Pain Reviews
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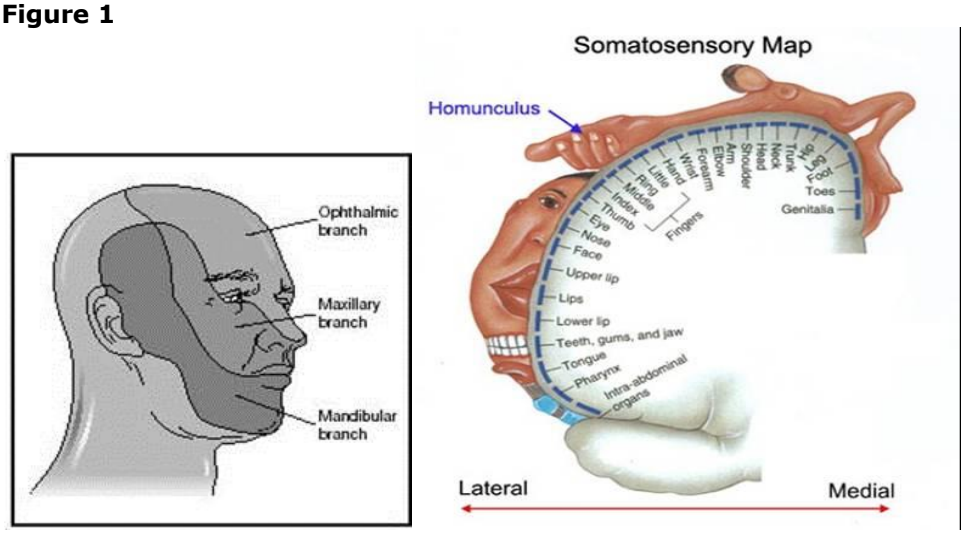
1. **Dental pain**

Introduction Orofacial pain is pain within the trigeminal system. The trigeminal nerve supplies general sensory supply to face, scalp, and mouth. A vast proportion of the sensory cortex represents the trigeminal input (over 40%).
Figure 1



The trigeminal sensory region is very complex, incorporating the cranium, ears, eyes, sinuses, nose, pharynx, infratemporal fossa, jaw joint, teeth, jaws, salivary glands, oral mucosa, and skin. As many medical students are rarely exposed to ear, nose, and throat (ENT), otolaryngology, and dentistry, this region remains an enigma to most, with their singular experience of trigeminal pain being based on trigeminal neuralgia in relation to neurosurgical procedures.

Aetiology of acute orofacial pain
Orofacial pain can be associated with pathological conditions or disorders related to somatic and neurological structures.1 There are a wide range of causes of acute orofacial pain conditions, the most common being dental pain (toothache) due to dental caries (tooth decay) the most common human infective disease worldwide. Interestingly periodontal disease (gum disease) the second most common infection is painless similar to other chronic macrobacteria infections for example Leprosy.

Prevalence
The prevalence of dental pain and its characteristics were recorded using standard measures of pain. Dental caries, dental trauma and dental plaque were assessed using WHO criteria. Multiple logistic and ordinal polytomous regression were used to assess which factors were associated with the dental pain outcomes. Results: 1,052 individuals participated in the study. The prevalence of reported toothache in schoolchildren in the last six months was 33.6% (31.1-36.8, 95% CI). The fully adjusted regression models showed a significant relationship between lower social class, later birth order, failure at school and

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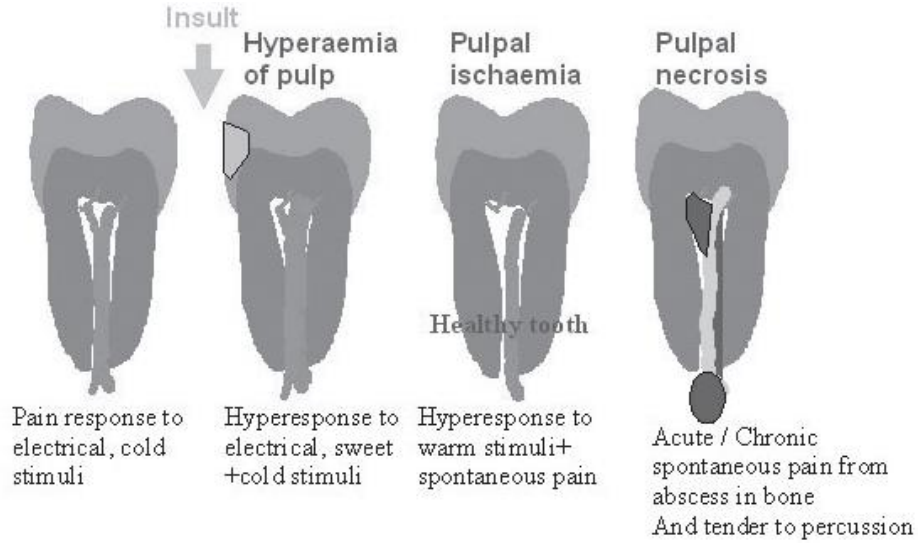
attendance at the dentist only when in trouble with both the prevalence and severity of dental pain. The major predictor of the prevalence and severity of pain was pattern of dental attendance ($p<0.001$)

Goes, P.S.A. and Watt, R.G. and Hardy, R. and Sheiham, A. (2007) The prevalence and severity of dental pain in 14-15 year old Brazilian schoolchildren. **Community Dental Health**, 24 . pp. 217-224.

Odontogenic pain

Odontogenic pain refers to pain initiating from the teeth or their supporting structures, the mucosa, gingivae, maxilla, mandible or periodontal membrane.

Figure 2 The stages and characteristics of dental pulpal pain.

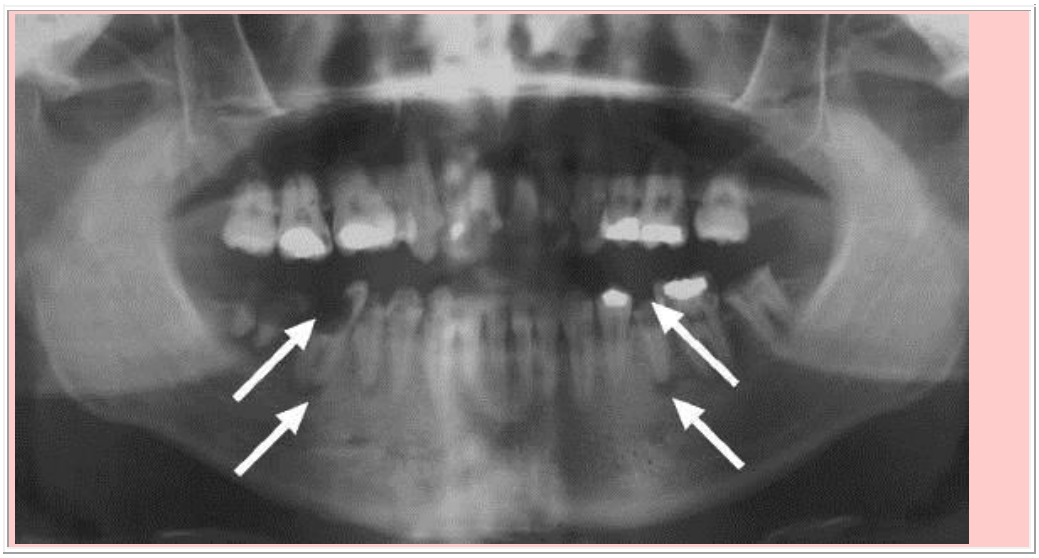


Dental pulpitis ('toothache')

In health teeth are only perceive pain often due to dentine sensitivity on cold, sweet or physical stimulus. Dental pulpitis may be due to infection from dental caries close to the pulp, inflammation caused by chemical or thermal insult subsequent to dental treatment, and may be reversible or non-reversible. Intermittent sharp, shooting pains are also symptomatic of trigeminal neuralgia, so care must be taken not to mistakenly label toothache as neuralgia.

Fig. 2

An orthopantomograph (OPG) showing extensive dental caries (radiolucent areas) affecting the crowns of several teeth, and abscess formation (radiolucent areas) around the periapical regions of the roots. Arrows show caries and abscess formation on two mandibular teeth.



Initially the tooth after insult due to caries (causing bacterial products infiltrating the pulp via the dentine tubules) or iatrogenic insult (dental restoration close to the dental pulp or trauma) will cause pulpal inflammation and results in extreme sensitivity to cold and sweet flavours with short sharp 'neuralgic' pain. Protection of teh pulp to bacterial infection and chemical irritation by dietary and salivary content must be undertaken promptly to minimise persistence of acute pulpitis thus evolving into chronic irreversible pulpitis

Fractured tooth If the crown of a tooth is fractured by trauma and the broken fragment is available, it should be stored in a physiological medium until a dentist can assess the patient. Coverage of exposed dentine on the fractured crown with a temporary restoration is desirable to protect the underlying pulp tissue.

Placement of temporary restorations Although it is unlikely that many general medical practitioners will have temporary filling materials available in their surgeries, dentine that has been exposed by caries, a lost filling or tooth fracture can be covered relatively easily with glass ionomer cement (GIC) or zinc oxide eugenol (ZOE) materials. Most GIC materials are dispensed in capsules but a hand-mixed material is available, consisting of a powder, liquid and conditioner. The surface of the cavity is painted with the conditioner, then rinsed and dried, before placement of the filling. Zinc oxide eugenol materials consist of a powder and liquid (oil of cloves) that are mixed to a putty-like consistency before placement in the tooth.

If the insult persists the pulpitis will become irreversible with increased pulpal vascularity and resultant pressure, inducing ischaemia causing sensitivity to heat with prolonged pain. Once necrosis of the dental pulp has occurred, the infection spreads through the apex of the tooth into the surrounding bone and periodontal membrane, initiating periodontal inflammation and eventually a dental abscess causing spontaneous long lasting pain on biting on the tooth. Typically the pain

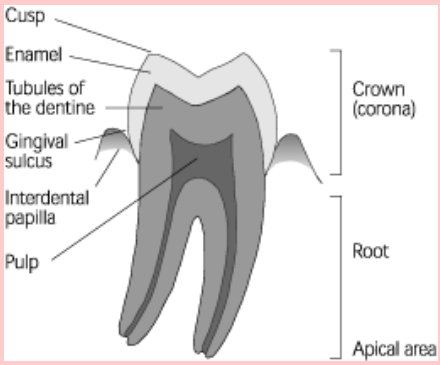
associated with an abscess is described as spontaneous aching or throbbing and if associated with swelling in the jaw, trismus or lymphadenopathy it may be indicative of an acute spreading infection. Thus different stages of infection have different clinical presentations (Figure 2).
Management for dental pulpitis is excavation of the tooth decay with restoration (filling) If the puplitis becomes irreversible then pupectomy (pulp removal) and root canal treatment will be required.

Which tests can assist in diagnosis? There are several simple tests that may assist in diagnosis of dental pain.

Pulp sensitivity test Dry ice, or an ordinary ice stick (made in a plastic or glass tube), is placed on the cervical third (neck region) of the tooth crown. A response to the stimulus indicates that the pulpal tissue is capable of transmitting nerve impulses. No response may indicate pulp necrosis.

Fig. 3

Diagram of a lower molar tooth



Percussion test Using an instrument handle, the tooth is tapped in the longitudinal axis. A painful response suggests possible periapical inflammation.

Probing Placing a fine, blunt probe gently into the gingival sulcus surrounding the tooth enables the health of the gingival tissues to be assessed. Bleeding and/or sulcus depths greater than 3-4 mm indicate gum disease.

Mobility test Holding a tooth firmly on the buccal (cheek) and lingual sides between the fingers enables mobility to be assessed. All teeth have a small amount of mobility (<0.5 mm), but visible movement suggests loss of bone support around the root of the tooth.

Palpation Careful palpation around the area of concern may reveal tenderness and the type and extent of swelling.

Radiographic examination If it is possible to obtain a screening radiograph, such as an orthopantomograph (OPG), this may assist in the diagnosis and

localisation of the cause of the pain. The radiograph should show clearly the apical and periapical structures of teeth and associated tissues. The relationship of the maxillary molars and premolars to the floor of the maxillary sinus can be examined, and radiographs may reveal recurrent caries or periapical radiolucencies associated with an established infection (Fig. 2).

Exposed cementum or dentine There is tooth sensitivity from cold fluids and/or air, a reflection of a healthy pulp. With gingival recession, recent scaling, or tooth wear due to a high acid diet or gastric reflux, there may be generalised dentine sensitivity. However, with caries, fractured fillings and cracked cusps, the pain tends to be localised to the affected tooth. The tooth root surface comprises of a thin layer of cementum overlaying dentine, is exposed from excessive and/or incorrect tooth brushing. Dentine underlying the enamel crown is constituted of tiny tubules which are fluid filled and connect directly to the nerve ending in the dental pulp. The current hypotheses for dental pain include the osmolality theory whereby the dentine fluids elicit an action potential within the A delta and C fibres in the pulp caused by mechanical stimulation.

Management For root sensitivity the use of a desensitising toothpaste and a reduction in acid in the diet will help resolve the symptoms. The use of a fluoride mouth-rinse may also help. In the case of caries, a lost filling or fractured tooth, coverage of the exposed dentine with a temporary restoration will usually relieve the symptoms.**Pericoronitis** Pain commonly arises from the supporting gingivae and mucosa when infection arises from an erupting tooth (teething or pericoronitis). This is the most common cause for the removal of third molar teeth (wisdom teeth). The pain may be constant or intermittent, but is often evoked when biting down with opposing maxillary teeth. This elicits pain in the inflamed mucosa and gingivae surrounding the partially erupted tooth. If recurrent, then pericoronitis is the main NICE indication for removal of wisdom teeth, however if the infection is acute and spreading then antibiotics must be prescribed. Chronic periodontitis with gradual bone loss, rarely causes pain and patients may be unaware of the disorder until tooth mobility is evident. There is quite often bleeding from the gums and sometimes an unpleasant taste. This is usually a generalised condition, however, deep pocketing with extreme bone loss can occur around isolated teeth. Food impaction in these areas can cause localised gingival pain. Poor contact between adjacent teeth and the presence of an occluding cusp forcing food into this gap can also cause a build-up of food debris and result in gingival inflammation.

Acute pericoronitis involves bacterial infection around an unerupted or partially erupted tooth and usually affects the lower third molar (wisdom tooth). The condition is often aggravated by the upper molar impacting on the swollen flap of soft tissue covering the unerupted tooth. There may be trismus.

Apical pain can be caused by infection spreading through the apical foramen of the tooth into the apical periodontal region causing inflammation (apical periodontitis) and ultimately a **dental abscess** if left untreated. Iatrogenic apical pain may result after dental treatment including **premature** contact if a restoration is left high in occlusion. This is characterized by an initial sharp pain which becomes duller after a period. The pain is due to a recent tooth restoration that is 'high' compared with the normal occlusion when biting

together and **Postendodontic surgery pain** This is severe aching pain following endodontic treatment such as root canal therapy or apicectomy. While the majority of patients improve over time (weeks), a few will develop a chronic neuropathic pain state (see section on persistent post surgical trigeminal pain)**.** There is considerable variation in the pain reported by patients, but it commonly starts as a sharp stabbing pain that becomes progressively dull and throbbing. At first the pain may be caused by a stimulus, but it then becomes spontaneous and remains for a considerable time after removal of the stimulus. The pain may radiate and be referred to other areas of the mouth. This type of pain tends to cause the patient to have difficulty sleeping and may be exacerbated by lying down. Heat may make the pain worse whereas cold may alleviate it. The pain may be intermittent with no regular pattern and may have occurred over months or years. If there is periapical infection present, patients may no longer complain of pain in response to a thermal stimulus, but rather of sensitivity on biting.

Management. Advise the use of an analgesic to relieve symptoms (Ibuprofen, or paracetamol if ibuprofen is contraindicated or unsuitable, is recommended first-line and Paracetamol and ibuprofen can be taken together if pain relief with either alone is insufficient. For adults, if taking paracetamol and ibuprofen together does not provide enough pain relief, consider adding codeine phosphate or switching to an alternative nonsteroidal anti-inflammatory drug (NSAID). For women who are pregnant or breastfeeding, paracetamol is preferred. A short course of codeine may be added if paracetamol alone is insufficient. Antibiotics are generally not indicated for otherwise healthy individuals when there no signs of spreading infection. Only prescribe an antibiotic: For people who are systemically unwell or if there are signs of severe infection (e.g. fever, lymphadenopathy, cellulitis, diffuse swelling).

Dental management for dental abscess is either root canal with removal of the necrotic pulp or tooth extraction, Periapical inflammation can lead to a cellulitis of the face characterised by a rapid spread of bacteria and their breakdown products into the surrounding tissues causing extensive oedema and pain. If systemic signs of infection are present, for example, fever and malaise, as well as swelling and possibly trismus (limitation of mouth opening), this is a surgical emergency. Antibiotic treatment alone is not suitable or recommended. If pus is present, it needs to be drained, the cause eliminated, and host defences augmented with antibiotics. The microbial spectrum is mainly gram positive including anaerobes. Appropriate antibiotics would include a penicillin or a 'first generation' cephalosporin, combined with metronidazole in more severe cases.**Alveolar osteitis** After extraction, the most common complication is a 'dry socket' which is a condition whereby the clot formation within the socket fails at 3–5 days; healing fails, resulting in an empty socket which traps food and debris. The resultant pain is caused by necrotic foodstuff aggravating bony nerve endings, causing intense pain following extractions. Interestingly this condition is devoid of the usual acute inflamammtory markers (absence of lymphadenopathy, local inflammation and swelling). dull throbbing pain develops two to four days after a mandibular tooth extraction. It rarely occurs in the maxilla. Smoking is a major predisposing factor as it reduces the blood supply. The tissue around the socket is very tender and white necrotic bone is exposed

in the socket. Halitosis is very common. The incidence of this condition is between 1-9% associated with patientsundergoing mandibular surgical tooth removal. Patients should be routinely warned of a possible incidence of 5%. *Dry socket*

Management Irrigation of the socket using saline or chlorhexidine and then an obtundant dressing usually soaked in bacteriorstatic solution (alvogyl paste, BIPP paste, cotton wool or gausze soaked in iodofrom). Immediate pain relief is usually attained and rarely patient re present for additional treatment. Patients should be shown how to irrigate the area and told to do this regularly. Analgesics are indicated, but pain may persist for several days. Although opinion is divided as to whether or not dry socket is an infective condition, we do not recommend the use of antibiotics in its management If the patient returns recurrently with ongoing pain then osteomyelitis should be excluded and localised bony sequestrate should be excluded.

Maxillary sinusitis 'mimicking' toothache Recurrent maxillary sinusitis may cause widespread pain in the maxillary teeth. The pain tends to be increased on lying down or bending over. There is often a feeling of `fullness' on the affected side. The pain is usually unilateral, dull, throbbing and continuous. Quite often the patient feels unwell generally and feverish. It can mimic the maxillary sinusitis-like symptoms in temporomandibular disease (TMD) (see below) or neuropathic pain. These dental conditions rarely present as chronic pain unless misdiagnosed. Inflammation of the maxillary sinuses is best treated using local and systemic decongestants and if persistent then antibiotics may be prescribed. Pain originating from the sinus arises mainly from pressure. Decongestants can help sinus drainage. Antibiotics probably have only a minor role in mild cases. Referral to an otorhinolaryngologist for endoscopic sinus surgery may be indicated in chronic cases.[3]

Non-odontogenic facial pain Non-odontogenic facial pain can be caused by inflammation due to tumour, infection, or trauma. Topographical classification is often applied to this complex region. Regions often presenting as orofacial pain complaints include the sinuses, salivary gland, ears, eyes, throat, mandibular, and maxillary bone pathology.

Acute necrotising ulcerative gingivitis is a rapidly progressive infection of the gingival tissues that causes ulceration of the interdental gingival papillae. It can lead to extensive destruction. Usually young to middle-aged people with reduced resistance to infection are affected (diabetes, HIV infection, chemotherapy). Males are more likely to be affected than females, with stress, smoking and poor oral hygiene being predisposing factors. Halitosis, spontaneous gingival bleeding, and a `punched-out' appearance of the interdental papillae are all important signs. The patients quite often complain of severe gingival tenderness with pain on eating and tooth brushing. The pain is dull, deep-seated and constant. The gums can bleed spontaneously and there is also an unpleasant taste in the mouth and obvious halitosis.

Management As there is an acute infection with mainly anaerobic bacteria, treatment follows surgical principles and includes superficial debridement, use of chlorhexidine mouthwashes and a course of metronidazole tablets. Treating the contributing factors should prevent a recurrence.

References

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2. Persistent pain after dental surgery

Introduction Chronic orofacial pain syndromes represent a diagnostic challenge for any practitioner. Patients are frequently misdiagnosed or attribute their pain to a prior event such as a dental procedure, ENT problem or facial trauma. Psychiatric symptoms of depression and anxiety are prevalent in this population and compound the diagnostic conundrum. Treatment is less effective than in other pain syndromes, thus often requires a multidisciplinary approach to address the many facets of this pain syndrome1.

Aetiology of orofacial pain
Facial pain can be associated with pathological conditions or disorders related to somatic and neurological structures2. There are a wide range of causes of chronic orofacial pain and these have been divided into three broad categories by Hapak *et al*.3—musculoligamentous, dentoalveolar, and neurological and vascular. The commonest cause of chronic orofacial pain is temporomandibular disorders, principally myofascial in nature4.

As mechanisms underlying these pains begin to be identified, more accurate classifications which are mechanism-based may come to be used. A major change in mechanism has been that burning mouth syndrome probably has a neuropathic cause using the newly defined definitions rather than being a pain owing to psychological causes.

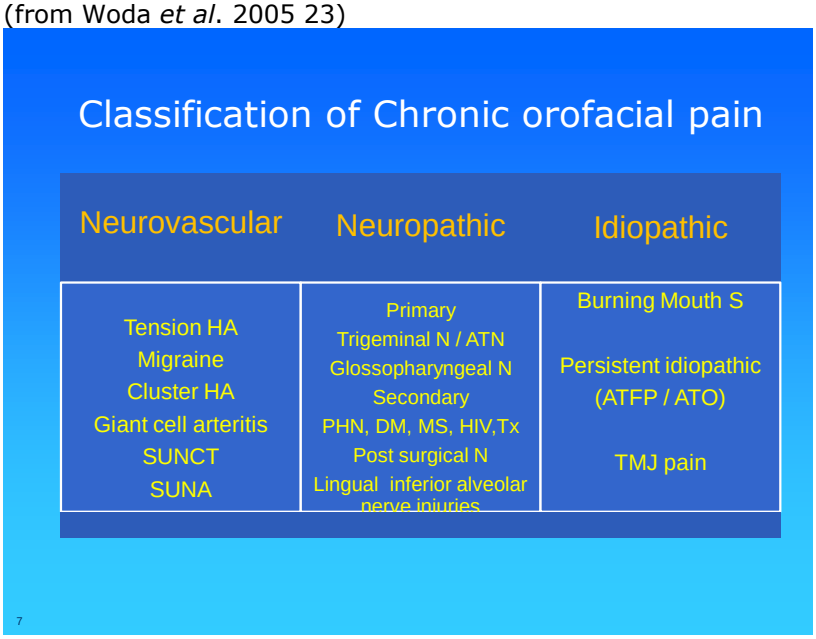
Incidence Chronic orofacial pain is comparable with other pain conditions in the body, and accounts for between 20 and 25% of chronic pain conditions4. A 6-month prevalence of facial pain has been reported by between 1%4 and 3%5 of the population. In the study by Locker and Grushka6, some pain or discomfort in the jaws, oral mucosa, or face had been experienced by less than 10% in the past 4 weeks. In 19807, Bonica estimated that 5–7 million Americans suffer from chronic pain in the face and mouth, and between 25 and 45% are affected at some time of life4. Most population-based studies have shown that women report more facial pain than men4,8,9, with rates approximately twice as high among women compared to men10. In clinic populations the rates for women are even higher1. On the other hand, other studies have found no sex difference in the prevalences of orofacial pain6,11. Several studies have also shown variability in the prevalence across age groups. The age distribution of the facial pain population differs from that of the most usual pain conditions. In contrast to chest and back pain, for example, facial pain has been suggested to be less prevalent among older persons than younger ones6,9. Conversely, in 19934 Lipton *et al*. found the prevalence of facial pain to remain relatively constant across the age groups, while in a study in 20015 by Riley and Gilbert, no difference in prevalence was observed between the age groups of 45–64 years and older.

Diagnosis The International Headache Society (IHS) has published diagnostic criteria for primary and secondary headaches as well as facial pain12,13. Criteria have also been published by the International Association for the Study of Pain (IASP) and by the American Academy of Orofacial Pain (AAOP), and the Research Diagnostic Criteria for Temporomandibular Disorders (RDCTMD)14,15.

The impact of trigeminal pain must not be underestimated. Consequences include interruption with daily social function such as eating, drinking, speaking, kissing, applying makeup, shaving, and sleeping16,17. Burning mouth syndrome has been reported to cause significant psychological impact in 70% of patients6. In temporomandibular joint (TMJ) pain, 29% patients report high disability resulting in unemployment18,19. A recent validated tool has been developed for the assessment of disability related to oral function (Oral Health Impact [OHIP 14])20,21.

Classification of orofacial pain The aim of this chapter is to address the causes of chronic orofacial pain (lasting >3 months). However, the most common causes of acute dental pain are due to trauma or infection of the dental pulp which contains the nerves and vessels supplying the tooth. Dental disease of the hard tissues (caries of enamel, dentine, and cementum), and soft tissues and supporting bone (gingivitis/periodontitis) are recognized as the most common diseases to afflict the general population. These conditions are largely diagnosed and treated by dental practitioners by history, dental clinical examination, and radiographs. By far the most common forms of oral pain are them acute form of pain that tend to last for short periods of time. These include toothache (dental pulpitis), gum pain (pericoronitis in 80% of the population), periapical periodontitis (owing to apical infection or postendodontic therapy of high occlusal contact). Dentine sensitivity affects 40% of the adult population; dry socket is postsurgical intense pain that affects 10% of patients after extraction of their teeth. Other orofacial acute pain conditions include trauma or infection of the orofacial tissues22.

Figure 1 Chart illustrating a suggested classification for chronic orofacial pain (from Woda *et al*. 2005 23)



Chronic orofacial pain The various suggested classifications of chronic orofacial pain do conflict with each other. Several classifications of chronic orofacial pain have been presented and the authors will use the fourth classification for this chapter as it presents a pragmatic and clinically useful alternative23

Group 1: neurovascular (predominantly VI pain)
Migrainel, Cluster headaches, Tension-type headaches, Medication overuse headaches and Chronic daily headache are covered elsewhere in review series

Short-lasting unilateral neuralgiaform conjunctival irritation and tearing (SUNCT) This is possibly a variation of the cluster tic syndrome. It is characterized by brief (15–120 seconds) bursts of pain in the eyes, temple, or face. The pain is usually unilateral and is described as burning, stabbing, or electric. It occurs frequently in a 24-hour period (>100 episodes). Neck movements can trigger the pain28–30. SUNCT syndrome is refractory to medical therapy31 but there is increasing evidence for treatment with lamotrigine32.

Temporal arteritis Temporal arteritis is characterized by daily headaches of moderate to severe intensity, scalp sensitivity, fatigue, and various non-specific complaints with a general sense of illness. Ninety-five per cent of patients are over 60 years old. The pain is usually unilateral, although some cases of bilateral or occipital pain do occur. Pain may also be felt in the tongue and is a continuous ache with superimposed sharp, shooting head pains. The pain is similar to and may be confused with that of CH, but CH tends to occur in younger patients. The two may also be distinguished on physical exam, when dilated and tortuous scalp arteries are noted. The erythrocyte sedimentation rate (ESR) is markedly elevated in temporal arteritis33. Definitive diagnosis is made by artery biopsy from the region of the pain, although negative biopsy may be caused by the spotty nature of the disease and does rule out the diagnosis. High dose steroid therapy usually precipitates a dramatic decrease in head pain. Failure to respond to steroid therapy with a negative biopsy should call the diagnosis into question. If the diagnosis seems likely based on history and physical examination, steroids should be started immediately to avoid vision loss, the most common complication of the disorder, occurring in 30% of untreated cases. The biopsy remains positive for 7–10 days from starting steroid therapy. Steroids may be tapered to an every other day maintenance schedule when the pain resolves and ESR normalizes. The disease is usually active for 1–2 years, during which time steroids should be continued to prevent vision loss.

Group 2: Neuralgia This group includes primary neuropathies -trigeminal neuralgia (typical or atypical), glossopharyngeal neuralgia, and secondary neuropathies including postherpetic neuralgia and post-traumatic V neuralgia, and other peripheral neuropathies affecting the trigeminal system (nutritional neuropathy, diabetes mellitus, human immunodeficiency virus (HIV), chemotherapy, and multiple sclerosis (MS) are not covered in this review but can present as orofacial pain.

Primary neuropathies
Trigeminal neuralgia (typical or atypical) covered elsewhere in review series

Glossopharyngeal neuralgia Glossopharyngeal neuralgia is characterized by pain attacks similar to those in trigeminal neuralgia, but is located unilaterally in the distribution of the glossopharyngeal nerve. Pain is most common in the posterior pharynx, soft palate, base of tongue, ear, mastoid or side of the head. Swallowing, yawning, coughing or phonation may trigger the pain. Management is similar to that for trigeminal neuralgia45.

Secondary neuropathies
Many conditions can cause peripheral sensory neuropathies that may present with pain, these include;

- Diabetes
- Post herpetic neuralgia
- Human Immunodeficiency Virus
- Chemotherapy
- Muliple Slcerosis
- Post surgical traumatic neuropathy
- Parkinson's
- Malignancy
- Drugs - Growth hormone injections
- Nutritional neuropathy

The most common causes of trigeminal neuropathy would include post traumatic neuropathy, PHN and idiopathic persistent post surgical pain.

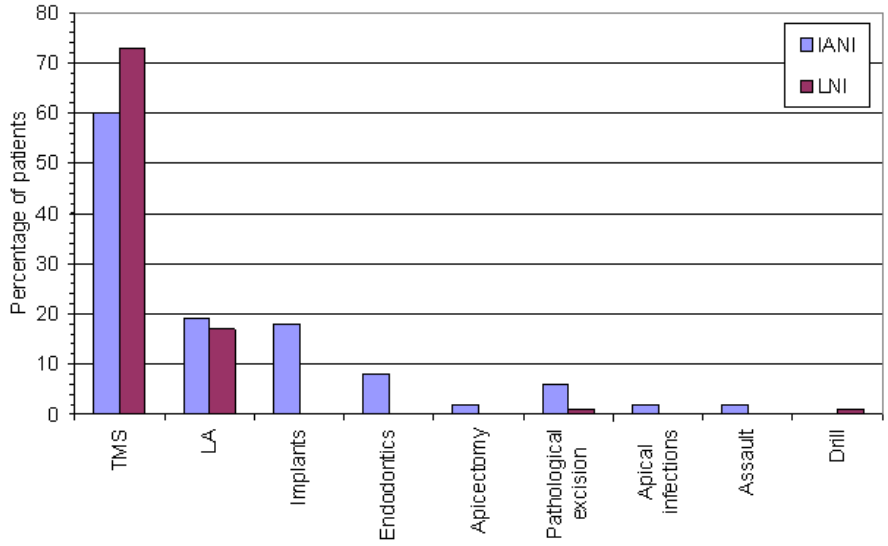
Postherpetic neuralgia In patients over 50 years of age there is a 60% incidence of developing postherpetic pain42. Herpetic skin eruption is caused by the reactivation of latent varicella zoster virus from the sensory nerve ganglia. The reactivated virus is carried via the axons distally to the skin where it produces a painful rash with crusting vesicles in a dermatomal distribution. The trigeminal nerve is the second most commonly affected after nerves in the thoracic region. Ramsay Hunt syndrome occurs when herpes zoster infection of the geniculate ganglion causes earache and facial palsy. Pain that persists 2 or more months after the acute eruption is known as postherpetic neuralgia. The pain is neuropathic in nature, severe, and it is associated with allodynia and hyperalgesia, most commonly affecting the VI distribution of the trigeminal nerve43. High doses of antivirals, steroids, and amitriptyline are often used for the acute eruption in otherwise healthy individuals. Antivirals, NSAIDs, and opiates are often used in immunocompromised patients. More recently, there is evidence that topical 5% lignocaine patches (Versatis) worn alternatively every 12 hours are very effective44.

Post-traumatic trigeminal neuropathy The most problematic outcome of dental surgical procedures with major medico-legal implications is injury to the trigeminal nerve (Caissie, 2005)[45]. The prevalence of temporarily impaired lingual and inferior alveolar nerve function is thought to range between 0.15–0.54% whereas permanent injury caused by injection of local analgesics is much less frequent at 0.0001–0.01% (Hillerup, 2007)[46]. Traumatic injuries to the lingual and inferior alveolar nerves may induce a pain syndrome owing to the development of a neuroma. The most commonly injured trigeminal nerve branches, the inferior alveolar and lingual nerves are different entities, whereby the lingual nerve sits loosely in soft tissue compared with the IAN that resides in a bony canal. Injury to the third division of the trigeminal may occur due to a

variety of different treatment modalities, such as major maxillofacial and minor oral surgery (Blackburn, 1990; Kraut & Chahal, 2002; Wismeijer et al., 1997; Hillerup and Jensen, 2006; Grotz et al., 1998)[4, 10, 13, 17, 33]. Peripheral sensory nerve injuries are more likely to be persistent when the injury is severe, if the patient is older, if the time elapsed between the cause of the injury and the review of the patient is of longer duration, and when the injury is more proximal to the cell body.

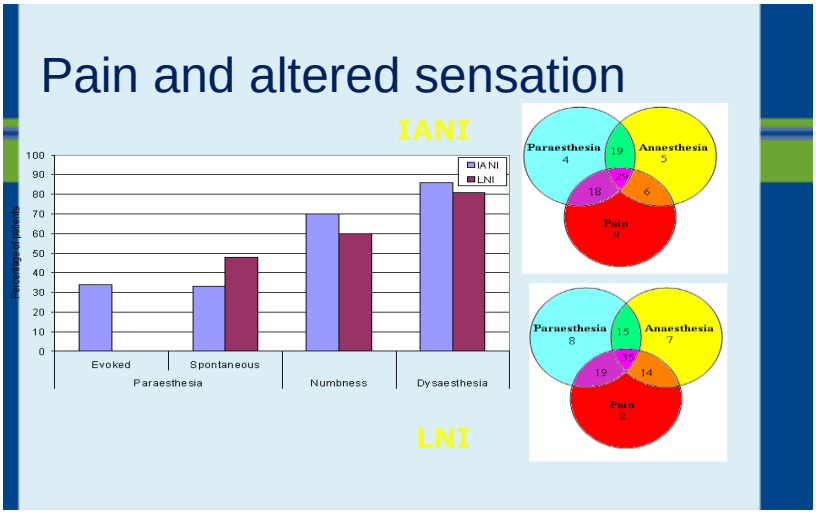
Subsequent to iatrogenic trigeminal nerve injury, the patient often complains about a reduced quality of life, psychological discomfort, social disabilities and handicap (Lam et al. 2003)[18]. Patients often find it hard to cope with such negative outcomes of dental surgery since the patient usually expects significant improvements not only regarding jaw function, but also in relation to dental, facial, and even overall body image after oral rehabilitation (Kiyak et al, 1990)[16]. Altered sensation and pain in the orofacial region may interfere with speaking, eating, kissing, shaving, applying make up, tooth brushing and drinking; in fact just about every social interaction we take for granted (Ziccardi and Zuniga, 2007)[36].

In a recent prospective assessment of 252 patients with iatrogenic trigeminal nerve injuries (Renton & Yilmaz 2010 in press) most were caused by third molar surgery but implants and local anaesthesia were significant contributors (Figure 2)

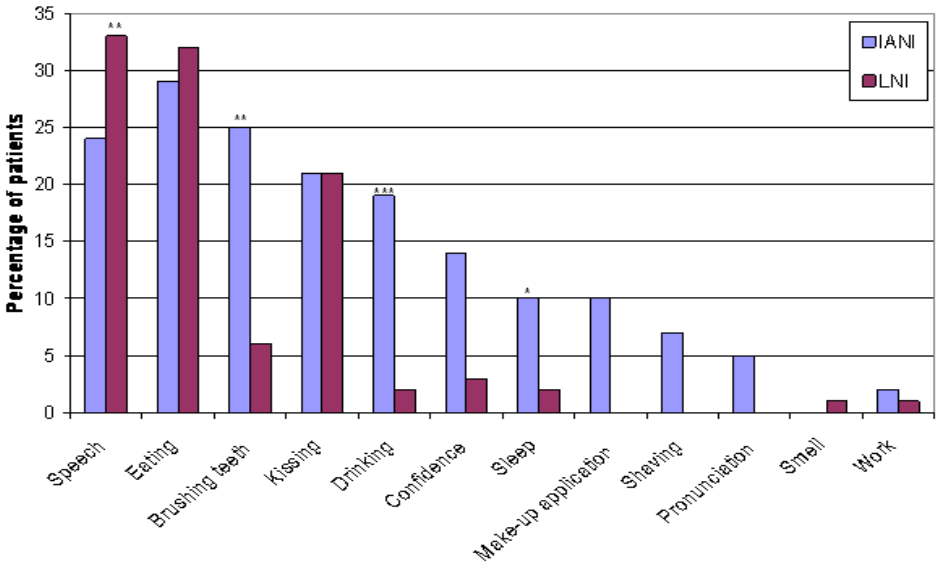


The diagnosis of posttraumatic neuralgia/ neuropathy is based upon a history of surgery or trauma temporally correlated with the development of the characteristic neuropathica pain. Age, poor wound closure, infections, foreign material in the wound, haematoma, skull fracture, diabetes mellitus or peripheral neuropathy elsewhere in the body predispose to neuroma development. The pains commonly persist 2– months after the injury and can be permanent **46,47**. Medical therapy is similar to that used in neuropathic pain

conditions depending on the patients' symptoms. In a recent survey of 252 iatrogenic trigeminal nerve injuries related to dental treatment, 70% of patients presented with pain (Figure 3). This highlights the problems related to postsurgical neuropathy aggravated by the fact that many patients may not have been warned at all about nerve injury or told that they would risk numbness**48**.



Any patients experienced significant daily disability predominantly caused by elicited mechanical or cold allodynia resulting in pain on eating, drinking, kissing sleeping and other essential functions (Figure 4).



Current management of these nerve injuries is inadequate. The focus remains on surgical correction or laser therapy with little or no attention to medical or

counselling intervention and the patients' psychological, functional or pain related complaints. The fault partly rests with how we assess these patients. Assessment tends to show little regard for the functional or pain evaluation with the main focus on basic mechanosensory evaluation, which is not necessarily reflective of the patients' difficulties. Oral Surgery specialists assessing these injuries should therefore follow guidelines from the World Health Organisation, which suggest that nerve injury outcomes should be assessed in terms of impairment, activity limitations, and participation restrictions (MacDermid, 2005)[19]. Guidelines set out by the International Association for the Study of Pain and European Federation of Neurological Societies should also be followed (Cruccu et al., 2004)[9]. Without exception these recommendations are holistic when compared with reports evaluating the management of trigeminal nerve injuries.

Traumatic injuries to peripheral nerves pose complex challenges and treatment of nerve injuries must consider all aspects of the inherent disability. Pain control is of paramount importance and rehabilitation needs to be instituted as first-line treatment. Early intervention is important for optimal physiologic and functional recovery (Robinson & Shannon, 2002)[24]. Reparative surgery may be indicated when the patient complains of persistent problems related to the nerve injury, however there remains a significant deficiency in evidence base to support this practice. The patients presenting complaints may include functional problems due to the reduced sensation, intolerable changed sensation or pain the latter being predominantly intransigent to surgery (Rutner et al., 2005; Hillerup and Stoltze, 2007; Robinson et al., 2000)[14, 26, 28] and less often expressed psychological problems relating the iatrogenesis of the injury and chronic pain. Generally for lesions of the peripheral sensory nerves in man, the gold standard is to repair the nerve as soon as possible after injury (Birch et al., 1991)[3]. However, the relatively few series of trigeminal nerve repair on human subjects relate mainly to repairs undertaken at more than 6 months after injury.

It is evident from the literature review that there needs to be a cultural change in the choice of intervention, timing and outcome criteria that should be evaluated for interventions for trigeminal nerve injuries. To date, there have been a very limited number of prospective randomised studies to evaluate the effect of treatment delay, the surgical, medical or counselling outcomes for trigeminal nerve injuries in humans.

Persistent post surgical pain without demonstrable neuropathy
This is defined as present at 1 year post-op or longer, unexplained by local factors and best described as neuropathic in nature

Nonodontogenic dentolalveolar pain is often difficult to diagnose (5, 8) because it is poorly understood (22). Even defining and categorizing such persistent pain is challenging. Nonodontogenic pain is not an uncommon outcome after root canal therapy and may represent half of all cases of persistent tooth pain. A recent systematic review of prospective studies that reported the frequency of nonodontogenic pain in patients who had undergone endodontic procedures. Nonodontogenic pain was defined as dentoalveolar pain present for 6 months or more after endodontic treatment without evidence of dental pathology. Endodontic procedures reviewed were nonsurgical root canal treatment, retreatment, and surgical root canal treatment. 770 articles retrieved and reviewed, 10 met inclusion criteria with a total of 3,343 teeth were enrolled

within the included studies and 1,125 had follow-up information regarding pain status. We identified nonodontogenic pain in 3.4% (95% confidence interval, 1.4%-5.5%) frequency of occurrence.
(Nixdorf N et al Frequency of Nonodontogenic Pain after Endodontic Therapy: A Systematic Review and Meta-AnalysisJ Endod 2010;36:1494–1498)

The prevalence of persistent pain post surgically in the trigeminal system may be low compared with other surgical sites (Kehlet *et al*, 2006 Lancet ~~Table 1~~)

	Estimated incidence of chronic pain	Estimated chronic severe (disabling) pain (>5 out of score of 10)	US surgical volumes (1000s)†
Amputation[2]	30–50%	5–10%	159 (lower limb only)
Breast surgery (lumpectomy and mastectomy)[3]	20–30%	5–10%	479
Thoracotomy[4-7]	30–40%	10%	Unknown
Inguinal hernia repair[8-10]	10%	2–4%	609
Coronary artery bypass surgery[11-13]	30–50%	5–10%	598
Caesarean section[14]	10%	4%	220

*Gall bladder surgery not included, since preoperative diagnosis of pain specifically from gall bladder is difficult and persistent postoperative pain could therefore be related to other intra-abdominal disorders. †National Center For Health Statistics, Ambulatory and Inpatients Procedures, USA, 1996.

Table 1*: Estimated incidence of chronic postoperative pain and disability after selected surgical procedures

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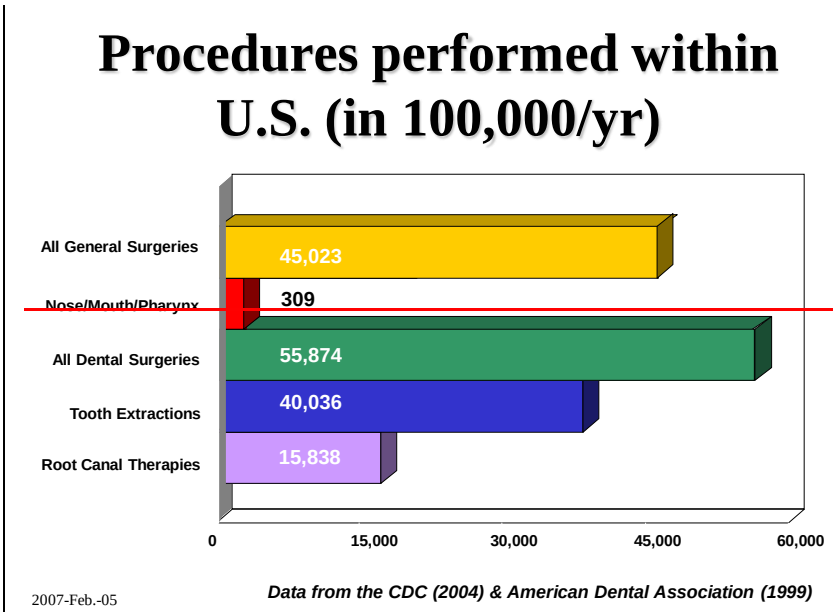
However when one considers the significant frequency of dental surgical procedure undertaken (Figure 5) then significant numbers of individuals may be affected by both post traumatic neuropathy and persistent post surgical pain.



Risk factors for developing persistent post surgical pain include; Genetics (catecholamine-O-methyltransferase), preceding pain (intensity and chronicity), psychosocial factors (*i.e.* fear, memories, work, SES, physical levels of activity, somtatization), Age (older = ↑ risk), Gender (female = ↑ risk) and the surgical procedure and technique (tension due to retraction).

All these persistent post surgical pain conditions may be attributable to post traumatic neuropathy but it is difficult to be conclusive without a demonstrable neuropathic area in relation to the previous surgery. The significant decreased ncidence in this condtion in the trigeminal region may reflect the lack of central sensitization due to most procedures being undertaken under local anaesthetic (Woolf et al ???).

3. Idiopathic chronic orofacial pain (Group 3) This group includes preauricular pain related to the TMJ, burning mouth syndrome (BMS), and persistent idiopathic facial pain.

Temporomandibular joint pain is covered elsewhere in review series

~~**Burning mouth syndrome** Burning mouth syndrome (BMS), glossodynia or stomatodynia is defined as a chronic, idiopathic oral mucosal pain or discomfort in which no clinical lesions or systemic disease are identified76. Clinical evidence (clinicalevidence.bmj.com) maintains a regularly-updated article on management of BMS and there is also a Cochrane Systematic Review on this topic77.~~
~~**Definition** According to the International Association for the Study of Pain (IASP),~~
~~**Epidemiology** There is a predilection for the condition for women in the menopausal to postmenopausal age group. The prevalence varies from 0.5 to 15% in this targeted group.~~
~~**Clinical presentation** Afflicted patients report a constant burning sensation. The preferred site for the pain is the anterior portion of the tongue, although the anterior portion of the hard palate and the labial mucosa of the lip region are other common sites of pain. There are increasing numbers of studies to suggest that this condition is not caused by psychological factors alone but may be a form of neuropathic pain which then results in psychological effects. Studies have noted that not only do patients have a sensation of burring in their mouths but there are often changes in taste and salivation.~~
~~**Diagnosis** Eliav *et al*.78, using patients with BMS and controls with a symptom of burning mouth which could be attributed to other causes, showed that BMS showed dysfunction of their chorda tympani and therefore this could account for these abnormal taste sensations as well as tingling sensations.~~
~~**Management** Of the RCTs it would appear that clonazepam used topically may be helpful as well as cognitive behaviour therapy76. In the last 2 years a well designed RCT reporting under CONSORT methodology showed that *Hypericum perforatum* (a form of St John's wort) did not result in a positive response79. There is increasing evidence that BMS is caused by a peripheral neuropathy80, the cause of which remains unknown.~~

Persistent idiopathic facial pain The term atypical facial pain was first introduced by Frazier and Russell in 1924. It has since been renamed persistent idiopathic facial pain (PIFP). PIFP refers to pain along the territory of the trigeminal nerve that does not fit the classic presentation of other cranial neuralgias12. The duration of pain is usually long, lasting most of the day (if not continuous). Pain is unilateral and without autonomic signs or symptoms. It is described as a severe ache, crushing or burning sensation. Upon examination and workup no abnormality is noted.
Definition According to the International Association for the Study of Pain (IASP), chronic facial pain refers to symptoms which have been present for at least 6 months. 'Atypical' pain is a diagnosis of exclusion after other conditions have been considered and eliminated (i.e. it is idiopathic), and is characterized by chronic, constant pain in the absence of any apparent cause in the face or brain. Many information sources suggest that all 'unexplained' facial pains are termed atypical facial pain but this is not the case. Categories of idiopathic facial pain conditions include neuropathic pain due to sensory nerve damage, chronic

regional pain syndrome (CRPS) from sympathetic nerve damage and atypical facial pain81. Atypical odontalgia, or phantom tooth pain, is a variation of atypical facial pain where intense discomfort is centred around a tooth or group of teeth with no obvious dental or oral disease.

Epidemiology Atypical facial pain is more common in women than in men; most patients attending a facial pain clinic are women aged between 30 and 50 years. Although any area of the face can be involved, the most commonly affected area is the maxillary region. In the majority of patients there is no disease or other cause found. In a few patients the symptoms represent serious disease. In a small number of patients the pain may be one consequence of significant psychological or psychiatric disease82.

Clinical presentation Atypical facial pain has a very variable presentation. Often it is characterized by continuous, daily pain of variable intensity. Typically, the pain is deep and poorly localized, is described as dull and aching, and does not waken the patient from sleep. At onset the pain may be confined to a limited area on one side of the face, while later it may spread to involve a larger area. Atypical facial pain is a diagnosis of exclusion for pain not meeting the diagnostic criteria of other facial pain syndromes. Mongini et al50 refers to the term atypical facial pain as outdated and includes its description in psychogenic facial pain. Indeed, the description of the pain may be inconsistent with bilateral pain that often changes locations over weeks to months. The pain is not triggered and is not electrical in quality. Intensity fluctuates but the patient is rarely pain-free. Pain is typically located in the face and seldom spreads to the cranium in contradistinction to tension headache9,83. It is more common in women aged 30–50 years old. Between 60 and 70% of these patients have significant psychiatric findings, usually depression, somatization or adjustment disorders, therefore psychiatric evaluation is indicated. Treatment is with antidepressants, beginning with low dose amitriptyline at bedtime and increasing the dose until pain and sleep are improved84. Accurate figures are difficult to obtain because of the lack of agreement on classification criteria12. Estimated incidence is 1 case per 100 000 population, although this number may be underestimated82. PIFP affects both sexes approximately equally, but more women than men seek medical care82. The disorder mainly affects adults and is rare in children82. PIFP is essentially a diagnosis of exclusion. Daily or near-daily headaches are a widespread problem in clinical practice82. According to population-based data from the United States, Europe, and Asia, chronic daily headache affects a large number (approximately 4–5% of the population) of patients12. Importantly, PIFP must be distinguished from various other chronic daily headache syndromes, including hemicrania continua84, TMJ syndrome, sidelocked migraine, chronic cluster headache, SUNCT, TN, and many others12. A careful history and physical examination, including a dental consultation, laboratory studies, and imaging studies, may be necessary to rule out occult pathology. Underlying pathology such as malignancy, vasculitis, infection, and central or peripheral demyelination may manifest early as neuralgia, and, not until focal neurological deficits, imaging abnormalities, or laboratory abnormalities are discovered, does the diagnosis become evident. Rare cases of referred pain must also be considered. Atypical odontalgia (AO) is characterized by continuous, dull, aching, or burning pain of moderate intensity in apparently normal teeth or endodontically treated teeth and occasionally in extraction sites. AO is not usually affected by testing the tooth and surrounding tissues with cold, heat or electrical stimuli. The pain remains constant despite repeated dental treatment, even extractions in the region, often rendering patients with persistent pain but

whole quadrants stripped of dentition. Moreover, the toothache characteristics frequently remain unchanged for months or years, contributing to the differentiation of AO from pulpal dental pain. Occasionally, the pain may spread to adjacent teeth, especially after extraction of the painful tooth. These patients are defined as having pain in a tooth or tooth region in which no clinical or radiological findings can be detected. Several studies have been conducted to define this group more clearly. AO patients have more comorbid pain conditions, higher scores for depression and somatization, significant limitation in jaw function, and lower scores on quality of life measures when compared with controls85. When compared to patients with TMD, AO patients were more likely to describe their pain as aching, find rest relieving but cold and heat aggravating. Over 80% relate the onset of their pain to dental treatment. Both groups show worsening of symptoms on chewing, but more patients with TMD have other chronic pain86. These patients have somatosensory abnormalities, suggesting that generalized sensitization of the nociceptive mechanism may be occurring87. The relationship with previous surgical intervention infers that this condition may, in some cases, be partial postsurgical neuropathy of the superior alveolar nerves.

The lack of RCTs makes evidenced-based care in AO difficult88. One of the major problems with this condition is convincing the patient, and informing their dentist, that there are no dental causes for their pain, so avoiding unnecessary irreversible invasive dental treatment. AO patients are often diagnosed late87 and therefore need a multidisciplinary approach. In her recent review, Baad-Hansen88 presents a sensible progressive approach to managing AO, beginning with topical lignocaine or capscasian, then TCAs. Ulltimately, the drugs used in neuropathic pain are often gabapaentin and pregablin, and finally tramadol or oxycodone.

Medical care Medical treatment of PIFP is usually less satisfactory than medical treatment for other facial pain syndromes88,89. Medications used to treat PIFP include antidepressants, anticonvulsants, substance P depletion agents, topical anaesthetics, *N*-methyl-D-aspartate (NMDA) antagonists, and opiate medications. Of these classes of medications, anticonvulsants and antidepressants appear to be the most effective. The neuropathic component of pain responds well to anticonvulsants and antidepressants. Pharmacotherapeutic knowledge is paramount in the treatment of this refractory pain syndrome. A multimechanistic approach, using modulation of both ascending and descending pain pathways, is frequently necessary. The goal of therapy is to manage the pain effectively with the fewest adverse medication effects. Anticonvulsants and antidepressants are the mainstays of medication treatment. Alternative therapies such as acupuncture and neuromuscular re-education have been tried and should be considered as part of a comprehensive treatment plan. Psychiatric treatment is important in the overall management of a patient with chronic pain. Holistic approach as many has other chronic pain. Available data on alternative treatments are limited.

Surgical care Details of neurosurgical interventions are beyond the scope of this review. Analgesic surgery should be considered at a centre well versed in these procedures88,90.

Consultations Psychometric testing may be of benefit in the evaluation and treatment of patients with headache and facial pain. Many tests have been applied, but probably the most widely used is the Minnesota multiple personality inventory (MMPI). While especially useful in the evaluation of chronic headache and facial pain patients, a thorough discussion of psychometric testing is beyond the scope of this discussion and is mentioned here only for completeness. Consultation with a dentist may be of benefit. All treatments should be provided in cooperation with the patient's primary care physician.

Future novel treatments in development include several phase three trials assessing specific pain receptor and channel blocking agents for neuropathic pain. Several studies have reported upregulation of peripheral TRPV receptor and sodium channel receptor expression in the human trigeminal system91,92. Recent recognition of genetic factors contributing to nociception, pain behaviour, and suffering may also lay the foundations for future strategies for improved treatment of patients with chronic pain. Of the 3.16 billion base pairs comprising the 23 pairs of chromosomes, the Human Genome Project has sequenced about 2.8 billion base pairs to date. Only 3% of the human genome actually codes for proteins, and about 15% of the non-coding DNA in humans is conserved (has functional importance). It is estimated that there are approximately 25 000 genes in the human genome and it is as yet unknown how many genes are involved in pain mediation, perception, and behavioural response. To date, gene coding for TRPV1 channel is associated with altered pain responses93, and sodium ion channels coded by an SCN9A mutation was found in a Pakistani family with an inability to experience pain94. Catechol-O-methyltransferase and the cytochrome P450 variant allele *CYP3A5* have been linked with pain behaviour attributed to dopamine metabolism which defined how patients coped with their pain experience95. The ability to evaluate the phenotype and genotype of the patient with pain may enable to clinician to provide specific and tailor-made treatment in the future.

Conclusion Chronic orofacial pain continues to present a diagnostic challenge for many practitioners. Patients are frequently misdiagnosed and they suffer from psychiatric symptoms of depression and anxiety. Treatment is less effective than in other pain syndromes and a multidisciplinary approach treatment is desirable.

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