ABSTRACT
Chronic pain in the orofacial region is a common complaint faced by clinicians. It is important for the dentists to have a thorough knowledge of various causes of jaw pain. Most common type reported is toothache. Since toothache is so common, it is important to determine if pain is from odontogenic or nonodontogenic origin. The need for careful diagnosis before undertaking any invasive treatment is the key to prevent misdiagnosis and mismanagement in patients with chronic orofacial pain. Emphasis in this article is on the differential diagnosis of jaw pain originating from muscular, neuropathic, cardiac, sinus and psychogenic origin.

Keywords: Toothache, Orofacial pain, Psychogenic, Nonodontogenic.

INTRODUCTION
Pain may be simply described as patient’s cry for help but the most widely accepted definition of pain is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” proposed by the International Association for the Study of Pain (IASP). Pain can have either acute or chronic nature. Acute pain serves a biologic purpose as either a protective mechanism or a warning signal. It has a sudden onset, is self-limiting, temporary and usually does not present a diagnostic problem. Chronic pain (more than three months duration) on the other hand, does not serve any biologic purpose, is not self-limiting and appears to be permanent. Riley et al found that 17.4% of the elderly population in a community reported some form of orofacial pain. The chronic pains were generally of four types—jaw pain, facial pain, burning and oral pain. The most common type of orofacial pain was toothache, which was reported by 12.2% of the population. Since toothache is so common, it is essential for the clinician to determine if the pain is odontogenic in origin or is referred from other orofacial structures. Unfortunately, there are many documented cases of misdiagnosis and mismanagement, wherein extensive treatments like multiple root canal therapies, extractions, etc., have been performed in patients with chronic orofacial pain especially those with neuropathic and myofacial pain.

This article reviews the clinical characteristics of jaw pain originating from odontogenic and nonodontogenic causes. First, pathways of pain and pain categories are described followed by the clinical characteristics of common odontogenic and non-odontogenic toothaches.

NEURAL PATHWAYS OF PAIN
Fields has described that the subjective experience of pain arises by four distinct processes: transduction, transmission, modulation and perception.

Transduction is the process by which noxious stimuli lead to electrical activity in the appropriate sensory nerve endings. Transmission refers to the neural events that carry the nociceptive input into the central nervous system for proper processing. There are three basic components of the transmission system: primary afferent neuron, second-order neuron and interaction of the neurons between thalamus, cortex and limbic system.

The peripheral sensory nerve called the primary afferent neuron carries the nociceptive input from the sensory organ into the spinal cord. The second order neuron carries the input to the higher centers. Actually this portion of the transmission process can involve a number of neurons that interact, as the input is sent to the thalamus. The third component represents interactions of neurons between thalamus, cortex and the limbic system as the nociceptive reaches these higher centers.

Modulation refers to the ability of the central nervous system to control the pain transmission neurons. Several areas of the cortex and brain stem have been identified that can either enhance or reduce nociceptive input arriving by the transmitting neurons.

Perception is the final process involved in the subjective experience of pain. If nociceptive input reaches the cortex, perception occurs, which immediately initiates a complex interaction of neurons between the higher centers of the brain. It is at this point that suffering and pain begins.
Sensory Receptors

At the distal terminalis of afferent (sensory) nerves are the specialized sensory receptors that respond to physical or chemical stimuli. Once these receptors are adequately stimulated, an impulse is generated in the primary afferent neuron that is carried centrally into the CNS. Sensory receptors are specific for certain types of stimuli. They can be classified into three main groups, exteroceptors (provide information from the skin and mucosa), proprioceptors (provide information from the musculoskeletal structures) and interoceptors (transmit the impulses from the viscera of the body).

The first-order neurons are classified based on their varying thickness, larger A-fibers and smaller C-fibers. Pain is conducted by A-delta (fast) and C-fibers (slow).

Second-order neurons are of three types, which include low threshold mechanosensitive neurons, nociceptive specific neurons and wide dynamic range neurons.

Neurotransmitters

These play an important role in modulation of pain by excitatory and inhibitory effects.

- Excitatory neurotransmitters include acetylcholine, norepinephrine, glutamate, aspartate.
- Inhibitory neurotransmitters include gamma-aminobutyric acid, glycine, dopamine.

THE TRIGEMINAL SYSTEM

In the periphery, the trigeminal nerve provides sensory input from the anterior part of the head including the extraoral structures. The sensory fibres are divided into A-beta mechanoreceptors and three types of nociceptors: A-delta fibers, C-polynodal nociceptors (C-PMNs) and silent or sleeping nociceptors.

The A-beta fibers that respond to light touch mechanostimulation, are large diameter, fast conducting and myelinated. The A-delta fibers are small in diameter, myelinated fast conducting fibres that respond to sharp, painful mechanical stimuli. Their output is in high frequency range that is perceived as painful. The C-PMNs are slow conducting, unmyelinated and respond to noxious mechanical, thermal and chemical stimuli. The silent nociceptors, recently discovered, are mechanically insensitive. They become active when tissue is injured and add to the nociceptive input to the CNS.

The afferent impulses from all these fibers travel from the periphery through the trigeminal ganglion and trigeminal root, enter the pons and descend in the trigeminal nucleus.

The trigeminal nucleus is subdivided into three parts, the uppermost subnucleus oratus, the middle subnucleus interpolaris and the inferior subnucleus caudalis. Most of the pain fibers synapse in the subnucleus caudalis.

PAIN CATEGORIZATION

Somatic Pain: It occurs in response to the stimulation of normal neural receptors. Mechanical deformation through pressure, excessive heat, cold or chemical irritants can stimulate pain receptors (nociceptors) which then transmit impulses to the brain resulting in the perception of pain. The clinical characteristics of pain that originates in superficial structures are distinctly different from those of deep origin (Table 1).

Neurogenous Pain: It is caused by structural abnormalities within the neural components that innervate the affected area. This pain arises in the absence of any noxious stimulation.

- Pain is bright, spontaneous, unremitting, triggered, burning type and often accompanied by paresthesia along a distinct nerve distribution.
- Severity of pain is intense and referred pain is not present.
- Although the patient can easily locate the pain, the site of pain perception may not be its source.
- Accompanied by other neurologic symptoms.

Psychogenic Pain: It arises from psychic causes and is not elicited by stimulus or an abnormality within the neural system. It can manifest as chronic facial pain syndrome.

- Pain can be felt in many areas that change location during the disease process.
- An anatomic relationship between the pain source and the site of pain is absent.
- Its clinical behavior and response to treatment is often inconsistent, unexpected and nonphysiological.

PAIN OF DENTAL ORIGIN

Pain of dental origin is usually inflammatory and arises from two tissues: pulp and periodontal structures. Pulpal pain and
periodontal pain can be perceived differently because the sensory capabilities of the dental pulp are similar to other visceral tissues, therefore pulpal pain is similar to other musculoskeletal pains (Table 2).

### TOOTHACHES OF NONDENTAL ORIGIN

Toothaches of nondental origin can be difficult to identify and puzzling for the dentist. Cardinal warning symptoms are as follows:

- Spontaneous multiple toothaches
- Inadequate dental care for the pain
- Stimulating, burning, non-pulsatile toothaches
- Constant, unremitting, non-variable toothache
- Persistent, recurrent toothaches
- Failure of the toothache to respond to reasonable dental treatment.

Hence, the following differential diagnosis should be considered:

- **Muscular toothache**
- **Neurovascular toothache**
- **Cardiac toothache**
- **Neuropathic toothache**
- **Sinus toothache**
- **Psychogenic toothache.**

### Muscular Toothache (Toothache of Myofacial Origin)

- Pain presents as nonpulsatile, constant aching deep pain which is not location specific.
- Not responsive to local provocation of the tooth.
- Pain occurs spontaneously or during functional movement of involved muscle.
- Presence of localized tender sites (trigger points) in the muscle can refer pain to distant sites.
- Treatment includes maintaining proper body posture, physical therapy (transcutaneous nerve stimulation (TENS), cryotherapy), spray and stretch, local anesthetic injection of the involved muscle and even low level laser. Other commonly used drugs include tramadol, tricyclic antidepressants such as amitriptyline, alpha-2 adrenergic agonists like clonidine and tizanidine. Botulinum toxin type A appears to be emerging as a promising but expensive new agent with efficacy in chronic myofascial pain (Table 4).

### Referral Pattern of Myofacial Pain in the Jaw/Orofacial Region

Tooth pain is referral of pain from muscles of mastication and cervical muscles. Two most common pain referral patterns from...
muscles of mastication are masseter and temporalis pain referral pattern and from cervical muscles are mainly from sternocleidomastoid and trapezius muscle.9

Myofascial trigger point is hyperirritable locus within a taut band of skeletal muscle or in its associated fascia or tendon.10 A significant relationship between temporomandibular joint (TMJ) pain and muscle tenderness in the orofacial region has been demonstrated. This can be attributed to the convergence patterns of afferent information from the TMJ and the masseter muscle in the trigeminal subnucleus caudalis in response to natural stimulation in anesthetized rats.11 A trigger point in the muscles can refer pain to teeth or jaw. The phenomenon of referred pain involves the trigeminocervical complex in the central nervous system (CNS). The CNS receives afferent input from the cervical region (C1, C2) and the areas supplied by trigeminal nerve (V1, V2, V3), i.e. the muscles of mastication. The secondary neurons which are in close proximity anatomically may cause nociceptive afferent input from one region to become misinterpreted in the cortex as coming from another region.

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Travell and Simons have mapped referral patterns of trigger points12 in the head and neck region referred to the teeth and jaw (Table 3).

### Neurovascular Toothache

Traditionally referred as vascular pains but recently it has been suggested the cause to be both neurologic and vascular, thus termed as neurovascular.

- Spontaneous, variable, pulsatile and throbbing with periods of remission and exacerbations over months or years.
- Absence of adequate of dental cause.
- Pain usually felt in maxillary canine and premolar.
- Over the time, pain complaint may spread to involve wider areas of the face, neck or shoulder and may evoke muscle pain and restricted movement.
- Pain may respond to ergotamine tartarate.
- Recurrence is characteristic of neurovascular pains. Episodes of pain may possess a temporal behavior appearing at similar times during the day, week or month.

Most common neurovascular pain is migraine. Migraine pain can be referred to the teeth.13 Generally, toothache occurs in conjunction with migraine with or without aura or cluster headache. Toothache subsides when the headache symptoms subside. Some migraine variants can occur called migrainous neuralgia, which can produce localized tooth pain without headache complaint posing diagnostic challenges.

Temporal arteritis is a systemic inflammatory disorder that often involves the extracranial carotid circulation. The temporal artery appears tortuous, tender and enlarged. It is rare in less than 50 years and mean age of onset is 70 years.14 Symptoms include unilateral headache and intermittent claudication (fatigue or pain on function) in the muscles of the jaw.15 One serious complication is complete or partial loss of vision. Erythrocyte sedimentation rate or C-reactive protein may be elevated.

- Management involves the use of NSAID’s, triptans (sumitriptan, zolmitriptan, etc.), ergot alkaloids (ergotamine, hydroergotamine).
- The first combination product of a 5-HT receptor agonist (i.e. sumatriptan) and an NSAID (i.e. naproxen sodium) Treximet was approved by the US Food and Drug Administration in April 2008. Efficacy was demonstrated in two randomized, double-blind, multicenter, parallel-group trials comparing the combination product to placebo and each individual active component (i.e. sumatriptan and naproxen sodium). The percentage of patients remaining pain free without the use of other medications through 24 hours postdose was significantly greater (p < 0.01) among patients receiving a single dose of Treximet (25 and 23%) compared with placebo (8 and 7%) or either sumatriptan (16 and 14%) or naproxen sodium (10%) alone16 (See Table 4).

### Cardiac Toothache

Cardiac distress may sometimes manifest solely as jaw pain or tooth pain. Lack of adequate dental cause for the pain complaint should always be an alerting sign for the dentist.

- Jaw pain or tooth pain is cyclic.
• The toothache is increased with physical exertion.
• Failure of analgesic block to arrest the pain completely is confirming evidence that pain is not from dental origin.
• Sometimes toothache or jaw pain is associated with chest pain and decreased with nitroglycerine tablet (See Table 4).

Neuropathic Toothache

It can radiate to tooth as a result of abnormality within the neural structures. Neuropathic pains may either be episodic (paroxysmal) or continuous.

• Episodic neuropathic toothache (trigeminal neuralgia)
  – Unilateral, sudden, sharp, severe, shock-like (paroxysmal) spontaneous pain felt in a tooth or in the jaw that lasts for seconds to minutes and then disappears.
  – Pain is consistent with trigeminal neuralgia and is likely to be a variant.
  – Provoked by a trigger.
  – Local anesthetic at the trigger zone will reduce the pain.
  – Lack of dental pathology to explain the pain.
  – A number of drugs have been used systemically based on randomized clinical trials, such as baclofen, carbamazepine, dexamethorphan, lamotrigine, pimozone, proparcaine, tizanidine, tocapain and topiramate. Based on the evidence, carbamazepine remains the drug of choice. In refractory cases, gabapentin is probably the most promising drug. In recalcitrant cases pregabalin, topiramate or older anticonvulsants (phenytoin) have been tried successfully.17 Topical medications can provide rapid pain relief either alone or in combination with systemic medication. The topical medication can be formulated from a pharmacy to contain carbamazepine 4%, lidocaine 1%, ketoprofen 4%, ketamine 4%, gabapentin 4%.18 (See Table 4).
• Continuous neuropathic pain (atypical odontalgia, post-traumatic neuropathy, postherpetic neuralgia).17
  – Constant pain persisting for more than 4 months.
  – Dull aching continuous pain located in a clinically and radiologically normal tooth, gingiva or extraction site and unrelieved by extensive dental treatment.19
  – Most common area affected is maxillary premolar or molar region affecting all ages except children with a preponderance among women in their 40s.20
  – Local provocation of the tooth or surrounding tissues does not alter the pain.
  – Accompanied by depression and responds in most cases to antidepressant therapy.21 Based on various trials, the best treatment options are tricyclic antidepressants (TCA), gabapentin, pregabalin, opioids, topical capciacin and topical lidocaine patches.22
  – Neuropathic signs, such as allodynia and hyperalgesia are common and suggest a neuropathic origin of this pain.23 A case-control study on somatosensory abnormalities in atypical odontalgia demonstrated significant abnormalities in intraoral somatosensory function, which reflects both peripheral and central sensitization in this pain condition.24
  – Local anesthesia has no impact.
  – Gabapentin or TCAs are the drug of choice to treat AO or painful traumatic neuropathies.25

Sinus Toothache

Pain arising from the sinus as a result of inflammation or infection is referred throughout the maxilla and maxillary teeth. Any history of upper respiratory infection and nasal congestion should arise suspicion of a sinus toothache.

• Pain perceived in multiple teeth rather than a single tooth in the maxillary arch.
• Dull, constant aching pain.
• Pressure below the eyes.
• Tenderness with palpation over the involved sinus.
• Local anesthesia does not eliminate the pain.
• Toothache is increased with lowering the head.
• Diagnosis is confirmed by appropriate imaging studies.
• Relief has been seen with the use of antibiotics, topical (oxymetazoline, phenypherine) and oral α-adrenergic decongestants (pseudoephedrine), nasal corticosteroid spray, saline, mucolytics and expectorants (guaifenesin, potassium iodine, iodinated glycerol, propylene glycerol) (See Table 4).

Psychogenic Toothache

(Somatoform Pain Disorder)

Somatoform pain disorders felt in the teeth are characterized as:

• Pain in multiple teeth with frequent change in character and location.
• No identifiable cause.
• Chronic pain pattern.
• Lack of response to reasonable dental treatment; responds to antidepressant therapy (See Table 4).
• Increased pain with emotional stress. Psychological causes like anxiety, depression, health anxiety and other somatic symptoms were significantly associated with new onset of chronic orofacial pain.26 Depression plays a very important role in women with chronic pain syndrome because it increases pain-perception threshold. 27

CONCLUSION

Sir William Osler's maxim should always be remembered “What you don’t know, you won’t diagnose”. Jaw pain can be difficult to diagnose and dentists are more likely to encounter these complex cases in their practices. Misdiagnosis of jaw pain can lead to unnecessary dental treatment. Unfortunately, dentists consider the nonodontogenic cause of pain only after the failure of invasive treatment. Thus, the most important concept for the clinicians to remember when diagnosing pain is to “Listen Carefully and Consider All Possibilities”.

REFERENCES