mixed' chronic migraine-chronic tension-type headache (CM-CTTH).<sup>20,26</sup> The 'gray zone' of CDH with features of both migraine and TTH needs further study. One practical solution to this impasse is to divide CM into two subforms: (i) CM solely with migraine features and (ii) CM with associated TTH features, as proposed by Solomon.<sup>34</sup>

#### *New daily-persistent headache (NDPH; code 4.8)*

New daily-persistent headache (NDPH) is coded as a separate primary headache type although the criteria, which were likely arbitrarily developed, are similar to those of CTTH. The ICHD-II criteria for NDPH require (i) that onset or rapid development be "clearly and unambiguously recalled," and (ii) history, physical and neurological examination should not suggest secondary headache disorders coded under 5-12.<sup>32</sup> The onset of NDPH was associated with infections or minor head injuries in one study (43% and 23% of 40 subjects, respectively);<sup>36</sup> hence, the designation of NDPH exclusively as a primary headache disorder is questionable. Furthermore, migraine features were common in children with NDPH in another report.<sup>37</sup> For these reasons and because, 'new daily' reflects a process that is the opposite of 'transformation', we suggest that the concept of NDPH be revisited in the next version of ICHD. Headaches should be classified by characteristics, an approach used by the IHS for almost all of the headache groups, types and subforms, not by mode of onset or evolution.

#### *Medication-overuse headache (Code 8.2 and appendix 8.2)<sup>32,33</sup>*

The designation of medication-overuse headache (MOH) as a separate headache type remains controversial and a source of considerable confusion.<sup>24,38</sup> The criteria for MOH are empirical and adult oriented.<sup>32,33</sup> In one study on TTH, the use of analgesics and ergotamine preparations was uncommon in children compared to adults.<sup>9</sup> Most pediatric studies suggest that the incidence of MOH is relatively low, although there are a few exceptions.<sup>5,8-12,14-16,23,39</sup> The absence of well defined criteria for children may explain some of the differences between studies, although selection bias and geography may also play a role. Hence, pharmacologically based criteria are needed for children.<sup>8</sup> Medication-overuse may reflect addictive behavior.<sup>40</sup> Medication-overuse should be considered a potential co-morbid risk with CDH, one that can contribute to transformation and persistence, and may not warrant listing as a specific entity.

### EPIDEMIOLOGY

The prevalence of CDH across the entire pediatric age spectrum is unknown as population studies have been based on schoolchildren. Precise comparisons between studies are not possible because of potential methodological differences. The prevalence of CDH was reported as 0.9% from Scotland,<sup>41</sup> 1.5% from Sweden,<sup>42</sup> 7.8% from China,<sup>43</sup> 1.5% from Taiwan<sup>16</sup> and 1.68% from Brazil<sup>22</sup>, respectively. The prevalence for CTTH was 0.1% in Sweden and 5.9% in Turkey respectively.<sup>42,44</sup> The

prevalence in both preadolescence and adolescence is two to three fold higher in girls than in boys.<sup>16,22</sup>

In a headache clinic based study, 105 (6.5%) of 1598 children were < 6 years-of-age; of these 105, five (4.8%) had CDH.<sup>13</sup> About one in three attending four pediatric headache clinics suffered from CDH.<sup>4,5,8,20</sup>

## GENETICS

There are three aspects to the genetics of CDH: (i) the genetics of the primary headache disorder (Codes 1-4) that has become CDH, (ii) the genetic propensity for developing CDH,<sup>45</sup> and (iii) the role of genetic factors in the neurobiological processes underlying central and peripheral sensitization responsible for chronification. The genetics of TTH, including CTTH, has been discussed recently.<sup>46</sup> The genetics of CH has been discussed eloquently by Montagna et al;<sup>47</sup> readers are directed to their paper, as a brief summary here will not do justice to the subject. In one study, 11 (16%) of 70 children with CDH had a family history of CDH in first degree relatives.<sup>20</sup> There are no data to help separate the roles of genetic influence and environment in this situation. The genetics of CDH in children needs further study.

## ASSOCIATIONS (POSSIBLY CO-MORBID CONDITIONS)

A number of conditions, especially psychiatric, associate with primary CDH, suggesting that it is a syndrome with many facets. Their recognition is essential for management.

### Anxiety and depressive disorders

Several publications have referred to the association between CDH on the one hand and anxiety and mood (specifically depressive) disorders on the other.<sup>1,6-8,11,12,17,18,20</sup> In a community based study of 12 to 14-year-old school children, almost half of the 121 subjects with CDH had at least one psychiatric disorder; depressive disorders were found in 30% (36 of 121) and anxiety disorders in 36% (43 of 121); additionally 20% (24 of 121) had high "current" suicidal scores.<sup>18</sup> These figures were much higher than those in the age matched general population. Migraine, especially migraine with aura, and female gender increased the risk of the association. In a population-based study on individuals older than ten years in rural Brazil, psychiatric co-morbidities were found in two-thirds of those with CDH.<sup>48</sup>

### Other psychiatric disorders

Mathew et al found an association between CDH in adults and "hysteria."<sup>1</sup> About 20% of 37 children with CDH in one study had "histrionic traits, as characterized by la belle indifference, in which symptoms described far outweighed disability seen by the family."<sup>3</sup> The diagnosis of somatoform disorder, factitious disorder and malingering in children with CDH was discussed in another report;<sup>20</sup> differentiation between these three entities even with DSM-IV-TR criteria,<sup>49</sup> is very dependent on the history and susceptible to subjective clinical opinion.<sup>20</sup> In a third, symptoms of anxiety, depression and somatization were more common in children with CDH than in controls.<sup>39</sup>

In a fourth study, children with CDH and school phobia were found to have a significantly higher incidence of psychiatric

disorders than those without school phobia; the psychiatric disorders included adjustment, anxiety and conversion.<sup>50</sup>

### Family history of psychiatric disorder

There is a higher incidence of psychiatric disorders in the parents of children with migraine compared to that in children with non-migraine headache.<sup>51</sup> A family history of anxiety disorder in first degree relatives was found in 7% (N=5), and of depressive disorder in 31% (N=22) of 70 children with CDH; these were not stratified by headache type.<sup>20</sup> Such illnesses in close family members were described as important stressors for child and family,<sup>8,20</sup> adding to the complexity of CDH.

### Disorders of sleep

Sleep disorders occur very frequently in adult headache subjects and morning headaches may be a clue to their presence.<sup>52-54</sup> Anxiety and depression may not entirely explain sleep disorders in adult migraineurs.<sup>55</sup> Several studies, the majority based on sleep questionnaires, including some that were population based, have drawn attention to the association between sleep disorders and childhood headache.<sup>56-62</sup> The association was stronger with migraine than TTH, although those with TTH (including CTTH) may not have been adequately represented. From polysomnographic studies, Vendrame et al found an association between TTH and bruxism; those with severe or CM had disrupted sleep architecture with reduced rapid eye movement and slow-wave sleep.<sup>59</sup> The data support the possibility of a close relationship between sleep and headache disorders. Twenty-three percent (N=16) of 70 children with CDH complained of disturbed sleep that was not necessarily related to headache but information was insufficient to identify associated sleep disorders.<sup>20</sup> A systematic study for sleep disorders/disturbances in children with CDH is needed.

### Other pain syndromes

Headache and other pain syndromes may be co-morbid in children and adults.<sup>63</sup> The issue needs prospective study as data specific for CDH is lacking.

### Obesity

There is an association between obesity and progression of episodic migraine to CM but not between obesity and TTH, in adults.<sup>64</sup> The incidence of obesity in two pediatric headache clinic based studies, one on those with CDH, was not different from that in the general population; subjects were not stratified by gender.<sup>20,65</sup> Overweight females had a near four fold excess risk of headache when compared to normal-weight girls; there was no relationship between weight and headache in males.<sup>66</sup>

## PRECIPITATING AND CONTRIBUTORY FACTORS

Clinical observations have shown that several factors may precipitate, contribute to transformation and maintain CDH. Their identification and management is also essential.

### Stressors/adverse life events/life changes

These terms are often used interchangeably. They may be positive or negative, minor hassles or major events. Stresses may

lead to post-traumatic stress disorder. Stress disorders are listed under anxiety disorders in DSM-IV-R.<sup>49</sup> Stressors, frequently multiple, contributed to transformation in forty to fifty percent of children with CDH and were also considered important in maintaining CDH.<sup>4,7,8,20,23</sup> For children, stresses are often family/home related, peer related or school related; bullying is an important school related stressor.<sup>8</sup> The risk of frequent headache in five year olds was increased by low socio-economic status and increasing number of leisure activities.<sup>67</sup> A higher incidence of divorce in the parents of children with TTH has been noted.<sup>68</sup>

There was a significant association between adolescent CDH and childhood adversity, specifically parental divorce and physical abuse, in a community based study; the authors did not find examples of sexual abuse but commented on the difficulty in identifying such victims.<sup>69</sup> Childhood maltreatment (physical abuse, sexual abuse, emotional abuse, and physical neglect) may be a risk factor for CDH in adults and is often associated with other pain syndromes, depressive and anxiety disorders.<sup>70,71</sup> The prevalence of specific adverse events is likely to be country and community specific. Greater attention has to be paid to the possibility of maltreatment in children with CDH and country/community specific epidemiological studies are needed.

### Head/neck trauma

Minor head injury, especially sports related, is often a cause of NDPH.<sup>8,10,36</sup> The cause may be overlooked unless history is sought. We are unaware of studies assessing the relationship between neck trauma and CDH in children. Chronic post-traumatic headache after head injury, whiplash and other head or neck trauma is discussed under code 5 of ICHD-II.<sup>32</sup>

### Other

Sleep deprivation, fatigue, irregular sleep habits, hunger, noise and bright lights often contribute to CDH. Caffeine is considered a risk factor in adults,<sup>1,72</sup> and is very like one in children.

### NEUROBIOLOGY

The neurobiology of TTH, including CTTH, has been discussed recently.<sup>46</sup> Chronic daily headache generally evolves from intermittent headache. The transformation to and the features of CDH can be explained by central and peripheral sensitization (the former more than the latter); changes in the trigeminal system, altered neuroimmunity and compromise to endogenous 'analgesia systems' (pain transmission and modulation) are considered central to the process; stress, anxiety and depressive disorders, and chronic analgesia exposure likely act through these mechanisms.<sup>73-77</sup> The putative mechanisms behind sensitization are likely common to all subtypes, although most investigators have focused on CM.

### CLINICAL FEATURES AND SUBTYPES OF CHRONIC DAILY HEADACHE

#### Primary subtypes (Codes 1-4)

Headache is generally bilateral, mainly frontal.<sup>5,10,20</sup> However, consistently unilateral headache has been reported in 3% to 16% of children with CDH, in some series.<sup>10,20,78</sup> The majority of primary CDH disorders are transformed from

intermittent headache. Transformation occurred in 78% of 630 patients in the series of Mathew et al.<sup>35</sup> A similar percentage has been reported in children.<sup>6,8,10,20</sup>

Chronic migraine, CTTH, mixed CM and CTTH, in variable proportion, have constituted the most frequent subtypes of primary CDH in clinic based studies.<sup>3,5-12,16,19,20</sup> In an adolescent community based study, the relative frequencies for CM and CTTH were 7% and 66% respectively (N=122) but 59% of those with CTTH also had migraine attacks.<sup>16</sup> Of note, the prevalence of CM increased (from 7% to 23%) when the revised criteria for CM were applied.<sup>17</sup> Even in those with preceding migraine, migraine characteristics often decline and TTH characteristics become prominent when CDH develops.<sup>5,79</sup> Conversely, migraine features may increase as CDH remits.<sup>17</sup> These patterns in some (but not all) with CDH further compounds the challenges of 'lumping' or 'splitting' CDH into CM, CTTH and mixed CM and CTTH subtypes respectively.

Unilateral headache, most striking over the orbital, supraorbital or temporal regions, with associated cranial autonomic features strongly suggests a TAC (Code 3) or HC (Code 4.7); response to indomethacin is considered essential under ICHD-II for diagnosing HC.<sup>32</sup> However, not all those with the clinical phenotype of HC respond to indomethacin.<sup>80</sup> The relative frequency of TAC and HC in children when compared to CM, CTTH or mixed CM and CTTH, must be extremely low; there were no cases in one population study conducted over eight years to date.<sup>16,17,21</sup>

Clinical features of psychological and psychiatric comorbidity are often present. Although headache may be constant and even severe or disabling through the day, they are usually not described as a problem during sleep.<sup>8,20</sup> When sleep is disturbed, then the possibility of associated mood, anxiety and sleep disorders must be considered.

#### Secondary subtypes (Codes 5-12)

In one study, 10% of seventy children with CDH had a secondary cause, the majority after minor concussion (code 5.6.2).<sup>20</sup> International Classification of Headache Disorders-II provides diagnostic criteria for the secondary subtypes.<sup>32</sup>

Chronic daily headache, CM in most reports, may associate with idiopathic intracranial hypertension (IIH; code 7.1.1) without papilledema.<sup>81-85</sup> Idiopathic intracranial hypertension may or may not be the sole cause of CDH in these cases. Chiari malformation type I (code 7.7) may cause CDH.<sup>32,86</sup>

#### RATING DISABILITY AND QUALITY OF LIFE

PedMIDAS was designed to assess the disability of children with migraine and can be used in those with with CM.<sup>87</sup> It was not intended for TTH; hence, we have reservations about its application in CTTH.<sup>46</sup> Universally accepted rating scales and quality of life measures are needed.<sup>88</sup>

#### DIFFERENTIAL DIAGNOSIS

The important elements in history, physical examination, differential diagnosis and the red flags for TTH, including CTTH, have been discussed.<sup>46</sup> They apply to CDH. Intractable CDH and persistent unilaterality of headache are additional red flags. Occipital or sub-occipital location and worsening with

coughing or Valsalva maneuver may suggest Chiari malformation type I.<sup>32,86</sup> Aggravation in the upright position with improvement by lying down may point to an intracranial hypotension syndrome; other associated clinical features include neck stiffness, tinnitus, hypacusia (Codes 7.2.2; 7.2.3).<sup>32</sup>

The possibility of IHH without papilledema must be considered under the following circumstances: (i) Intractable CDH, (ii) tinnitus or noise in the head as a symptom (important to seek this information), particularly in the presence of obesity, although subjects may be of normal weight.<sup>32,81-85</sup> A detailed ophthalmologic examination, not only testing of visual acuity, examining fundii and assessing for venous pulsations but also blind spot charting, visual field assessment and contrast sensitivity, must be done in all those suspected of having IHH.

## INVESTIGATIONS

The majority of children with CDH will not need specific investigation, especially neuroradiological.<sup>8,20,89,90</sup> If secondary CDH is suspected, magnetic resonance imaging of the head including magnetic resonance angiography and venography is preferred to computed tomography not only due to potential risks of radiation from computed tomography but also because of the broader range of information that is provided.<sup>46</sup> The cervical spine should be included in the study to identify a Chiari malformation. Continuous cerebrospinal fluid pressure monitoring may be more helpful than an isolated measurement if IHH or low cerebrospinal fluid pressure syndromes are suspected.<sup>46,91</sup>

Other investigations will be determined by the differential diagnosis entertained.

## MANAGEMENT

There may be regional or personal differences in the availability and use of specific non-pharmacologic and pharmacologic treatments. Therefore, the suggestions that follow should be tailored to the individual. The general principles are similar to those outlined for TTH,<sup>46</sup> and will not be detailed. The first step is to identify and treat the factors, including lifestyle issues that have precipitated and contributed to CDH. Chronic daily headache, especially primary, must be handled in a multi-disciplinary biopsychosocial manner. Immediate family members have to be involved in the assessment of stressors or illnesses in them, as these may contribute to the child's CDH.<sup>8,20</sup> The team can determine if stressors and associated psychiatric disorders should be treated before or in conjunction with pharmacologic management of pain. The relative contributions to impaired quality of life by headache and associated conditions are central to decision making. Analgesics are frequently ineffective in CDH. When there has been overuse, gradual withdrawal of the offending agent should be done.

## Psychological therapies

There is good evidence for the effectiveness of psychological therapies, especially relaxation and cognitive behavioral, in reducing severity and frequency of CH.<sup>92</sup> Hence, if readily available, such treatment should be offered as an alternative to drugs. Space does not permit a detailed description of psychological interventions.

## Other non-pharmacologic

Needling acupuncture was found superior to sham acupuncture and medication in improving CH in adults.<sup>93</sup> Laser acupuncture has been reported to be effective in children with headache.<sup>94</sup> Therefore, acupuncture is another potential non-pharmacologic treatment for CDH in children but further studies to firmly establish efficacy are needed.

## Pharmacologic

When considered necessary because of the impact of pain on quality of life, the specific choice of drug is dependent not only upon the subtype of CDH but also the presence of associated conditions such as anxiety, depressive or other psychiatric disorders. The relatively high placebo effect in children makes assessment of benefit difficult.<sup>95</sup> Most if not all of the drugs used are off-label, and the evidence for benefit is based on open label studies. Doses are empiric, since there are no studies based on doses calculated by body weight or surface area. The role of pharmacogenetic factors has not been addressed. Three of 122 participants with CDH in a community based study received treatment; only 25% of the total had CDH after two years of follow-up;<sup>17</sup> this 'natural history' must be factored into the outcomes of any treatment trial.

With these provisos, dihydroergotamine and metoclopramide given intravenously in the out-patient or emergency room setting may ameliorate or abolish the pain of CTTH, CM or mixed CTTH-CM, even in a single dose.

### *Chronic tension-type headache and mixed chronic migraine-chronic tension-type headache*

The management has been discussed recently.<sup>46</sup>

### *Chronic migraine*

We have no evidence for the efficacy of triptans once a CDH pattern is established. Open label data suggest a role for intravenous valproic acid (VPA) in adults.<sup>96</sup> We are not aware of information in children. Chronic migraine remitted in seven adolescents given dihydroergotamine, dexamethasone and hydroxyzine parenterally once a week for three weeks.<sup>97</sup>

We are unaware of evidence for the benefit of oral cyproheptadine, flunarizine, propranolol or riboflavin but these were considered effective in one clinic based study.<sup>10</sup> Riboflavin and Coenzyme Q10, singly or in combination, are worthy of trial because they are innocuous. Amitriptyline, gabapentin and topiramate have a beneficial effect on pain and can be used orally for CM in the same manner as for frequent episodic TTH and CTTH;<sup>46,98</sup> they are our other choices in this situation. Topiramate is preferred in obese subjects. Limitations to the use of VPA include: potential for weight gain, possible risk of polycystic ovary syndrome and teratogenicity. Hence, VPA may not be a suitable choice for adolescent females who constitute a high proportion of those with CDH. Improvement with any prophylactic drug is often delayed for about a month, and in some, the CDH then resolves. Treatment is then generally continued for a three month headache period before gradual discontinuation, a practice for which there is no evidence.

*Hemicrania continua*

A trial of indomethacin should be given to any child who presents with unilateral headache.<sup>99</sup> Indomethacin has troublesome side-effects, and alternatives include gabapentin and topiramate.<sup>100</sup> Other non-steroidal anti-inflammatory drugs may also be effective if these have not already been tried.

*In-patient Management*

In-patient management in an age appropriate facility is generally reserved for children who have high pain intensity, are disabled by pain (i.e. unable to participate effectively in school or extracurricular activities), who are suspected of having severe anxiety or mood disorder, or in whom significant adverse social factors are suspected. The protocol for management is similar to that outlined for CTTH.<sup>46</sup> Secondary causes must be excluded in those with intractable CDH.

*Other treatments for chronic daily headache*

Mexilitene may be useful in adults with refractory CDH;<sup>101</sup> we are unaware of data in children. Botulinum toxin type A may be an effective option in children with CDH, and the authors felt that a controlled trial was warranted.<sup>102</sup>

**OUTCOME**

Outcome data are limited and confounded by the differences in length of follow-up and criteria for improvement. The ideal outcome is the headache-free state. In one communication, headaches resolved completely and were not considered a management issue by 48 (68%) of 70 children with CDH; however, 5 (10%) of the 48 relapsed within the three-year follow-up period, four of the five being girls.<sup>20</sup> In another, over a ten-year follow-up, 86.5% (32/37) were improved, 8% (3/37) were worse, and 5% (2/37) were unchanged;<sup>103</sup> the authors felt that the comprehensive biopsychosocial approach provided in their centre contributed to the results. From an adolescent community based study, at the end of eight years, 11% (11 of 103) were headache free, 27% (28 of 103) still had moderate to severe headache disability and 12 (11%) continued to meet criteria for CDH.<sup>21</sup> Prognosis may be less favorable in girls, in those with migraine, those with medication-overuse, those with CDH onset < 13 years-of-age, CDH duration  $\geq$  2 years, and those with associated psychiatric disorders.<sup>11,17,20,21,104</sup> Fifty-nine (59%) of 100 adults with CDH recalled having headaches as children.<sup>105</sup> Thirteen percent of adults (8 of 60) in another study, recalled onset of CDH in childhood.<sup>106</sup> These data suggest that CDH may not remit or may only improve partially in a clinically significant number of children;<sup>104-107</sup> therefore, those at high risk for chronicity (see above) should be targeted for early "aggressive" intervention.<sup>104</sup> Additionally, children with CDH should be followed into late adult life to better define long term outcome; data bases such as those used in Taiwan provide a model to achieve this end.

**A MULTI-AXIAL APPROACH TO CDH?<sup>20,26</sup>**

The information presented shows that primary CDH is a multi-factorial, often complex syndrome (Figure). Hence, it would lend itself well to a multi-axial system of classification such as that used in Psychiatry.<sup>49</sup> A tentative multi-axial classification has been proposed [Table].<sup>20,26</sup> There is merit in

exploring and refining such a classification for CDH in particular and headache disorders in general.

**CONCLUSIONS**

With a prevalence of at least 1% in school children, CDH is an important pain syndrome in childhood. A clinically significant percentage continues to have frequent headache and CDH into adult life. In the preface to ICHD-II, Professor Olesen wrote, "It is important for any field of medicine to have a generally-accepted classification that is used throughout the world."<sup>32</sup> Hence, the absence of universally acceptable nomenclature and classification for CDH needs to be rectified. Many conditions, particularly psychiatric and psychological, are co-morbid with and contribute to primary CDH. Therefore, a multi-axial approach may improve management.<sup>20,26</sup> A multi-axial classification may also enhance uniformity in the clinical, education and research settings,<sup>49</sup> a key goal of the IHS. A classification for CDH could be incorporated as an appendix to

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**Table: Proposed axes for classification of CDH<sup>20,26</sup>**

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Axis I: Main headache Group (CDH; Type Primary or Secondary)

Axis II: Subtype/s (ICHD codes)\*

Primary

Chronic migraine (CM; 1.5.1): (i) Solely with migraine features (ii) with associated TTH features

Chronic tension-type headache (CTTH; 2.3)

Chronic cluster (3.1.2)

Chronic paroxysmal hemicrania (CPH; 3.2.2)

Hemicrania continua (HC; 4.7)

New daily-persistent headache (NDPH; 4.8)

Secondary (specify diagnosis/code)

Axis III: Associated medical conditions (examples: Psychiatric disorders such as anxiety or depression; other pain syndromes; obesity etc)

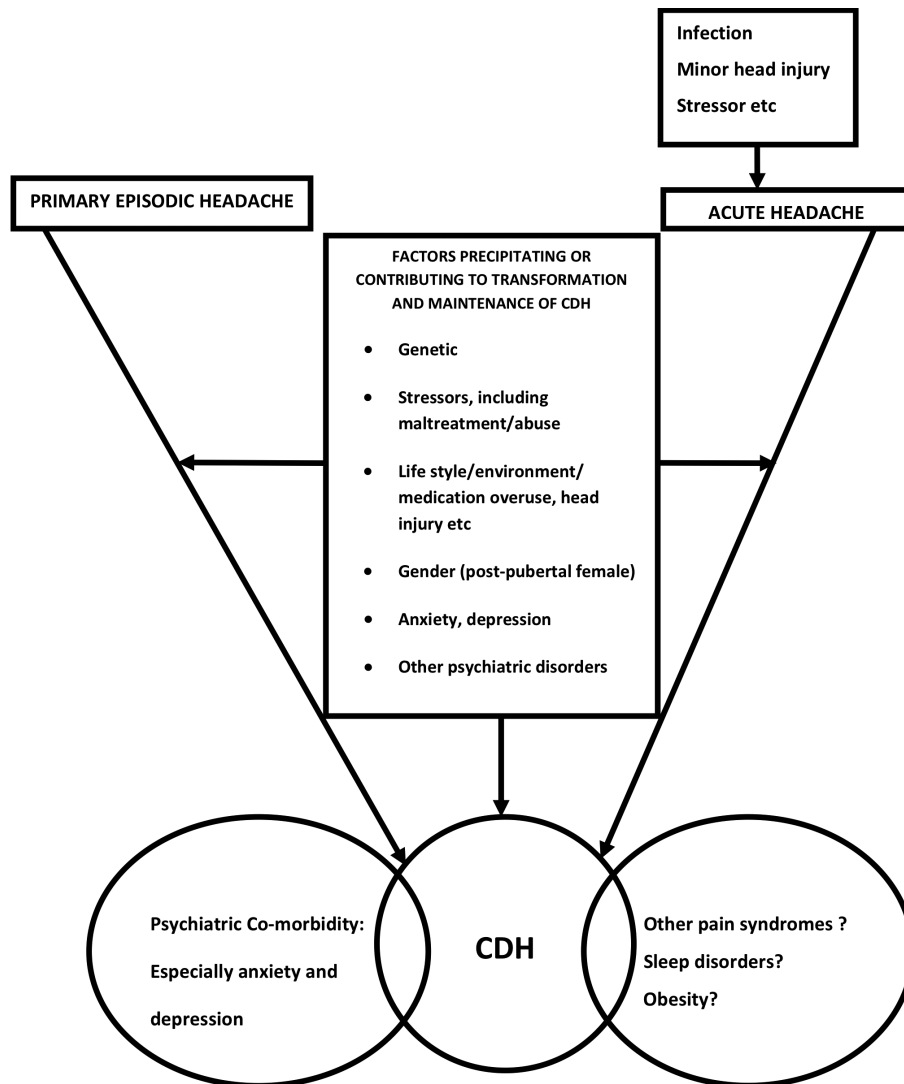
Axis IV: Contributory factors (examples: adverse life events: specify; concussion; analgesia-overuse; caffeine etc)

Axis V: Functional impairment (specify sphere of activity) †

Axis VI: Pain Severity\*\*

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Multi-axial classification for CDH. Note: \*Please see discussion in the text pertinent to the subtypes. † There may be dissociation of functional impairment for different activities. \*\* Standardized universally accepted tools needed. We are grateful to Wiley-Blackwell & Mac Keith Press (Publishers of *Developmental Medicine and Child Neurology*), and John Wiley & Sons, Inc., (Publishers of *Cephalalgia*) for permission to adapt the Table from Table V in reference 20 and Table 1 in reference 26 respectively, the former being the original and the latter a reproduction.



**Figure:** Multi-faceted nature of primary CDH (chronic daily headache). Please see text for details specific to the variables listed. The question mark (?) after some variables reflects the uncertainty of information regarding their association with CDH. Life style/environmental factors include: sleep deprivation, fatigue, noise, bright lights, caffeine, etc. The information on the transformation of primary episodic headache to CDH applies best to chronic migraine, chronic tension-type headache and mixed chronic migraine and tension-type. Acute headache may progress to new daily-persistent headache.

the main ICHD classification, as suggested by Welch and Goadsby.<sup>31</sup>

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#### DEDICATION

We dedicate this paper to the late Professor Giovanni Lanzi (formerly of Pavia, Italy), a pioneer in the discipline of Childhood and Adolescent Neuropsychiatry and in the field of Child Neurology, especially headache in children and adolescents.

**Foot-Notes**

(i) Readers are advised to refer to current Pediatric Drug Dosage references specific to their population, for doses of drugs discussed and for information about toxicity, drug interactions etc. Some of the drugs mentioned may not be available in all countries.

(ii) The literature on adult CDH is vast. Only those pertinent to our review have been cited.

(iii) We have attempted to minimize duplication of information provided in reference number 46. The current review and reference 46 should be considered companion papers.

(iv) Depression (colloquial) and depressive disorder (DSM IV) have been used synonymously in this review.

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**Appendix: Abbreviated ICHD-II classification<sup>32</sup>**


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**The primary headaches**

1. Migraine
2. Tension-type headache
3. Cluster headache and other trigeminal autonomic cephalalgias
4. Other primary headaches

**The Secondary headaches**

5. Headache attributed to head and/or neck trauma
6. Headache attributed to cranial or cervical vascular disorder
7. Headache attributed to non-vascular intracranial disorder
8. Headache attributed to a substance or its withdrawal
9. Headache attributed to infection
10. Headache attributed to disorder of homeostasis
11. Headache or facial pain attributed to disorder of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cranial structures
12. Headache attributed to psychiatric disorder

**Cranial neuralgias, central and primary facial pain and other headaches**

13. Cranial neuralgias and central causes of facial pain
  14. Other headache, cranial neuralgia, central or primary facial pain
- 

Abbreviated ICHD-II classification. Numbers refer to code for headache group. Subtypes would be coded to the two digit level (example, 1.2 for migraine with aura), and subform at the three digit level (example, 1.5.1 for chronic migraine). Reproduced from reference 32 with permission of International Headache Society, to whom we are grateful. The classification is available for download without cost at <http://www.ihs-classification.org/en/>

**DISCLOSURES**

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