

The classification and differential diagnosis of orofacial pain

Expert Rev. Neurother. 12(5), 1–xxx (2012)

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There are currently four main pain classification systems relevant to orofacial pain (OFP): the International Association for the Study of Pain (IASP), International Classification of Headache Disorders (ICHD-II), the American Academy of Orofacial Pain (AAOP) and the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD). Of the four, the RDC/TMD is the most biopsychosocial system with the remaining three focusing more on the biomedical. Unsurprisingly clinical scientists and clinicians have both reported perceived deficiencies in the published systems and have proposed further modified classifications and nomenclature for OFP. Establishing a standardized biopsychosocial classification of OFP is essential for ensuring continuity for patient care as it creates a standard language with which to communicate healthcare information, thus enabling improved and more specific (epidemiological) research and patient care. Despite ongoing attempts, an accepted overarching classification of OFP is still a work in progress. There is an urgent need for a robust classification system for OFP. This review aims to highlight the recent debate and continued struggle to attain a consensus on a classification of OFP and highlight some recent developments that assist differential diagnosis of these conditions.

KEYWORDS: classification • oral and facial region • temporomandibular disorders • trigeminal neuralgia • trigeminal neuropathy

Pain in the oral and facial region (OFP) produces significant biopsychosocial impacts [1–5]. A recent US Surgeon General's report states that 'oral health means much more than healthy teeth, it means being free of chronic OFP conditions' [1]. Epidemiologists report a significant burden of OFP affecting the community: estimates place this at 39 million persons (22%) of the American adult population suffering from chronic OFP and approximately 7% in the UK [6–9].

Risk factors for chronic OFP include chronic widespread pain, female age, gender and psychological factors with most studies reporting that females reporting OFP twice as frequently as males [10,11].

OFP may be due to various conditions affecting numerous structures local to or distant to the oral cavity including: the meninges, cornea, oral/nasal/sinus mucosa, dentition, musculature, salivary glands and temporomandibular joint. The region's unique neurophysiologic characteristics, which are different to the spinal nociceptive system, can present diagnostic challenges to clinicians specializing in this area [12]. The

region's sensory supply is from both spinal (C2 and 3) and cranial nerves (III, V, VII [nervous intermedius], IX, X), the latter providing both sensory and autonomic supply. The main sensory supply to the orofacial region is from the trigeminal nerve and its large representation in the sensory cortex means that pain in the orofacial region can have significant functional and social impacts: for example, interruption with daily social function such as eating, drinking, speaking, kissing, applying make-up, shaving and sleeping [13], and in some cases reportedly compromising the patient's self identity [14].

Over recent times there have been significant developments in understanding pain mechanism, the implications of which are spread over many different fields including: neuroimaging, psychometrics, neuro-immunity, neurophysiology and pain genetics [15]. This, in part, may explain the difficulty in reaching and or maintaining a consensus for the taxonomy of pain itself. Woolf eloquently highlights this by posing the question 'what is this thing we call pain?' [16]. Woolf classifies pain into three groups: nociceptive (detects noxious stimuli), inflammatory

Box 1. Hierarchical International Headache Classification (IHCD) 11.**Hierarchical International Headache Classification (IHCD) II**

Part I: the primary headaches

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

• Part II: 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 nonvascular 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

• Part III: 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

Chapter 13. International Headache Society Classification of cranial neuralgias and central causes of facial pain (ICD-10 G44.847, G.44.848 or G44.8)

- 13.1. Trigeminal neuralgia
- 13.2. Glossopharyngeal neuralgia
- 13.3. Nervus intermedius neuralgia [G51.80]
- 13.4. Superior laryngeal neuralgia [G52.20]
- 13.5. Nasociliary neuralgia [G52.80]
- 13.6. Supraorbital neuralgia [G52.80]
- 13.7. Other terminal branch neuralgias [G52.80]
- 13.8. Occipital neuralgia [G52.80]
- 13.9. Neck–tongue syndrome
- 13.10. External compression headache
- 13.11. Cold-stimulus headache
- 13.12. Constant pain caused by compression, irritation or distortion of cranial nerves or upper cervical roots by structural lesions [G53.8] + [code to specify etiology]
- 13.13. Optic neuritis [H46]
- 13.14. Ocular diabetic neuropathy [E10-E14]
- 13.15. Head or facial pain attributed to herpes zoster
- 13.16. Tolosa–Hunt syndrome
- 13.17. Ophthalmoplegic ‘migraine’
- 13.18. Central causes of facial pain

Chapter 14. Other headache, cranial neuralgia, central or primary facial pain (ICD-10 R51)

- 14.1. Headache not elsewhere classified
- 14.2. Headache unspecified

Data from [26].

(adaptive and protective) and pathological (neuropathic with a lesion present or dysfunctional with no identifiable cause). He emphasizes that the processes driving these pain types are different and that treatments should be specific and preferably directed at the distinct mechanisms responsible [16]. The pathological group is the group that is the focus of developing pain-related diagnoses, because it is viewed as a true dysfunction of the somatosensory

system, as opposed to pain being a symptom of different disorders, such as sinusitis or symptomatic apical periodontitis. Within the orofacial region there has been significant progress in advancing the understanding and the assessment of musculoskeletal pain and neuropathic pain related to the orofacial region [17–21].

Taxonomy is the science of identifying and naming species, thereby allowing them to be arranged into a classification [101–102]. Pain naturally involves three different levels of classification – our current understanding of pain mechanisms, possible primary causes (etiology and genetics) and related clinical signs and symptoms. In addition, the response to medical or surgical interventions may also provide potential for further classification of pain conditions [22]. Diagnosis, on the other hand, determines the nature of a disease case and involves a process whereby, after a thorough assessment of a patient’s disorder, the findings are used to determine the precise type of problem that exists. Pain character, duration, pattern, intensity and associated comorbidities often help establish diagnoses. In addition, to assist in diagnosis, an established classification of disorders helps to group different symptoms with common etiologies.

Taken as a whole, the measurement and classification of chronic pain is important for the following reasons [23]:

- To identify the perceived intensity and characteristics (quality, time course) of the pain so that differences between presenting conditions can be identified and further investigated;
- To provide diagnostic clues in the history or examination of the patient, thereby enabling a provisional diagnosis or differential diagnoses;
- To identify the most efficacious management strategy for the presenting pain;
- To allow the assessment of the outcome of management strategies being employed.

Classification systems clearly need to be valid, reliable, comprehensive, generalizable and flexible, and they need to be tested using consensus views of experts as well as the available literature [101]. There is an urgent need for a robust classification system for OFP, recently highlighted by the confusion arising amongst practitioners understanding of chronic OFP

conditions and the preliminary report of a working group in this area [24].

This review aims to: outline the main classification systems in current use; present a short summary of the published critique of these systems and current developments in classification; and briefly outline the processes involved in reaching a differential diagnoses for OFP.

Classification systems for OFP

There have been several attempts to classify OFP conditions by pain associations. The main categories most have used have either been topographical (odontogenic versus nonodontogenic) and/or chronological (chronic vs acute). Several associations with interest in pain have published classifications: The International Association for the Study of Pain [25] (IASP); The Scheme for coding chronic pain diagnoses based on axes (see below) [25]; International Headache Society (IHS) [26] (International Classification of Headache Disorders [ICHD-II]; Box 1); The American Academy of OFP [27] (Box 2) and the Research Diagnostic Criteria for Temporomandibular Disorders [28] (RDC/TMD [103]). As one would expect there has been published critique and suggestions for modification for most of these systems [29–36].

The Scheme for coding chronic pain diagnoses based on axes is detailed below [25];

- Axis definition
- Regions (e.g., head, face or mouth)
- Systems (e.g., nervous system)
- Temporal characteristics of pain (e.g., continuous, recurring irregularly and paroxysmal)
- Patient's statement of intensity: time since onset of pain (e.g., mild, medium or severe; 1 month or less, or more than 6 months)
- Etiology (e.g., genetic, infective or psychological)
- IASP Regional Classification of Localized Syndromes of the Head and Neck [25]
- Neuralgias of the head and face
- Craniofacial pain of musculoskeletal origin
- Lesions of the ear, nose and oral cavity
- Primary headache syndromes, vascular disorders and cerebrospinal fluid syndromes
- Pain of psychological origin in the head, face, and neck
- Suboccipital and cervical musculoskeletal disorders
- Visceral pain in the neck

The IASP classification categorized OFP into 'relatively localized syndromes of the head and neck' and is composed of five axes. The IASP system does not, however, fully address the psychosocial aspects of pain, which are required in order to provide a more

Box 2. American Academy of Orofacial Pain classification†.

Vascular and Nonvascular Intracranial Disorders
 Primary Headache Disorders
 Episodic and continuous neuropathic pain
 Intraoral Pain Disorders
 Temporomandibular Disorders
 Cervicogenic Mechanisms of Orofacial Pain and Headaches
 Extracranial and Systemic Causes of Head and Facial Pain
 Axis II: Bio behavioral Considerations

†Taxonomy is based on a mixture of regional, temporal and Axes.
 Data taken from [27].

comprehensive view of OFP. Turk and Rudy have suggested a modification of pain classification, which may be applicable to the IASP (the Multiaxial Assessment of Pain [MAP]) as it integrates physical, psychosocial and behavioral data [34]. Their further work with the MAP based a classification of chronic pain patients on psychosocial and behavioral data alone [35]. Their hypothesis was that certain patterns exist in chronic pain patients regardless of the medical diagnosis: dysfunctional patients, interpersonally distressed patients and adaptive copers. The study indicated that despite differences in medical/dental diagnoses, patients had similar psychosocial and behavioral responses. Lynch and Elgeneidy [36] suggested further adaptations of the IASP classification in order to: account for neuropathic injury and be consistent with DSM-IV terminology by using the term 'not otherwise specified' instead of 'atypical facial pain' (AFP) for a condition that does not conform to criteria in another category [37].

The term AFP may now, however, fall into disuse as the new IHS classification (IHS 12.8) uses the term, 'facial pain not

Box 3. Woda *et al.* (2005) classification for chronic orofacial pain.

Neurovascular and tension

- Tension headache
- Migraine
- Cluster headache

Neuralgia

- Primary
 - Trigeminal neuralgia
 - (Classical and nonclassical)
- Secondary neuropathy
 - Post herpetic neuralgia
 - Diabetes mellitus
 - Multiple sclerosis
 - HIV
 - Post traumatic neuropathy
 - Lingual inferior alveolar nerve injuries

Persistent idiopathic

- Stomatodynia/burning mouth syndrome
- Persistent idiopathic facial pain (e.g., atypical facial pain)
- Arthromyalgia

Reproduced with permission from [44].

Box 4. Systemic diseases associated with headache and orofacial pain.

- Paget's disease
- Metastatic disease
- Hyperthyroidism
- Multiple myeloma
- Hyperparathyroidism
- Vitamin B deficiencies
- Systemic lupus erythematosus
- Vincristine and other chemotherapy for cancer
- Folic acid- and iron-deficiency anemias

fulfilling other criteria' for AFP (Table 10-7 or persistent idiopathic facial pain (PIFP) [38]. The IHS have recently updated their original classification of headache disorders by providing a second edition of ICHD-II; (Box 1) [26,39]. For most instances, primary headache disorders, defined in IHCD, do not have a more specified location besides within the head or laterality, and some authors contend that the orofacial region is excluded [40]. A paper comparing the IASP (Box 2) and IHS (Box 3) diagnostic categories shows the significant differences between the two systems, but both focus mainly on the biomedical as opposed to the biopsychosocial [41].

The major stakeholder in OFP classification, the AAOP (Box 2) [27] used the IHS classification as the basis for their classification of OFP disorders with a separate axis for defining psychosocial factors and diagnosing mental disorders.

Two papers have recently focused on both the ICHD-II and AAOP definitions of traumatic nerve injury, presenting new terminology for posttraumatic trigeminal nerve injuries [13,29]. The two new terms, 'painful posttraumatic trigeminal nerve injury' and 'nonpainful posttraumatic trigeminal nerve injury' have operationalized and tested criteria [42], and provide a more comprehensive recognition of the increasing cohort of patients experiencing chronic trigeminal pain as a result of surgical injuries.

An OFP condition specific operationalized set of diagnostic criteria for TMDs were created in 1992 (RDC/TMD) [28]. The triggers for their creation included both the problems within

the literature with respect to the classification of subjects for trials of management strategies, and the growing appreciation of TMDs as a biopsychosocial entity. The RDC/TMD takes a dual-axis approach to assessing and classifying TMDs with axis 1 providing a physical (biomedical) classification and axis 2 providing a psychosocial classification of the patient's condition. The RDC/TMD is currently undergoing revision and a revised, more clinically applicable, version is in press (Diagnostic Criteria for Temporomandibular Disorders [DC/TMD]) [103]. Axis 1 of the current version groups TMDs into three categories: group 1: muscle disorders; group 2: disc disorders; group 3: arthritides. Further details on the subgroup diagnoses possible within each of these groups can be found on the RDC's website [103]. A reduced version of the RDC, the CEP-TMD (Clinical Examination Protocol for TMD) [43], was produced independent of the RDC/TMD consortium and therefore blinded to the developments within the consortium who was producing a shorter more clinically applicable version of the RDC/TMD, the DC/TMD. The CEP-TMD and the DC/TMD both share the same aim, that is, to allow clinicians to make TMD diagnoses in everyday practice that correlate to those produced by the longer RDC [43]. Given the international group involved, and the preliminary results on the DC/TMD's reliability and validity, the CEP-TMD system is likely to fall into disuse once the DC/TMD is published.

Recent developments

Several studies have recently critiqued the established classification systems, highlighting potential weaknesses in their application to the diverse OFP population [40]. One of the recurring themes amongst these critiques tends to be the omission of diagnostic entities from the various systems leading to patients OFP becoming unclassifiable in between 7 to 44% of cases without the use of multiple diagnostic classification systems [32,33,40]. One of the more recent studies examining this applied ICHD-II diagnostic criteria to a series of 328 consecutive patients with OFP [32]. Just over half (56%) of the patients were successfully diagnosed with the ICHD-II. The remaining 44% of patients in the sample then had the AAOP and RDC/TMD criteria applied, thereby diagnosing a further 37% of the total sample, resulting

Box 5. Red flags: orofacial pain symptoms that may indicate serious or malignant disease.

- Spontaneously occurring focal neuropathy with pain and or altered sensation confirmed by physical examination may indicate tumor invasion of nerve
- Pain at the angle of the mandible, brought on by exertion, relieved by rest may indicate cardiac ischemia
- Patient over 50 years of age and/or with known history of carcinoma
- Jaw claudication, visual symptoms, palpably tender superficial temporal arteries – suggestive of temporal arteritis
- Systemic symptoms of fever, weight loss, anorexia, malaise, myalgia, chills, sweating - unlikely to be associated with OFP
- New-onset headache in adult life of increasing severity with: nausea and vomiting without evidence of migraine or systemic illness; nocturnal occurrence; precipitation or exacerbation through changes in posture; confusion, seizures or weakness; any abnormal neurologic sign – suggests a mass effect in cranial cavity (through intracranial tumor)
- Earache, trismus, altered sensation in the mandibular branch distribution – suggests infratemporal fossa or acoustic nerve impingement, for example, by tumor
- Trigeminal neuralgia in a person less than 50 years of age may be suggestive of multiple sclerosis

in 93% of the sample possessing a diagnosis after the application of three diagnostic classifications (ICHD-II, AAOP, RDC/TMD). Benoliel *et al.*'s conclusion at the end of their study was that masticatory muscle pain (MMP) is only clearly defined by AAOP and the RDC/TMD and neurovascular OFP (NVOP) is not defined by any of the four major OFP classification systems (IASP, ICHD-II, AAOP, RDC/TMD).

Other recent studies have suggested novel strategies for OFP classifications including: temporal pain patterns, cluster analysis and ontological principles.

Benoliel *et al.* tested the temporal definitions of chronic daily headache (CDH) in a wholly OFP population [40]. They aimed to examine the definition of 'chronic OFP' (COFP), which is a term in abundance in the literature, but that probably most accurately refers to a group of conditions as opposed to one defined entity. Using the temporal definitions of CDH only 50% of the sample were defined as 'chronic', with remainder split between 'daily' and 'episodic' OFP. They found no distinctive defining characteristics of 'chronic OFP' in either the history or examination process employed and therefore concluded that COFP was a temporal definition and not a diagnostic entity.

Given the wide-ranging presentations and putative sources for OFP conditions, it is perhaps unsurprising that a recent cluster analysis [44] has regrouped the various conditions comprising OFP (Box 3). The slight disadvantage to this system is that despite being based on a sound study design and statistical procedure, it relies on sometimes putative, etiology in order to group conditions. This has resulted in an idiopathic group, which includes somewhat discarded terminology for burning mouth syndrome and TMDs. The existence of an idiopathic group may lead to a lack of a label and explanation for patients within that group and, in turn, lead to problems in their daily lives. Furthermore, the output of such an analysis is only valid if all notable factors of each of the disorders has been included – and at sufficient numbers – so that the 'true' relationship of these factors is observed.

Given that ontology underpins the majority of classification systems, it is unusual that it has remained unreported in the development of the majority of current OFP classification systems. Nixdorf *et al.* have proposed a new taxonomy model based on ontological principles for a specific OFP condition known by a variety of pseudonyms, including atypical odontalgia and phantom tooth syndrome [42]. Diagnostic criteria for persistent dento-alveolar pain disorder (PDAP) were formulated using ontological principles in to provide an exemplar for other OFP conditions. The criteria produced have the advantage of being concisely and operationally defined with the potential for subtypes of PDAP to be developed. As the paper acknowledges, these criteria have yet to be tested.

At the time of writing there is a working group reassessing Chapter 13 (painful cranial neuropathies and other facial pains) of the IHS classification who aim to achieve a consensus on its revision in 2012. Any future over-arching classification of OFP will need to take into account the developments in etiology, and specifically the genetic and pathophysiological basis of OFP conditions.

Box 6. Orofacial disorders that may be confused with toothache.

- Trigeminal neuralgia
- Trigeminal neuropathy (due to trauma or tumor invasion of nerves)
- Atypical facial pain and atypical odontalgia
- Cluster headache
- Acute and chronic maxillary sinusitis
- Temporomandibular disorders

Differential diagnosis

The following sections are aimed at giving the reader an overview of the processes involved in formulating a differential diagnosis for patients presenting with OFP. They are not meant to be exhaustive and interested readers are referred to several excellent texts on the subject [45–51].

A recent paper on the differential diagnosis of OFP highlights some important strategies to help distinguish between OFP conditions and come to a diagnosis or differential diagnoses [12]. History-taking remains of paramount importance in facilitating the diagnostic process. Blau suggested 15 questions to facilitate the history taking process in OFP, which cover the following aspects of the presenting pain [52]: onset, frequency, duration, provoking factors, site of initiation of pain, radiation and referral of pain, whether the pain deep or superficial, aggravating or exacerbating factors, relieving factors, characteristics of the pain, severity, other associated features (e.g., lacrimation or other autonomic signs and symptoms), previous management strategies attempted and response, and patient's perceived cause(s) of pain.

Several recent recommendations for the assessment of OFP patients cover the necessity for a full history (medical, dental,

Box 7. Hematology and imaging investigations used in classification of orofacial pain.

Hematology investigations

The most frequently employed hematological investigations for orofacial pain include:

- Full blood count – predominately looking for anemias
- Hematinics: ferritin, B12, folate – looking for deficiency states causing secondary burning mouth syndrome
- Zinc levels – necessary for Fe absorption
- Hypothyroidism – causing headache
- HBA1c – examining likelihood of diabetes related neuropathy
- Antibody screen to exclude connective tissue disorders
- Extractable nuclear antigens antinuclear antibody test
- Erythrocyte sedimentation rate or C-reactive protein if inflammatory condition suspected

Imaging investigations [60]

- Plain dental radiography (dental pantomogram DPT) to identify caries, infection, bone loss and more
- MRI to exclude space occupying lesions, demyelination and vascular compromise of the trigeminal nerve

social history and the history of the presenting complaint) pain profiling, quantitative sensory assessment, and functional psychological assessment, ideally undertaken by a multidisciplinary team [53–59].

The examination of a patient with OFP should include the following as a bare minimum, and more detailed examination of some tissues or systems may be added as the diagnostic process refines:

- Inspection of the head and neck, skin and topographic anatomy, and swelling or other orofacial asymmetry;
- Palpation of the temporomandibular joint and masticatory muscles, tests for strength and provocation, with assessment and measurement of the range of mandibular movement;
- Palpation of soft tissue (including lymph nodes);
- Palpation of cervical muscles and assessment of cervical range of motion;
- Cranial nerve examination;
- General inspection of the ears, nose and oropharyngeal areas;
- Examination and palpation of intraoral soft tissue;
- Examination of the teeth and periodontium (including occlusion).

Systemic conditions that can be associated with OFP are detailed in Box 4. Neoplastic processes and other non-neoplastic pathology with serious adverse outcomes can occasionally mimic or masquerade as OFP and Box 5 summarizes the salient details of the more commonly presenting pathologies. Conversely some OFP conditions may masquerade, or be misdiagnosed or misinterpreted as toothache and these are outlined in Box 6.

Time taken in eliciting a thorough pain history may often clarify the diagnosis, as in any other pain condition. Multidisciplinary OFP assessment, ideally, also includes psychometrics, pain profiling, quantitative sensory testing, hematology and imaging (Box 7) where indicated. A psychometric assessment must also consider the role of stress in the persistence of pain. Often clinicians focus on a biomedical approach and assume a ‘diagnose–treat–cure’ approach. Where psychosocial

factors are known to influence persistence of pain, this approach will be far from effective. There is good epidemiological evidence to indicate that stress plays an important role in the persistence of OFP [11].

An outline of the presenting features of acute OFP related to inflammatory conditions is given in SUPPLEMENTARY TABLE 1 (table available at: www.expert-reviews.com/doi/suppl/10.1586/ern.12.40). This is followed in SUPPLEMENTARY TABLE 2 (table available at: www.expert-reviews.com/doi/suppl/10.1586/ern.12.40) by an outline of the presenting features of chronic OFP conditions.

Expert commentary & five-year view

Chronic OFP continues to present a diagnostic challenge and it is possible therefore to make a misdiagnosis. Improved education for clinicians, in recognizing neuropathic pain, is required, which may prevent unnecessary dental surgery and other interventions often experienced by these patients. The biological, psychological and social impact of OFP should always be examined and patients should receive a diagnosis, albeit provisional in some cases, as soon as possible. It is important that the diagnosis is appropriately communicated to the patient with particular emphasis on a simple explanation of how and why their pain symptoms have developed, despite the absence of an underlying organic pathology as may be the case in some chronic OFP conditions. Achieving patients understanding of the fact that organic pathology has been thoroughly investigated and excluded as a possibility is also crucial to prevent ‘doctor shopping’ in the search for an organic cause. An overarching, comprehensive, OFP classification system that is under development under the auspices of the IASP and several other international stakeholders will help further advance research and management of this complex group of conditions.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Key issues

- The goal of an accepted classification system of chronic orofacial pain (OFP) conditions would facilitate research and management of patients with these conditions.
- Despite four leading authorities with interest in chronic OFP having published guidelines, a consensus on the classification of OFP remains elusive.
- This lack of a universal classification system may be due to rapid and expanding reported development in understanding pain and its management.
- There is an urgent need for a robust classification system for OFP.

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