Neuropathic Orofacial Pain including Burning Mouth Syndrome

Lecture Topic Specific Learning Outcomes:

Outline the aetiology, pathogenesis, clinical features, diagnosis and management of neuropathic orofacial pain conditions.

These lecture slides and associated module materials must not be reproduced, distributed or shared without prior permission. Unauthorised use of this material breaches UWA's student conduct regulations and may also constitute a violation of the Copyright Act 1968.

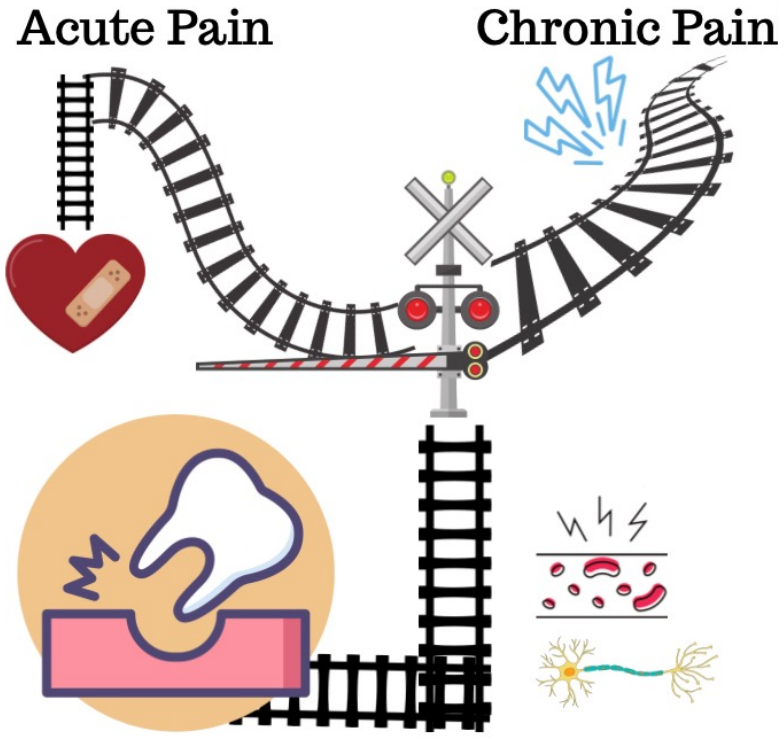
Dr Amanda Phoon Nguyen

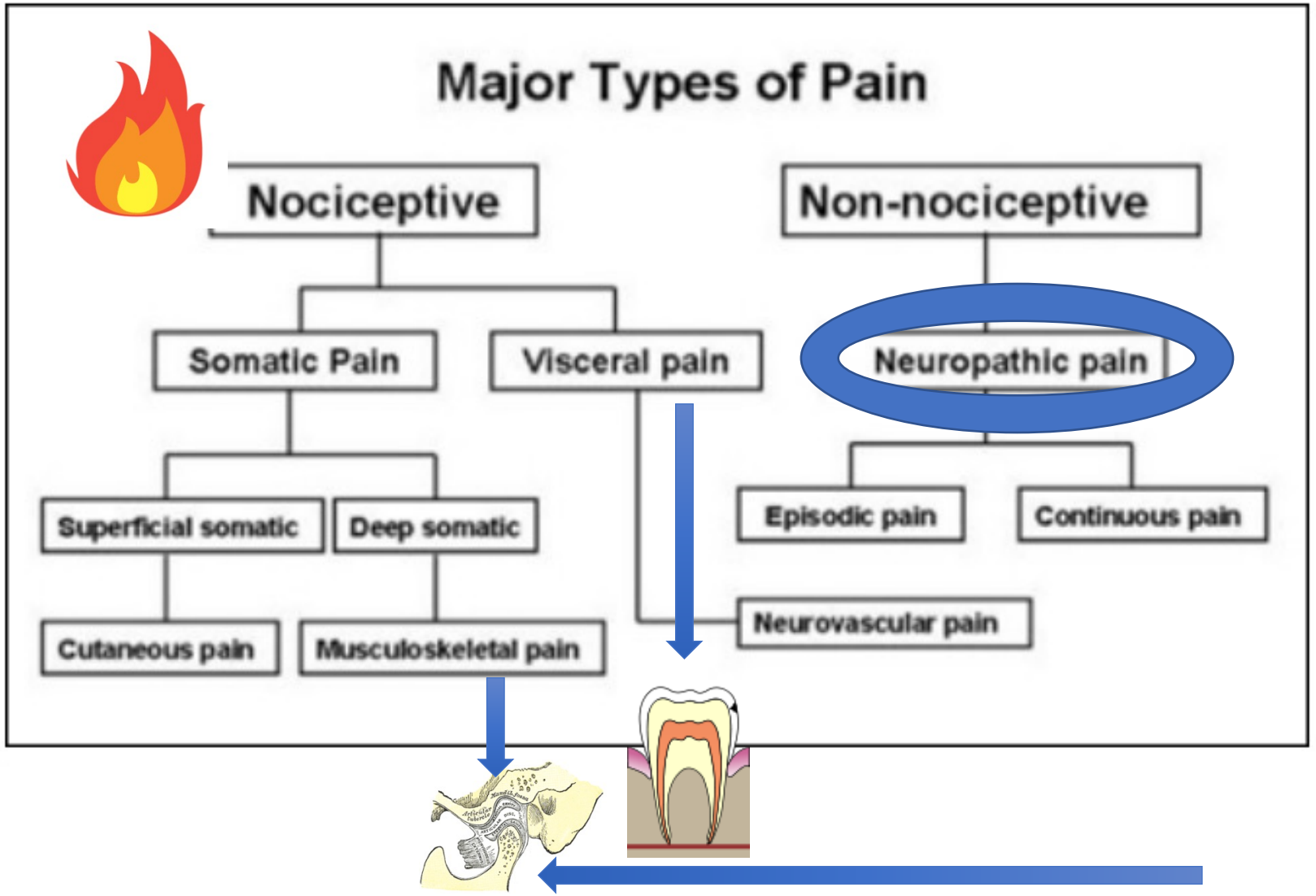
BDSc (UniMelb), MRACDS (GDP), DClinDent (Oral Med) (UWA), MRACDS (OralMed), Cert ADL, FOMAA, FPFA, FICD,FADI, MAICD, GCHL, MICDA, FDSM

Oral Medicine Specialist

AUSTRALIAN DENTAL ASSOCIATION
PERTH ORAL MEDICINE & DENTAL SLEEP CENTRE
Specialists in Oral Medicine
Perth Children's Hospital
Australasian Sleep Association
OMAA Oral Medicine Academy of Australasia
Royal Australasian College of Dental Surgeons
Let knowledge conquer disease

Is all pain the same?





“Good and Bad” Pain

Nociceptive Pain

- “Normal Pain” / protective
- Consequence of tissue injury or noxious stimuli
- Site of injury = source of pain

- When noxious stimuli is removed, inflammation resolves and pain ceases

Neuropathic Pain

- Chronic pain
- Lesion / dysfunction of the PNS or CNS
- No protective or reparative role

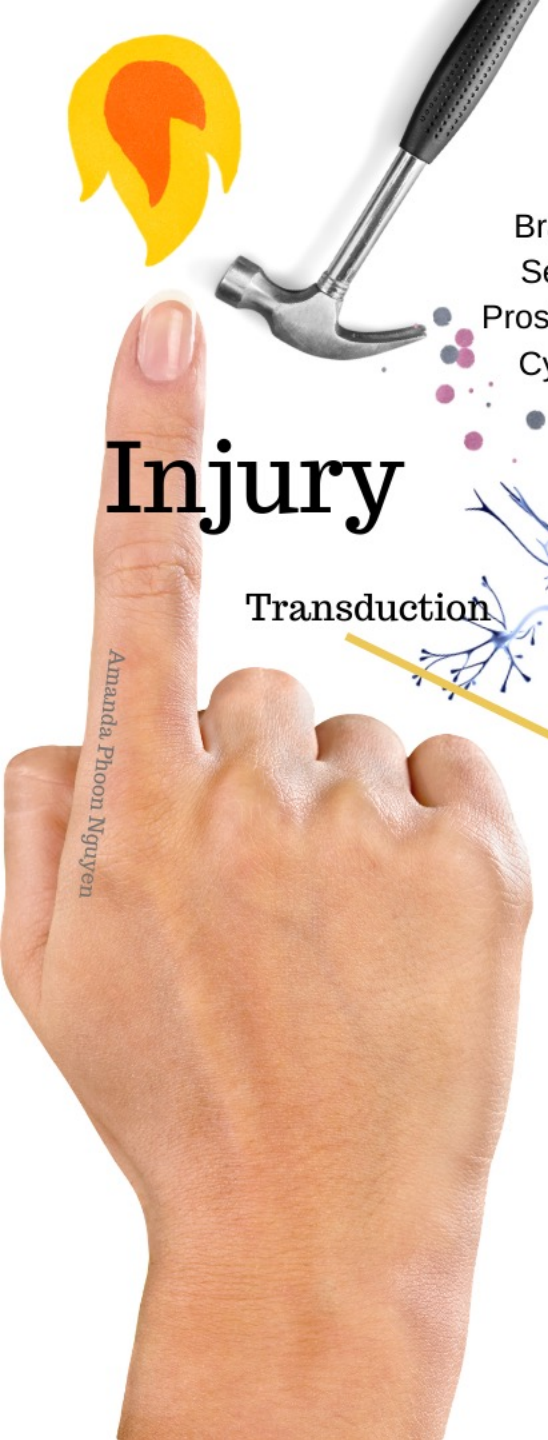
- Pain persist after noxious stimuli has ceased and tissue healed

- Nociception: The neural process of encoding noxious stimuli.
- Nociceptive pain: Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors. Normally functioning somatosensory nervous system
- Neuropathic pain: Pain caused by a lesion or disease of the somatosensory nervous system. Abnormally functioning somatosensory nervous system
- Neuralgia: Pain in the distribution of a nerve or nerves.
- Neuritis: Inflammation of a nerve or nerves.
- Neuropathy: A disturbance of function or pathological change in a nerve. Neuritis is a special case of neuropathy, the term being reserved for inflammatory processes affecting nerves.

Is there something missing?

What happens if someone has pain but there is no demonstrable tissue damage or lesion / dysfunction of the PNS or CNS?

NOCIPLASTIC PAIN



Injury

Bradykinin
Serotonin
Prostaglandins
Cytokines
H+

Transduction

Nociceptive afferents

Dorsal root ganglion

1st order neuron

Transmission

Spinal interneuron

2nd order neurons
Rexed laminae of the spinal cord

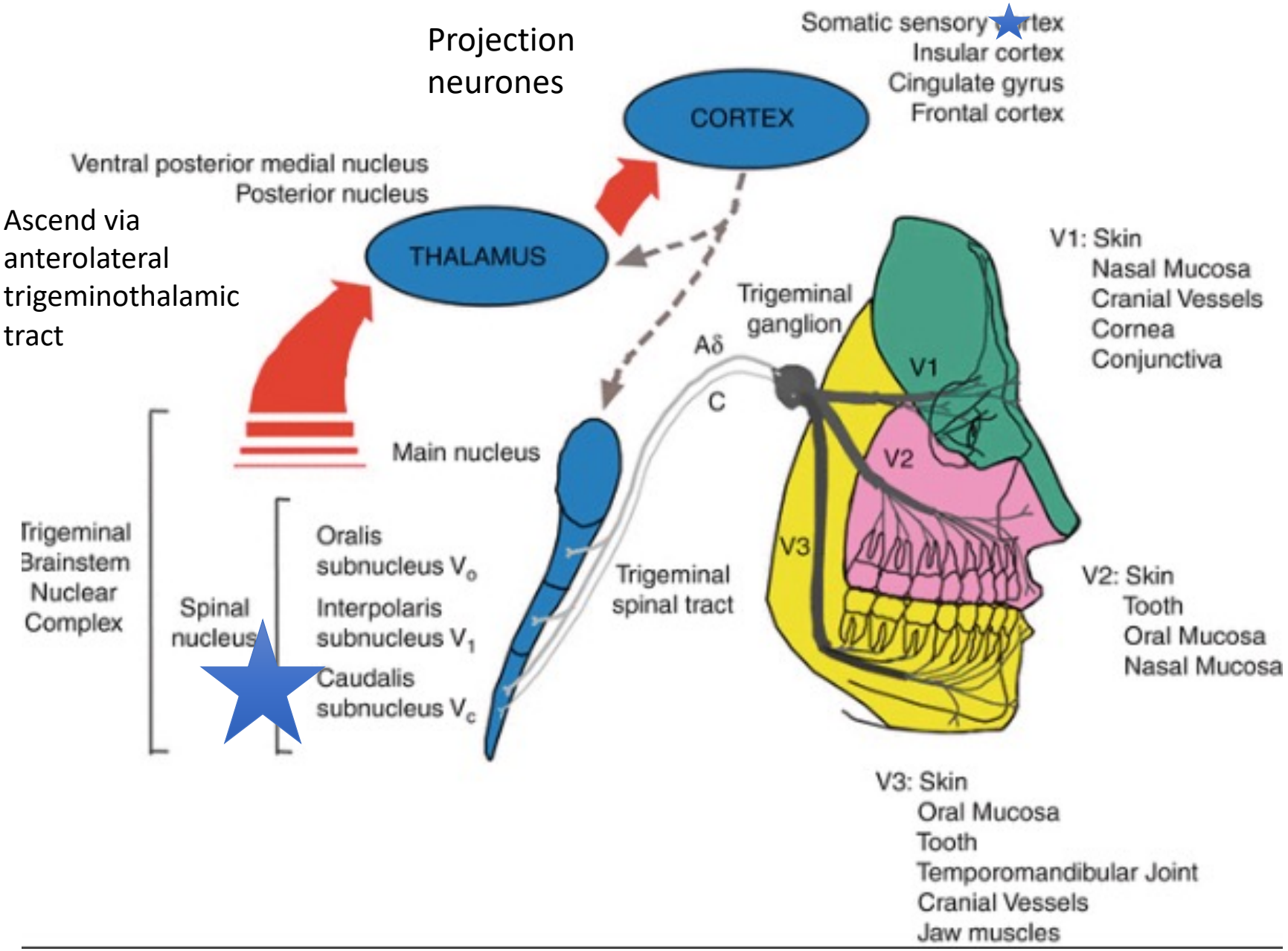
Ascending pathway

Spinothalamic tract to the ventral posterolateral (VPL) nucleus of the thalamus

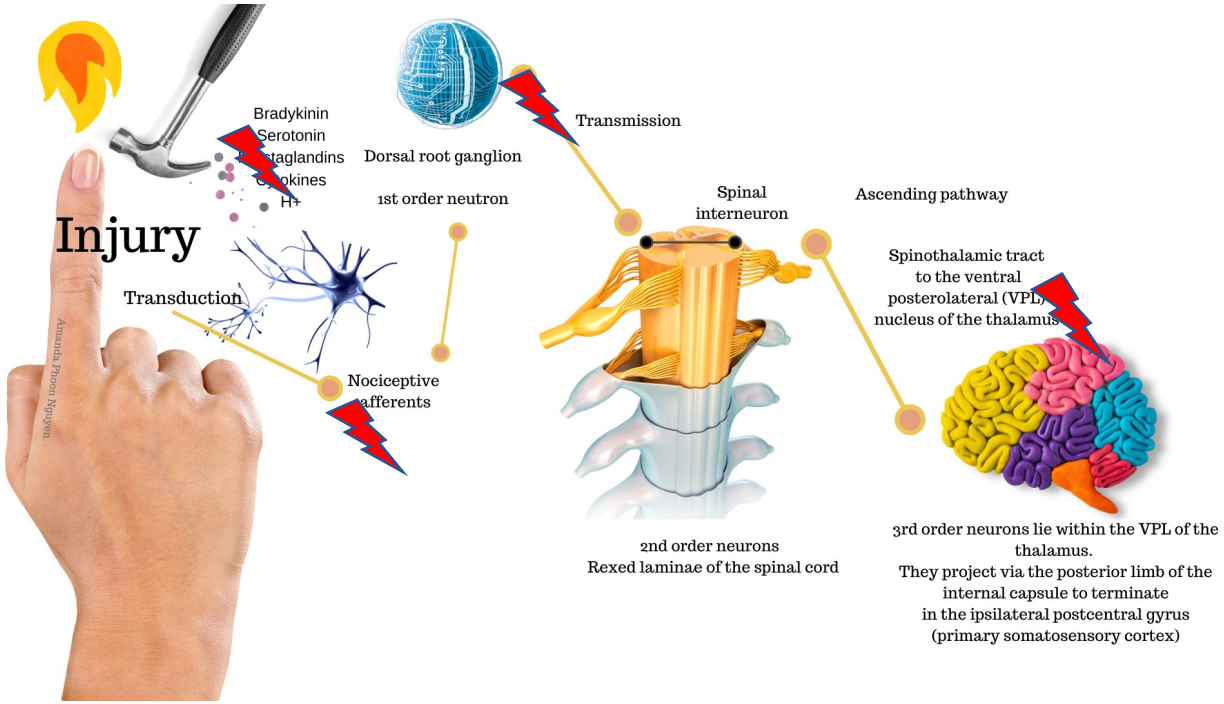
3rd order neurons lie within the VPL of the thalamus.
They project via the posterior limb of the internal capsule to terminate in the ipsilateral postcentral gyrus (primary somatosensory cortex)

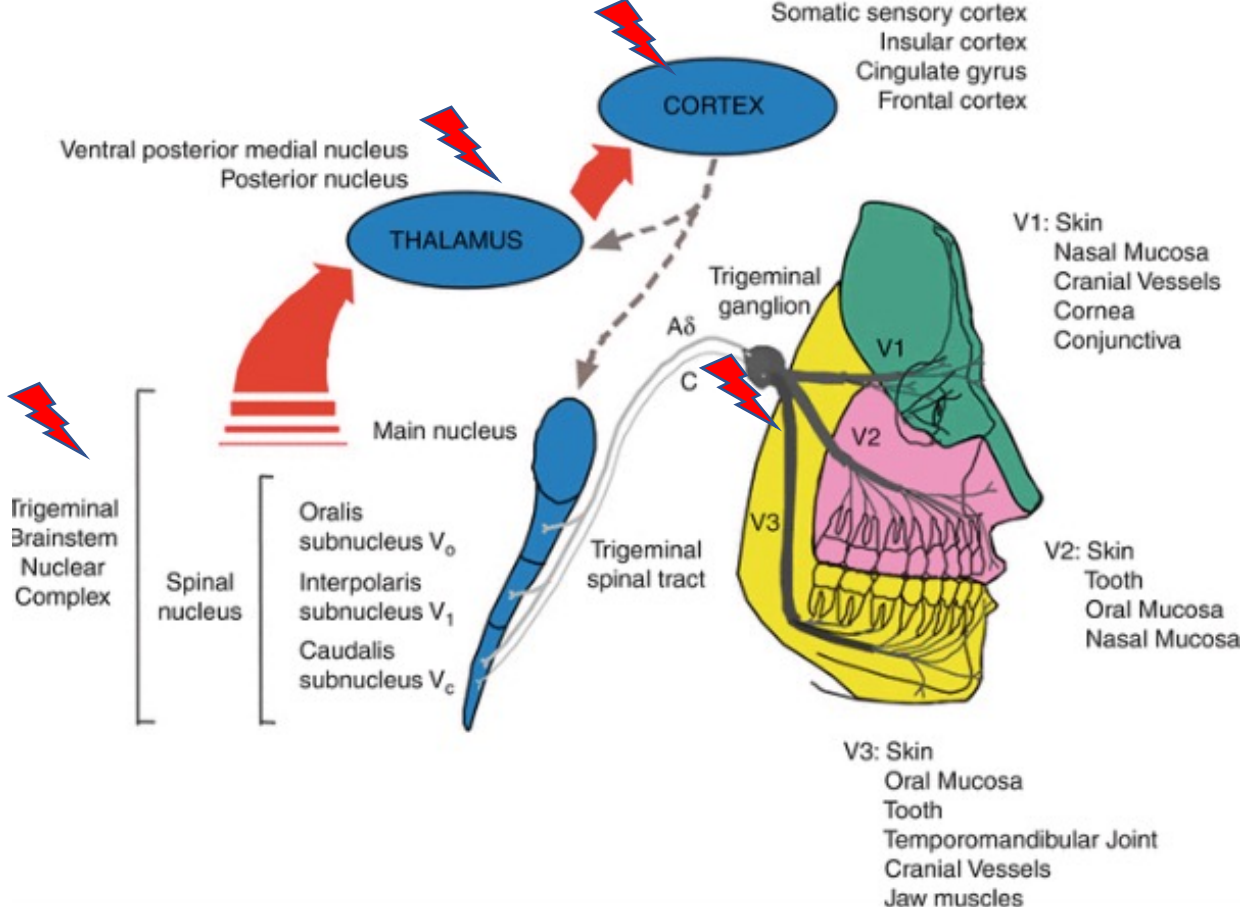
Projection neurones

Ascend via anterolateral trigeminothalamic tract



Hu J.W., Woda A. (2013) Trigeminal Brainstem Nuclear Complex, Physiology. In: Gebhart G.F., Schmidt R.F. (eds) Encyclopedia of Pain. Springer, Berlin, Heidelberg

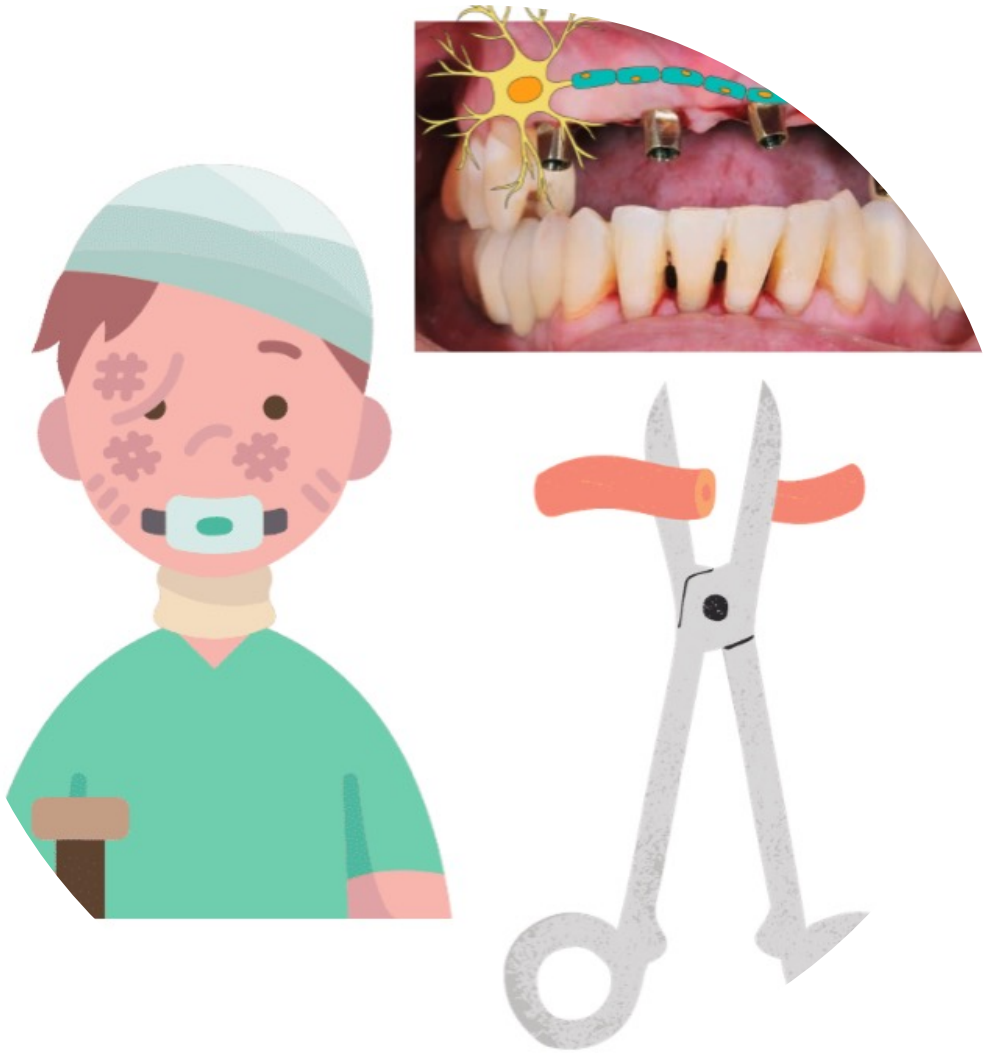




Postsurgical Pain

- Nociceptive pain from activation of nociceptors
- Inflammatory pain from release of inflammatory mediators
- Neuropathic pain from injury of nerves

- Neuropathy is classified into 3 main types: axonotmesis, neurotmesis, and neuropraxia.
- Neurotmesis indicates rupture of the nerve trunk where both the axon and axon continuity is completely severed
- Axonotmesis indicates the rupture of axons where the surrounding connective tissue of the nerve has been maintained
- Neuropraxia is a transient blockage of nerve conduction without axon alteration.



Chronicity of Pain

- In general, pain lasting for more than 3 months

In orofacial pain:

- Pain occurring on >15 days per month and lasting for >2 hours a day for at least 3 months

Chronicity of Pain

- Neuroplasticity!
- Repeated pain exposure changes pain pathways in the brain, making them more sensitive to future pain and increasing the risk of developing chronic pain.

- Peripheral and Central Sensitization

Sensitization

Long-term consequences of noxious stimuli result from central as well as from peripheral changes.

The hallmarks of central sensitization include decreased threshold firing, firing from non-noxious stimuli and pain spread.

Hyperalgesia: Exaggerated responses to noxious stimuli (hyperalgesia).
Allodynia: Sensitivity to normally non-noxious mechanical and thermal stimuli

Published: 15 December 1983

Evidence for a central component of post-injury pain hypersensitivity

Clifford J. Woolf

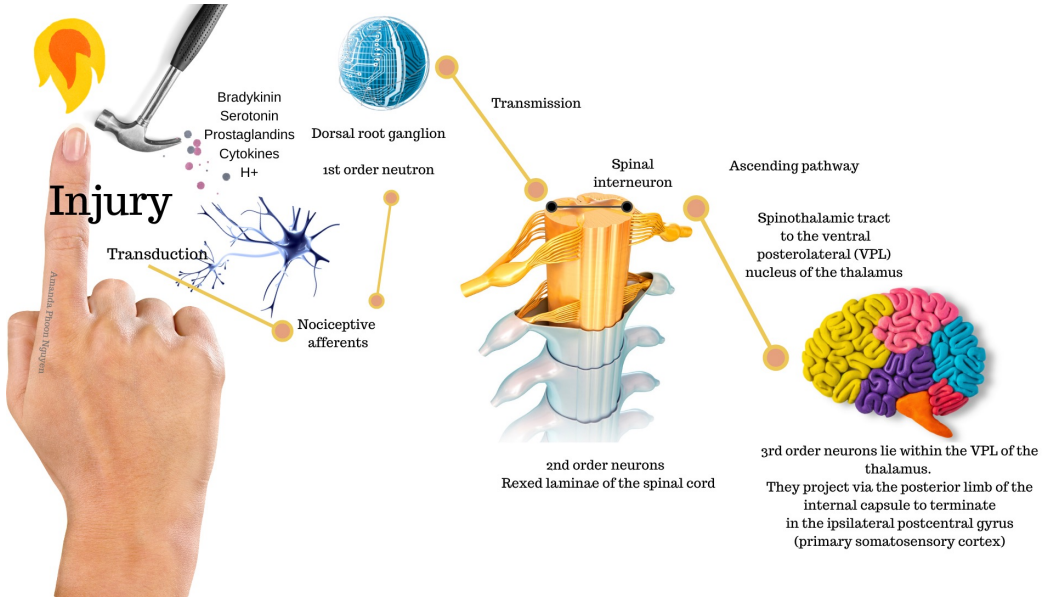
Nature **306**, 686–688 (1983) | Cite this article

3659 Accesses | **1529** Citations | **84** Altmetric | Metrics

Abstract

Noxious skin stimuli which are sufficiently intense to produce tissue injury, characteristically generate prolonged post-stimulus sensory disturbances that include continuing pain, an increased sensitivity to noxious stimuli and pain following innocuous stimuli. This could result from either a reduction in the thresholds of skin nociceptors (sensitization)[1,2] or an increase in the excitability of the central nervous system so that normal inputs now evoke exaggerated responses[3,4]. Because sensitization of peripheral receptors occurs following injury[5–7], a peripheral mechanism is widely held to be responsible for post-injury hypersensitivity. To investigate this I have now developed an animal model where changes occur in the threshold and responsiveness of the flexor reflex following peripheral injury that

- Repetitive noxious stimulation of primary C-fiber afferents results in a ‘wind-up’ phenomenon
- Escalation of nociceptive transmission by cells in the dorsal horn.
- Wide-dynamic range neurons recruited resulting in the amplification and prolongation of nociceptive transmission in ascending pathways in the central nervous system.
- Central sensitization is mediated via activation of the *N*-methyl-D-aspartate (NMDA) glutamate receptor and is a feature of many chronic pain states.



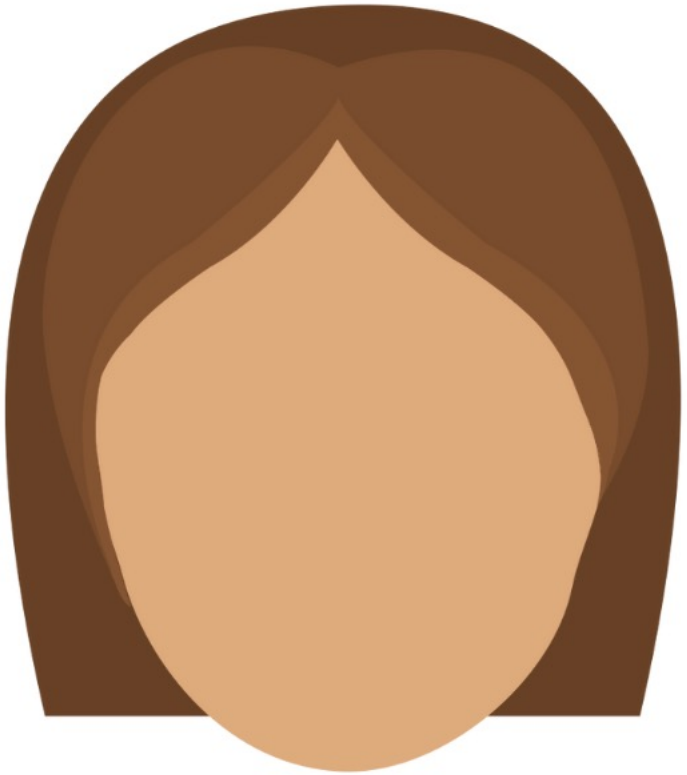
Neuropathic Pain Prevalence

Prevalence of neuropathic pain in the general community > 2%

One-third of cancer patients have neuropathic pain (alone or with nociceptive pain)

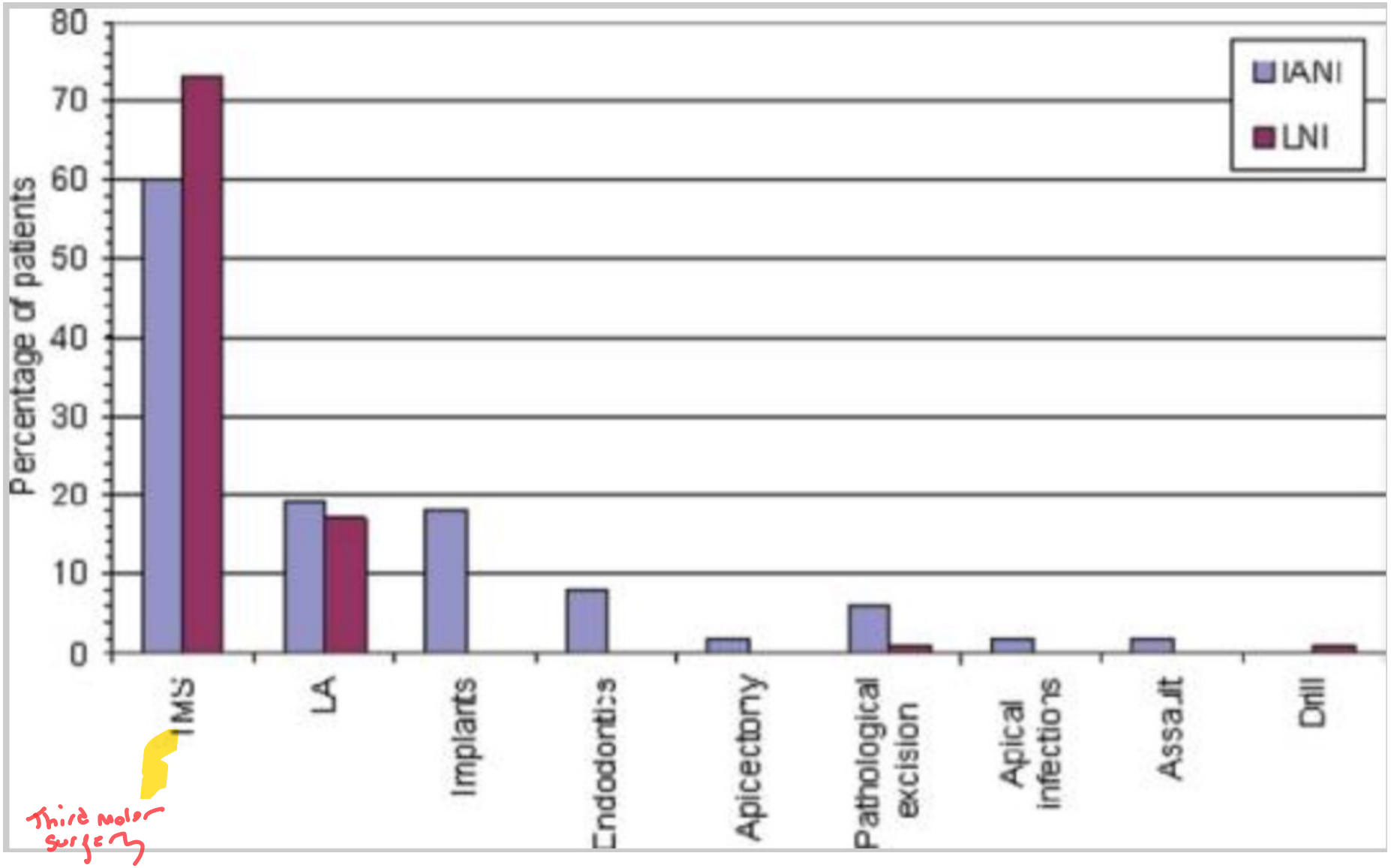
>50% of low back pain patients have associated neuropathic pain

SPHERE Positive Management of Persistent Pain Algorithms (2006). Schmader KE. *Clin J Pain* 2002; 18: 350-4. Stevens PE, *et al*. *Pain* 1995; 61: 61-8. Davis MP, Walsh D. *Am J Hosp Palliat Care* 2004; 21: 137-42. Deyo RA, Weinstein JN. *NEJM* 2001; 344: 363-70



- Incidence following injury to the peripheral branches of the trigeminal nerve following implants, 3rd molar extractions, orthognathic surgery, mid face fractures and root canal therapy: 3-5%

IASP 2016



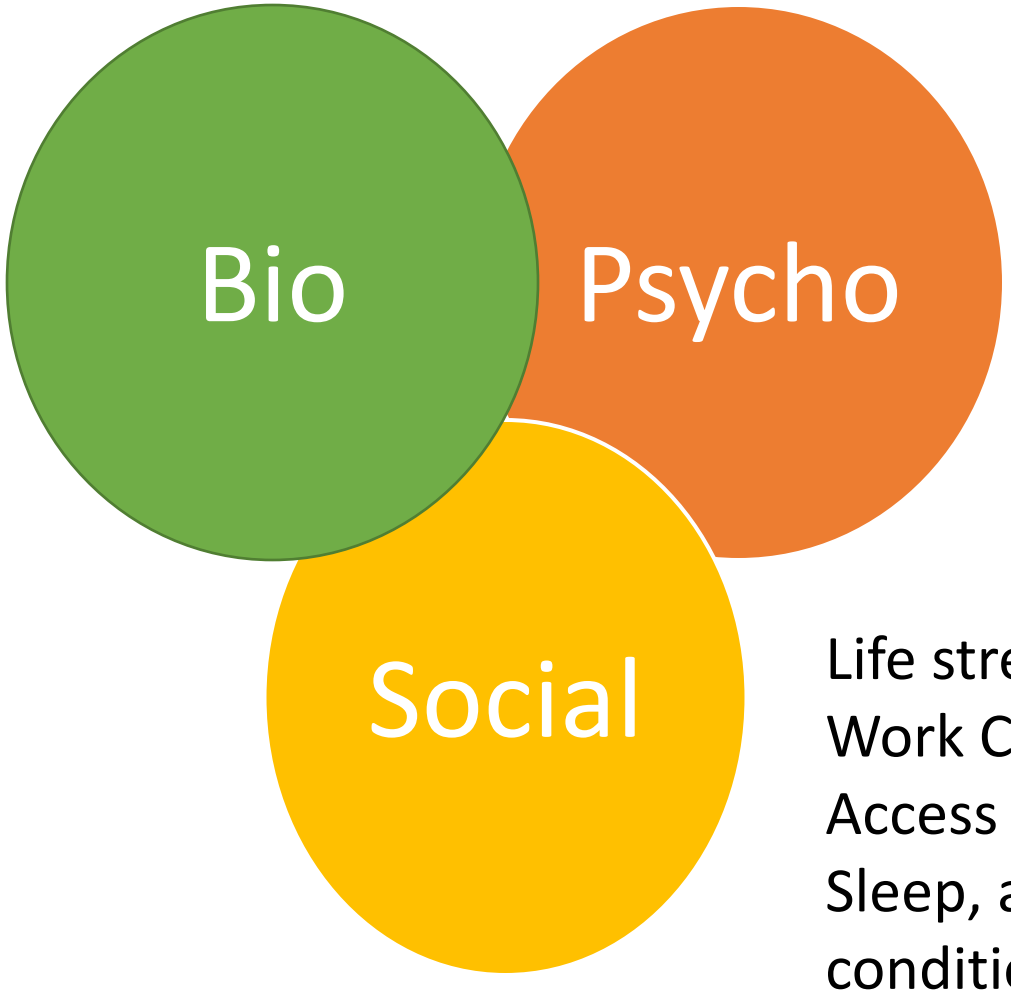
Renton T, Yilmaz Z. Profiling of patients presenting with posttraumatic neuropathy of the trigeminal nerve. J Orofac Pain. 2011 Fall;25(4):333-44. PMID: 22247929.

Who can Get Chronic Pain?
Anyone

Biopsychosocial Model

Partial genetic susceptibility

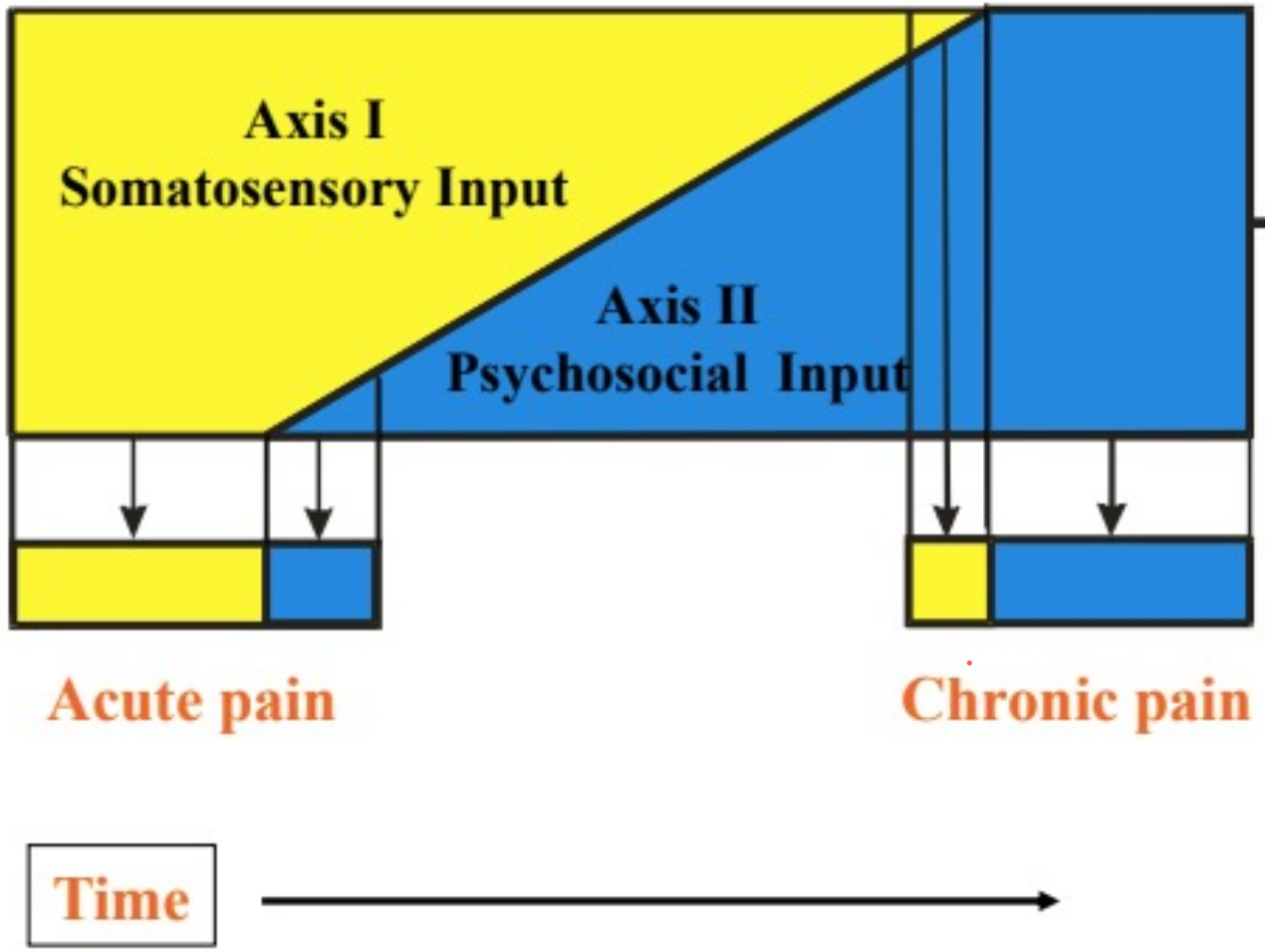
Biological pain processes



Psychological

Perpetuating Factors

Life stressors
Work Claim
Access to care
Sleep, alcohol, other pain conditions, smoking



↳ this chart helps to predict pain
↳ learning the risk factors is ↑↑

Orbach and Durham 2017

Pain Vulnerability Predictors

- Female
- Comorbid chronic pain conditions
- Stress
- Anxiety
- Neuroticism
- Catastrophizing

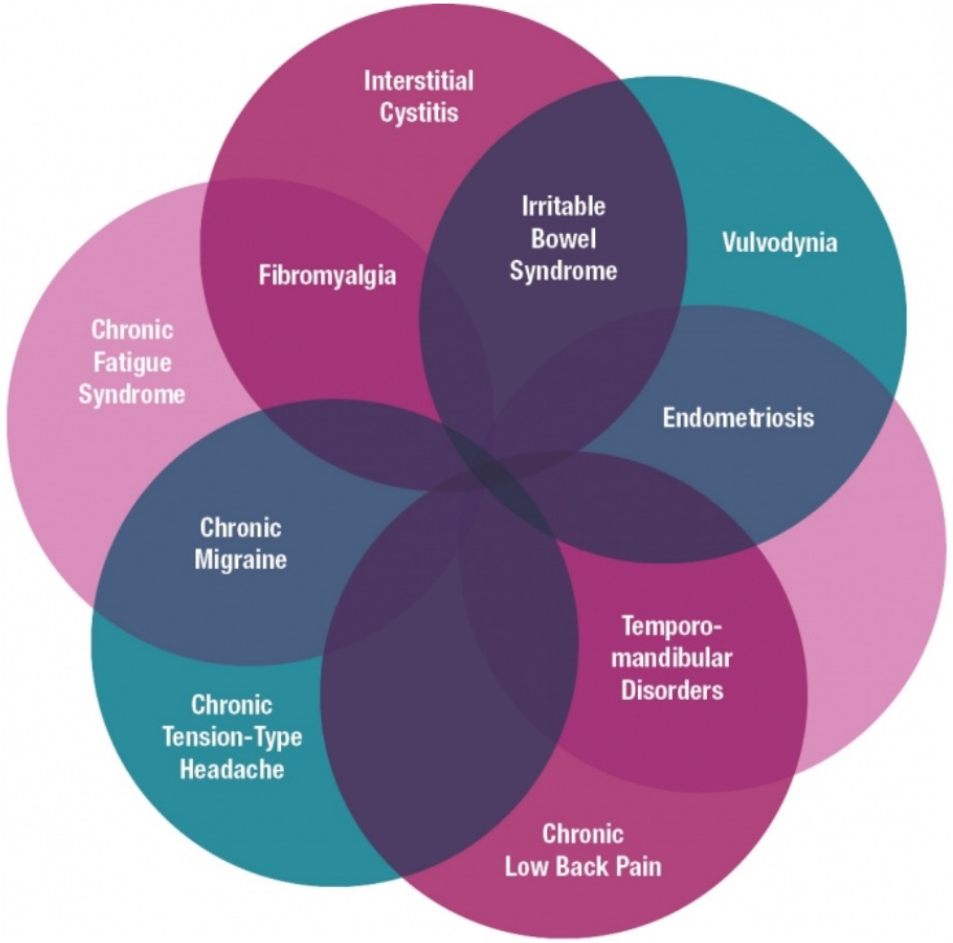


Figure 1. A sample of chronic overlapping pain conditions (Courtesy CRPA).

PracticalPainManagement.com

Case 1

https://doi.org/10.1016/j.adaj.2020.10.014

A middle-aged woman reached up for a small plastic box of facial wipes from a closet shelf. It slipped out of her hand and struck her upper lip. There was no bleeding either externally or on the mucogingival tissue over teeth 21 and 22. There was a localized pain that she believed was a toothache in no. 21. Within a few days, she saw her primary general dentist (dentist no. 1). His examination found that the tooth was vital and responded normally to testing; that is, radiograph, electric pulp testing, tapping with blunt instrument, and manual palpations. He advised waiting to see what would happen, and the patient continued to have fluctuating symptoms of pain.

Over the next 6 months, the patient was referred back and forth to dentist no. 2, an endodontist, who could not reach a diagnostic conclusion about tooth no. 21. He eventually was persuaded to perform a nonsurgical root canal therapy (RCT) on that tooth and found a vital pulp that might have been slightly hyperemic; the procedure was completed in 1 visit. After the endodontic treatment, the patient developed more severe pain, and the endodontist was unable to explain this outcome. He advised her to wait it out with the help of prescription analgesics. A limited field of view cone-beam computed tomography (CBCT) study of the area failed to show any cracks or other radiographic findings that could explain the etiology.

At this point, the patient became frustrated with these 2 dentists and decided to search for a more expert practitioner.

Online she found a prosthodontist (dentist no. 3) who had been a part-time faculty member at a local dental college. He examined her approximately 2 months after the RCT was performed. He examined her by tapping on tooth 21 with a blunt instrument and found her responses to be indicative of a DAP problem, so he referred her to a periodontist (dentist no. 4). This led to the following series of evaluations and treatments by these 2 dentists and 3 other colleagues within 2 dental group practice offices. First, dentist no. 4 concluded that tooth 21 was cracked, and he extracted it; an immediate implant was placed during that visit. Afterward, a temporary crown was placed by dentist no. 3. Because the pain persisted, the patient was seen by an endodontist (dentist no. 5) within that same group practice, and he performed RCT on tooth 22. The same cycle of events as described for 21 was repeated as the pain was getting worse, and extraction was recommended. Also, owing to a questionable radiographic finding around the tip of implant for tooth 21, that implant was removed during the same visit. At this point, the patient went to a different dental office to see another periodontist (dentist no. 6), who asked the endodontist in his practice (dentist no. 7) to evaluate the completed RCT on tooth 22. Together they decided to extract this tooth on the basis of a cracked root. An implant was placed, and it has not been removed to date.

Throughout all of this treatment, provided over a 3-year span, the patient's symptoms steadily worsened. During this entire 3-year period, not 1 of the 7 dentists ever mentioned an alternative diagnosis other than toothache or cracked root, nor was it ever suggested that the patient should consult with an OFP or oral medicine specialist or with a physician of any kind. Finally, the patient sought an opinion at the Mayo Clinic, where within 30 minutes a diagnosis of atypical odontalgia was offered; this diagnosis has changed nomenclature over the succeeding years, but essentially it was a correct description of a neuropathic pain problem. A first attempt to treat with gabapentin did not help. The patient returned home and began a cross-country odyssey seeking treatment. One neurologist in New York suggested a microvascular decompression surgical procedure to treat what he diagnosed as trigeminal neuralgia, but another neurologist warned her against it. She saw oral surgeons in a Midwestern state who advertise treatment for neuralgia-inducing cavitational osteonecrosis (NICO) (also described as holes in bone), for which they recommended performing a surgical excavation procedure of the dentoalveolar bone.

At this time, the patient was referred to the article's first author (C.S.G.) and was advised to avoid that NICO procedure. An oral stent containing a custom-compounded mixture of various medications for neuropathic pain (that is, pregabalin, cortisone, and lidocaine) was fabricated; this was inserted over the painful area, and that was moderately helpful for some time, but ultimately it did not provide adequate relief. The patient then was referred for Somehow, she has managed to continue working as a teacher most of this time. neurologic care, and a series of medications for neuropathic pain was tried with limited success. Ultimately, after failing to improve with stellate ganglion blocks for a supposed sympathetically maintained pain disorder, she was prescribed opioid medications to be taken 4 times per day combined with other centrally acting medications.

The patient understandably was distressed and consulted with an attorney. She wanted to sue all 7 dentists but ultimately was persuaded that dentist no. 1 had done the best he could with vague symptoms and no findings and that his 6-month collaboration with the endodontist (dentist no. 2) was acceptable. Performing the RCT on 21 also seemed reasonable at the time, but it is unfortunate that the endodontist did not understand the negative outcome; instead, he attempted prescribing medications and hoping for resolution of the pain.

Clearly, it is fair to think that dentist no. 3 erred by failing to consider a nonodontogenic diagnosis when this new patient with 1 year of progressively increasing DAP sought treatment at his office. Instead, he initiated the cycle described above, and the following 6 years of pain could be attributed to the combination of omissions (failure to diagnose or refer) and commissions (extractions, implant placement and removal, etc.) committed by him and his 4 colleagues. Therefore, a malpractice suit was brought against all 5 of those dentists; the outcome of that action is still pending.

Case 2

27-year-old woman

- Wanted to continue her search for someone who might be able to correct her occlusal problem or to make her pain disappear without any centrally acting drugs.
- Nonacceptance of working diagnosis of neuropathic pain

https://doi.org/10.1016/j.adaj.2020.10.014

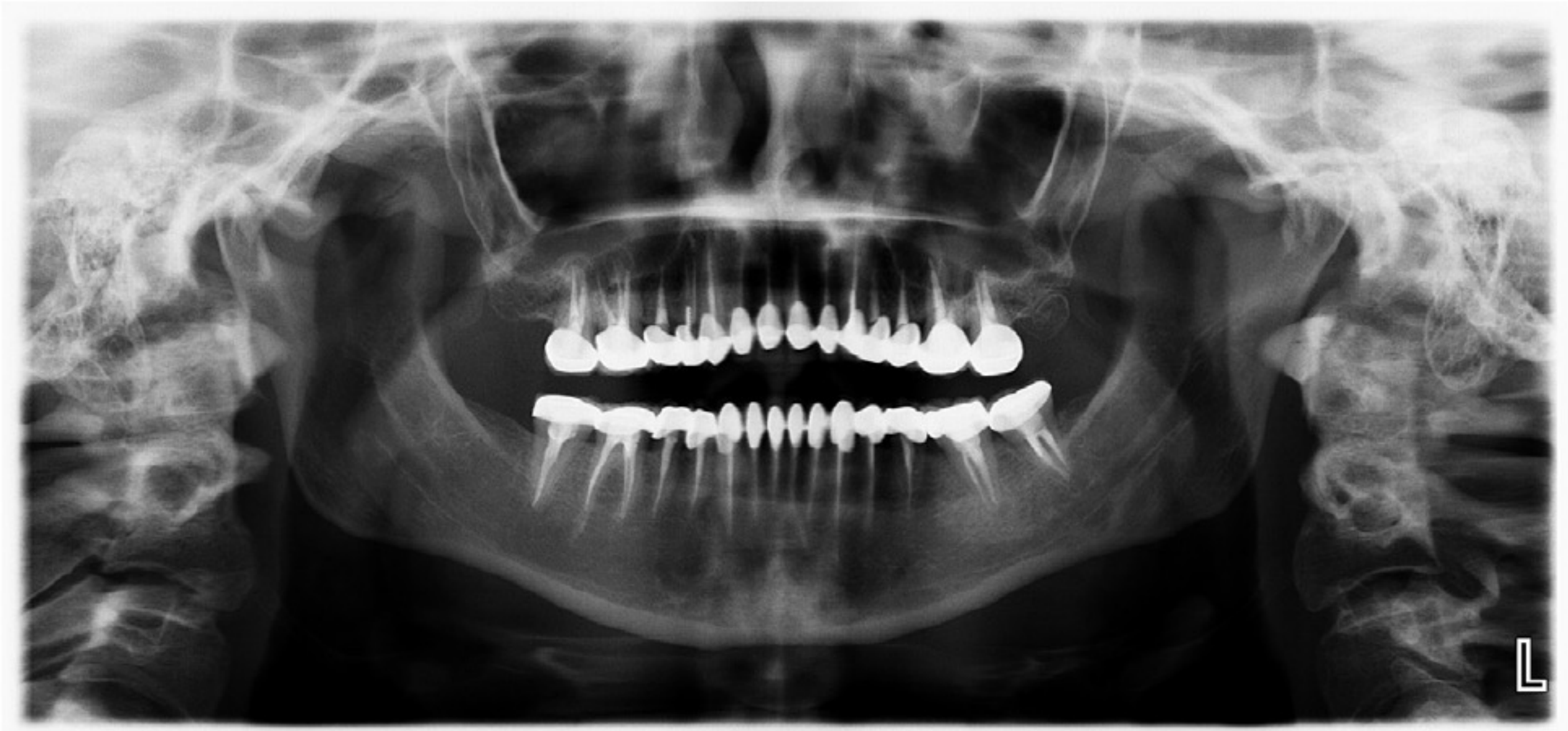
She recalled her initial problem as pain in the maxillary right arch, in the area of premolars, approximately 5 years earlier.

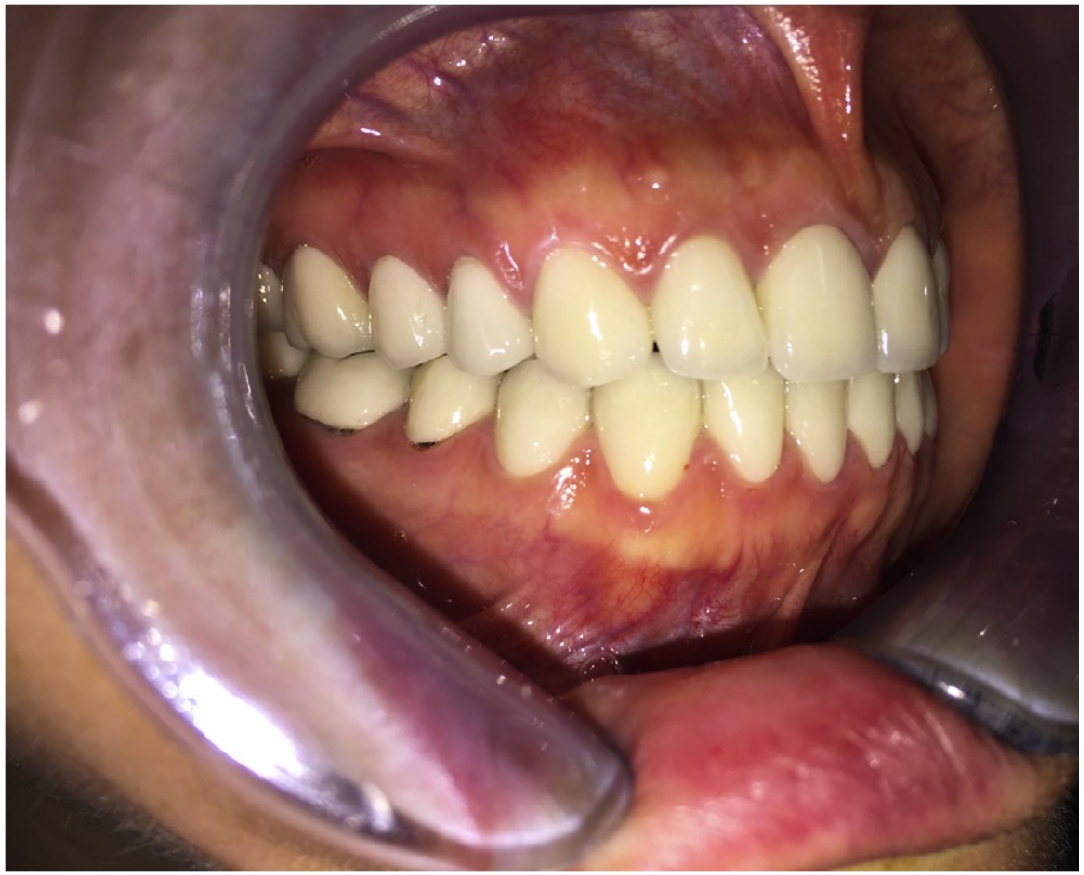
Her general dentist attributed the pain to pulpal inflammation of the first premolar and performed an endodontic treatment. After an initial improvement, the pain soon reappeared, and the dentist attributed the pain to sensitivity of the neighbouring teeth. He proceeded with additional sequential RCTs of teeth to provide possible relief from pain, which was migrating from 1 tooth to another.

How many?

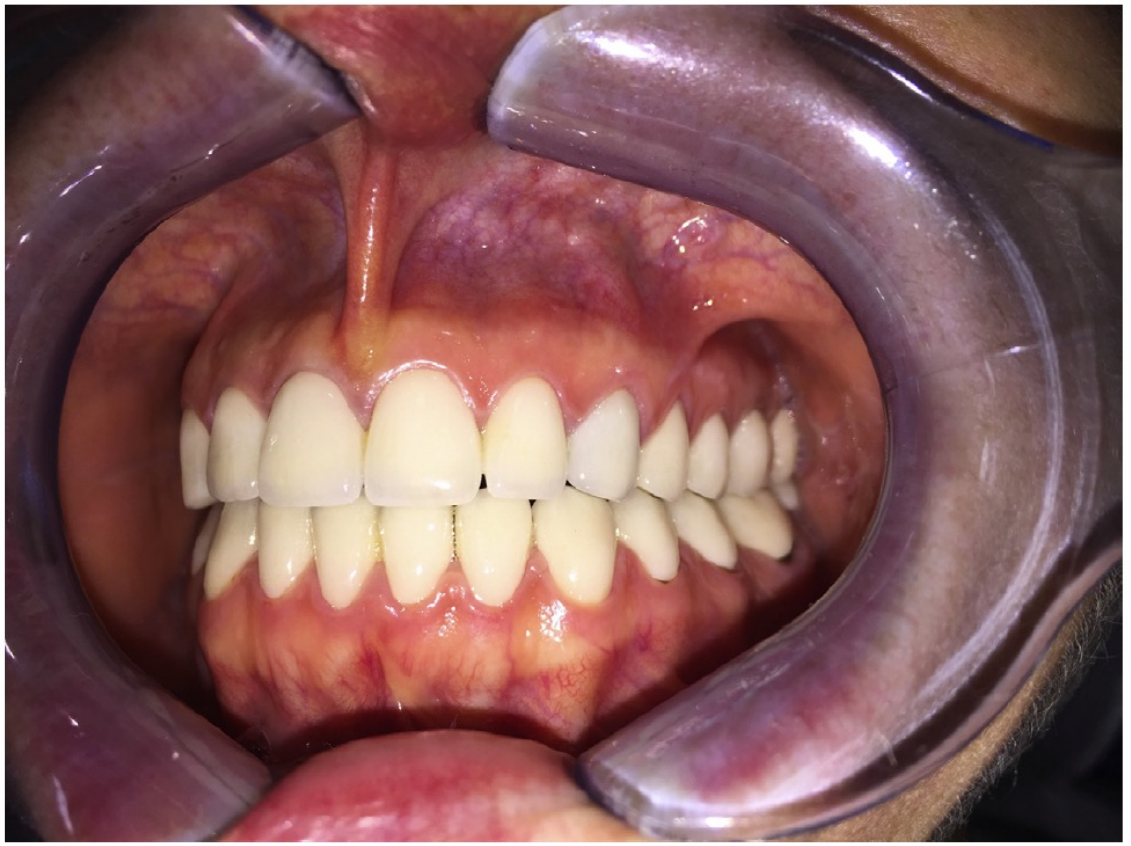
28

Persistent Idiopathic Dentoalveolar Pain





al photograph of the patient in case report 2, showing full crowns on all z



2. Clinical photograph of the patient in case report 2 (left-side view).

https://doi.org/10.1016/j.adaj.2020.10.014

- After these extensive procedures, her overall pain increased, with alternating periods of slight remissions and worsening episodes.
- Pain was described by the patient as feeling like an electrical stimulus that is never too intense but sometimes reaches 7 of 10 on a numeric rating scale.
- The location of the pain was variable from time to time, primarily in the original quadrant but also migrating to the other quadrants.
- The patient was not able to identify any particular trigger for the pain but described some occasional associated symptoms, such as a burning sensation in the gingiva as well as a bad taste in the mouth.
- She reported headaches with a frequency of no less than 7 days per month.
- Prosthetic treatment was proposed to adjust her occlusion and exclude any cause for pain related to misalignment of the teeth.
- Time passed without any improvement, and her dentist suggested an escalation to a third step of treatment: full-mouth extractions and provision of an implant-supported prosthesis.
- At that point the patient, frightened over the prospect of this extensive proposed surgical intervention, decided to ask for a second opinion, 5 years after the first appointment with the first dentist.
- The patient never returned for a second consultation and communicated that she would instead continue her search for someone who might be able to correct her occlusal problem or to make her pain disappear without any centrally acting drugs.

Post-traumatic trigeminal neuropathic pain

previous terminology

- Anaesthesia dolorosa, painful post-traumatic trigeminal neuropathy, persistent dentoalveolar pain, deafferentation pain, phantom tooth pain, atypical odontalgia, atypical facial pain.

- Unilateral or bilateral facial or oral pain following and caused by trauma to the trigeminal nerve(s), with other symptoms and/or clinical signs of trigeminal nerve dysfunction and persisting or recurring for more than 3 months.

- Post-traumatic trigeminal neuropathic pain rarely, if ever, crosses the midline but, over time, it may in some cases become more diffusely distributed.

Epidemiology

- Rare
  - Good estimates of the prevalence of PTTN lacking
  - ? Shifting diagnostic terms and criteria
  - Traumatic injuries to the trigeminal nerve only rarely lead to a painful neuropathy
- Onset usually in middle age (40-50 years)
- More common in females
- Associated with significant psychosocial stressors

Clinical Presentation

- Oral or facial pain developing within 6 months
- Identifiable traumatic event to the trigeminal nerve
- The pain persists beyond the normal healing time
- Usually unilateral

- Pain is localised to the distribution of the trigeminal nerve

- Symptoms vary considerably.

- Quality: Often burning or shooting
- Swollen or foreign body sensation, heat or cold, or redness/flushing.

- Moderate to severe intensity.

- Duration: Often continuous, but may be paroxysmal or mixed.

- There may be clinical signs of hyperalgesia/allodynia or hypoaesthesia /hypoalgesia.

Management

- Avoid irreversible dental treatment if an obvious dental cause cannot be identified

- Often difficult to manage once established
- Minimise pain and inflammation around the time of injury/surgery (consider pre, peri and post op adequate anesthesia)
- Pharmacologic:
  - Topical – e.g. local anaesthetics, capsaicin
  - Systemic – e.g. tricyclic antidepressants, gabapentanoids, anticonvulsants, selective noradrenaline reuptake inhibitors
- Psychological, cognitive behavioural approaches

Table II. Most common drugs in neuropathic pain

Drug	*Mechanism of action*	*Active ingredient*	*Daily dose*
Tricyclic antidepressants (TCAs)[1,2]	Inhibit the reabsorption (reuptake) of serotonin and norepinephrine	Amitriptyline	10-200 mg
Phenothiazines[18]	Block dopamine D2 receptor	Chlorpromazine	60-300 mg
Beta-blockers[19]	Beta-blockers work by blocking the effects of the hormone epinephrine, also known as adrenaline	Propanolol	5-50 mg
Anticonvulsivants[20-25]	Intervene on the canals' Ca^{2+}	Gabapentin	300-3600 mg
		Pregabalin	300-600 mg
		Clonazepam	1-10 mg
Agonist of GABA receptor[19]	Acts on the CNS to produce its muscle relaxant effects	Baclofen	30-200 mg
Topical medications[1]	Capsaicin encourages the release of substance P, inhibiting its biosynthesis and axonal transport, leading to a depletion of substance P in the central and peripheral nervous system.	Capsaicin	0.025% topical
Minor opiate analgesics[26]	Minor opiate analgesics act to relieve pain in the CNS	Tramadol Codeine	100-400 mg

Don’t have to know this table, but please be familiar with the types of meds used.

- Amitriptylline
- Pregablin
- Gabapentin

Renton, Dawood, Shah, Searson & Yilmaz, 2012

*Referral delay

Table 1 Reported incidence and risk factors for implant related inferior alveolar nerve injury[7,9–16]

Study, author, year Implant type, number	Descriptive	Incidence of nerve injury %
Balshi (1989)[9]	Chronic pain resolved after implant removed	Therefore concluded that prosthodontic technique is the source of trouble
Delcanho (1995)[10] Opinion paper and literature review.	Neuropathic implications of prosthodontic treatment.	Lip parasthesia is mentioned but pain is rarely mentioned
Rubenstein and Taylor (1997)[11] Nobelpharma 1 case, 10 year follow-up	Apical nerve transection resulting from implant placement: a 10 year follow-up report.	"Sensitivity" noted at 5 m post placement (1 m after Stage 11) Paraesthesia of lower lip at 6 m Complete resolution 2 years
Wismeijer *et al.* (1997)[12] 110 patients Straumann 102 followed-up to 16 months	Patients' perception of sensory disturbances of the mental nerve before and after implant surgery 110 patients.	10% reported at 16 months after surgery of which one third reported a disturbance before surgery, therefore reported incidence = 7%.
Bartling *et al.* (1999)[13] 94 patients (43 female, 51 male) 405 implants placed	The incidence of altered sensation of the mental nerve after mandibular implant placement.	8.5% at 1 week post placement. 0% at 121 days post placement.
Walton (2000)[14] 75 patients (47 female, 28 male)	Altered sensation associated with two Branemark implants in the anterior mandible	24% at 2 weeks post placement. 4% at 6 months post placement. 1% at 12 months post placement.
Von Arx *et al.* (2005)[15] 30 patients (15 female, 15 male) 51 sites augmented	Neurosensory disturbances following bone harvesting in the symphysis:	18.6% at 10 days post surgery when sutures removed. 8.1% at 6 months post surgery. 0.6% at 12 months post surgery.
Hillerup (2007)[16] 449 nerve injuries referred	Iatrogenic injury 3.6% due to implant surgery	33.2% IAN injuries.

Table 2 Summary of data on referral delay, radiographic proximity to the inferior alveolar nerve (IAN) canal, and mechanosensory function

	Frequency
Referral Delay:	
Within 24 hours	2
Within 48 hours	1
Within 3 days	1
6 days	2
12 days	1
<6 months	6
<6 months in total	13
7-12 months	7
>12 months	10
Radiographic proximity:	
Preparation breach of IAN canal	13
Implant breach of IAN canal	6
Either cross the IAN canal	6
Unknown	4
No breach or crossing of the IAN canal	1
Mechanosensory function:	
Increased	1
Normal	5
Reduced to none:	12
Slight decrease	2
Moderate decrease	8
Significant decrease	2
None	

*earlier referral = better prognosis :)

Summary points from paper

- Patients were aware of signing consent forms for the surgery in 11 cases and 8 of those felt they were not explicitly warned about nerve injury.
- Over 70% of patients were referred after six months post injury.
- CBCT (10%), dental pantomograph (50%) and long cone periapical radiographs (48%). However, no radiographic evidence pre- or postoperatively in 15% of cases!
- Permanent IAN neuropathy was sustained in 27 patients.
- 3 patients achieved resolution of neuropathy after removal of the implant within 30 hours of placement.

Persistent Idiopathic Facial Pain

- Other names: atypical facial pain, phantom toothache
- AO as a subform of PIFP?

- Persistent oral and/or facial pain with varying presentations, in the absence of clinical neurological deficit
- Characterised by daily (or near daily) pain that may spread to different locations
- May be part of a continuum with PPTTN

Epidemiology

- Rare
- Onset usually in middle age
- Female predominance
- Associated with central sensitivity syndrome, with comorbidities such as chronic widespread pain, fibromyalgia, and irritable bowel syndrome

- Associated with high levels of psychiatric comorbidity and psychosocial disability.

Clinical Presentation

- Oral and/or facial pain that is poorly localised, and does not follow the distribution of a peripheral nerve. Pain persists beyond the normal healing time.
- The pain is initially confined, but may subsequently spread in a non-dermatomal pattern.
- Onset of symptoms may not necessarily be associated with a physically traumatic event.
- Clinical neurological examination is normal.

- Symptoms vary considerably.
- Quality: often dull, aching or nagging, sometimes with sharp exacerbations, but other pain qualities may also be described.
- Mild to severe intensity.
- Duration: often continuous, and recurs daily.
- Aggravated by stress.
- Often co-existing chronic orofacial pain or headache.
- No dental cause identified.

ICHD-3 NOT ON EXAM

- Facial and/or oral pain fulfilling criteria B and C
- Recurring daily for >2 hours/day for >3 months
- Pain has both of the following characteristics:
  - poorly localized, and not following the distribution of a peripheral nerve
  - dull, aching or nagging quality
- Clinical neurological examination is normal
- A dental cause has been excluded by appropriate investigations
- Not better accounted for by another ICHD-3 diagnosis

Management

Difficult to manage.

Usually requires management by pain specialists in a multidisciplinary setting

May involve pharmacological therapy (e.g. tricyclic antidepressants, gabanoids, anticonvulsants, selective noradrenaline reuptake inhibitors), cognitive behavioural therapy and psychotherapy.

Trigeminal Neuralgia

* EXAM

- Other names: Tic douloureux.
- A severely painful disorder characterised by brief electric shock-like pain in the distribution of the trigeminal nerve, triggered by innocuous stimuli.

- **Epidemiology**
- Uncommon.
- Middle to old age.
- More common in females.

Is this a trigeminal neuropathy?

Aetiopathogenesis

- Classical Trigeminal Neuralgia – neurovascular conflict at the trigeminal nerve root entry zone
- Secondary Trigeminal Neuralgia – space-occupying lesion, multiple sclerosis or other abnormality
- Idiopathic Trigeminal Neuralgia – no obvious cause
    - Trigeminal nerve root atrophy (demyelination) and/or displacement leading to ectopic firing of neurons.

Clinical Presentation

Recurrent severe paroxysmal pain in one or more divisions of the trigeminal nerve

Usually unilateral

Quality: Electric shock, shooting, stabbing, sharp

Usually lasts a fraction of a second

Triggered by innocuous stimuli (e.g. light touch, talking, chewing)

Can present with concomitant background pain between the attacks

Other cranial neuralgias: These clinical features can also occur in the distribution of other sensory nerves (e.g. glossopharyngeal neuralgia, occipital neuralgia)

Diagnosis

- Clinical diagnosis
- Investigations – MRI to assess for cause
- Atypical presentations (e.g. bilateral pain in a younger patient, involvement of multiple cranial nerves, coexisting sensory or motor disturbances) may suggest other pathology and requires specialist assessment

Management

- Pharmacologic
- First line therapy is carbamazepine
- Severe adverse effects!
- E.g. Stevens-Johnson Syndrome and bone marrow depression

- Other medications
  - anticonvulsants, gabapentinoids and baclofen

- Neurosurgery
  - Microvascular decompression, rhizotomy, balloon compression, gamma knife

Trigeminal Post-Herpetic Neuralgia

- Other names: Post-herpetic trigeminal neuropathy

- Unilateral neuropathic facial pain in the distribution of the trigeminal nerve caused by herpes zoster
- Can persist for months to years.

- **25-50% of patients >50 years with herpes zoster develop PHN (≥3 months after healing of rash)**

Epidemiology

Risk factors for developing post-herpetic neuralgia include:

- Over 60 years of age.
- Severe herpes zoster rash.
- Severe pain during herpes zoster.
- Immunocompromised individuals.
- Ophthalmic involvement.

Clinical Presentation

Unilateral facial pain in the same trigeminal nerve branch(es) as the herpes zoster infection

Quality: Burning, itching

Moderate intensity

Pain may be continuous, or sometimes display intermittent shooting/electric shock-like attacks

Allodynia and hyperalgesia

Most commonly affects the ophthalmic division of the trigeminal nerve.

Management

- Difficult to manage

- The risk of developing post-herpetic neuralgia may be reduced by treating herpes zoster early, and vaccination of adults over 50 years of age to minimise varicella zoster virus reactivation.

- Topical therapy – e.g. capsaicin (watch the eyes!), lidocaine
- Systemic therapy – e.g. gabanoids, tricyclic antidepressants, serotonin-noradrenaline reuptake inhibitors

Oral Burning

“Jane”

- 55-year-old female who presents with a 4 month history of oral burning.
- Constant, predominantly affecting her dorsal tongue, and she feels that it is gradually getting worse.
- Hx Type 2 diabetes, asthma, gastroesophageal reflux, hypertension, depression and anxiety.
- Her daily medications include metformin, warfarin, escitalopram, pantoprazole, ramipril, fluticasone puffer
- Never smoker, 1–2 standard alcoholic beverages per week.

What are the possible causes of oral burning?

Most common?

Is it Burning Mouth Syndrome?

Is BMS the best name for it?

- Nomenclature
- Subjective xerostomia, dysaesthesia and dysgeusia (altered taste) are present in two-thirds of cases reported.

POSSIBLE CAUSES OF ORAL BURNING

A SPOONFUL OF ORAL MEDICINE

ORAL BURNING

ORALMEDICINEORALPATHOLOGY

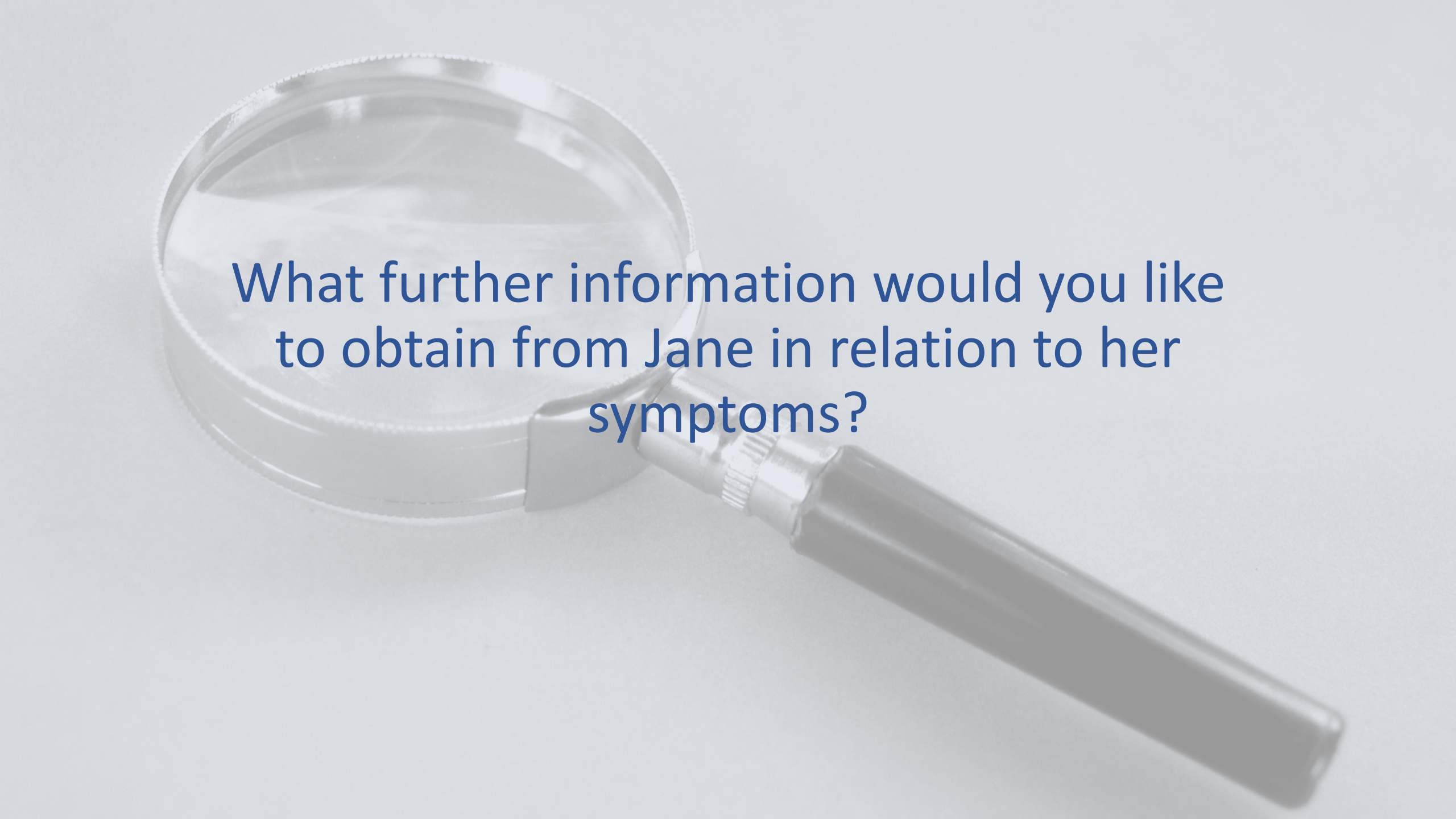
- INFECTIVE E.G. CANDIDOSIS, VIRAL
- IDIOPATHIC E.G.BURNING MOUTH SYNDROME ORAL DYSAESTHESIA
- NEOPLASTIC- E.G. CNS PATHOLOGY
- IMMUNE-MEDIATED E.G ORAL MUCOSAL DISEASES SUCH AS ORAL LICHEN PLANUS
- DEGENERATIVE E.G. ALZHEIMER'S
- SYSTEMIC E.G.NUTRITIONAL DEFICIENCIES, HEMATINIC DEFICIENCIES, HORMONAL CHANGES, AGE RELATED CHANGES, RENAL PROBEMS, PSYCHIATRIC ISSUES
- AUTOIMMUNE E.G. SJOGRENS
- METABOLIC E.G. DIABETES, THYROID. DYSFUNCTION
- IATROGENIC E.G. MEDICATION RELATED
- TRAUMATIC (IATROGENIC) E.G. RADIOTHERAPY, SURGERY
- TRAUMATIC E.G. DAMAGE FROM CAUSES SUCH AS GORD/ANOREXIA, DEHYDRATION

Most common cause

Thank you for reading!
ADr Amanda Phoon Nguyen

Possible causes of oral burning include:

- medication related (most common)
- traumatic, including iatrogenic causes (e.g radiotherapy to the oral cavity), or physical, thermal or chemical trauma
- autoimmune/immune mediated (e.g Sjogren's syndrome or oral lichen planus)
- neoplastic (e.g central nervous system pathology)
- idiopathic (e.g oral dysaesthesia or BMS)
- infective (e.g oral candidosis)
- degenerative (e.g Alzheimer's disease)
- systemic conditions (e.g nutritional deficiencies)
- metabolic conditions (e.g diabetes)



What further information would you like to obtain from Jane in relation to her symptoms?

Medical History

- Thorough!
- Consider by a range of systemic and local factors

- Some considerations include:
- Jane’s medications, diabetic control, asthma and hypertensive control
- nutritional deficiencies and diet

History taking

It is important to seek a history of the oral burning, including:

- Symptoms
- Date of onset
- Precipitating event
- Previous treatments trialled
- other investigations undertaken
- Quality of the pain
- Intensity of the symptoms
- Exacerbating or relieving factors.

Medications

- Medication-related adverse effect

- Extensive list
- Examples include: antihypertensives, antibiotics, neurological medications, cardiac medications, endocrine medications and psychotropic medications

- Most commonly implicated: ACE inhibitors and angiotensin receptor blockers

Supplements

- **Vitamin B_6 /pyridoxine**
  Doses ≥200 mg/day of vitamin B_6 have been associated with severe sensory peripheral neuropathies. Risk often arises from multiple products being taken all containing pyridoxine.

- **Zinc**
  Often associated with altered or impaired taste and smell. Intranasal zinc can cause anosmia. Doses ≥80 mg/day in clinical trials were associated with adverse prostate effects.

AM GM. The safety of commonly used vitamins and minerals. Aust Prescr 2021;44:119-23. https://doi.org/10.18773/austprescr.2021.029

NTUC FairPrice

Australian Government
Department of Health
Therapeutic Goods Administration

Home » Safety information » Alerts » All alerts

Share

Andrographis paniculata

Related information

- Products containing Andrographis paniculata

Safety advisory - potential to change sense of taste

20 May 2020

For info and resources about COVID-19, visit the COVID-19 Information Center.

- loss of taste
- metallic or soapy taste
- altered taste
- loss of appetite

Psychosocial history

- Psychological and psychiatric comorbidities are more prevalent in patients experiencing oral burning.

- Some patients with oral burning have a high incidence of anxiety, depression and personality disorders.

No supplements, no diet changes.

Dental History and Examination

- Associated symptoms?
  - Xerostomia, salivary gland hypofunction, dysaesthesia and dysgeusia
- A history of trauma
- Chemical, mechanical or thermal trauma
- Parafunctional habits- tongue thrusting
- Mucosal lesions/diseases such as oral infections (e.g oral candidosis), mucocutaneous lesions (e.g oral lichen planus) and other mucosal reactions such as hypersensitivity, contact allergy and lichenoid reactions can be associated with oral burning

You find out..

- Jane is partially edentulous and wears a full upper denture. She rarely removes it at night. Her upper denture is more than 10 years old and poorly fitting
- She also does not rinse out her mouth after steroid puffer use

- Clinically, you see creamy, semi-adherent plaques in the maxillary buccal sulcus

- The rest of her E/O and I/O examination is unremarkable
- Her CN exam reveal no remarkable findings

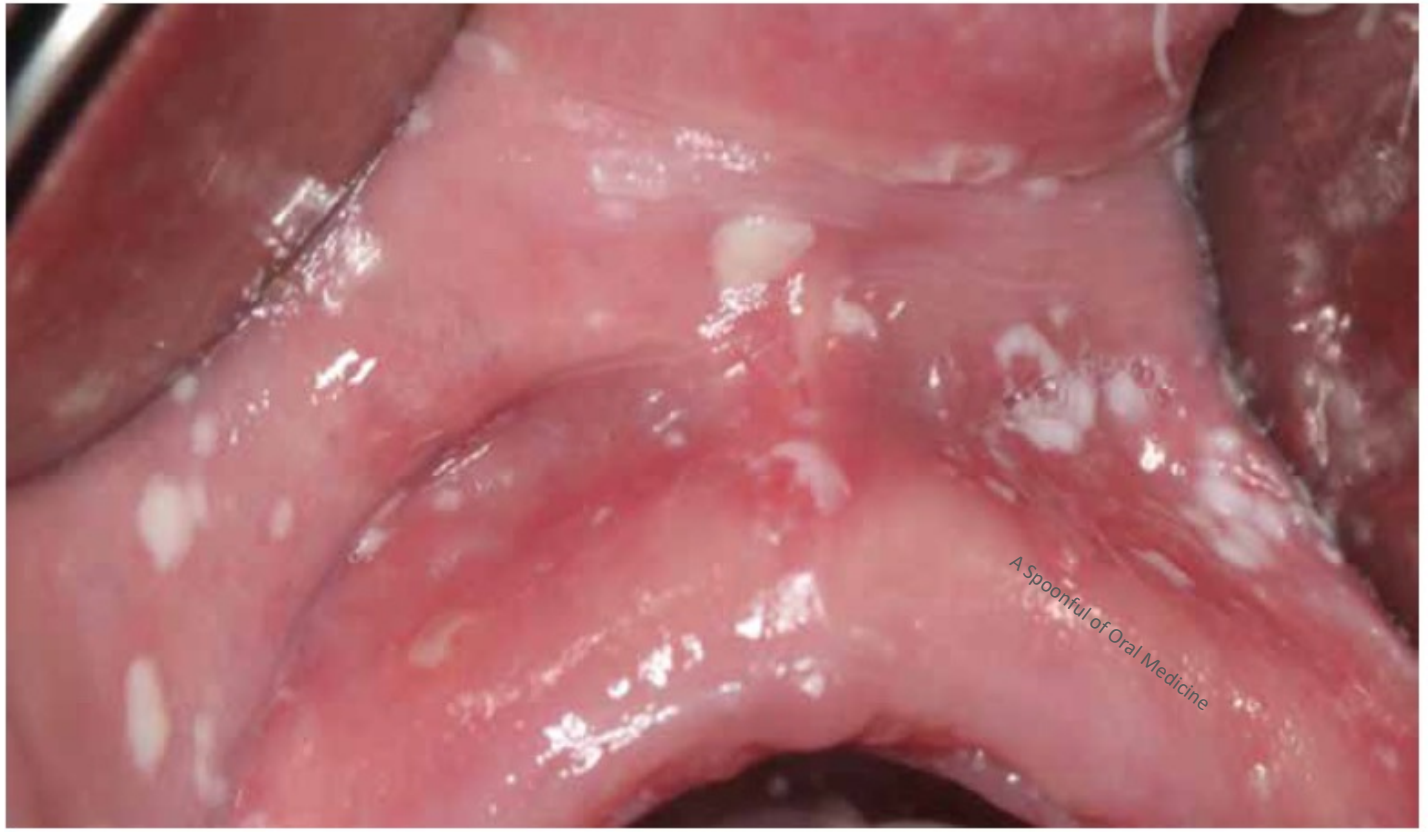


Figure 1. Creamy, semi-adherent plaques in the maxillary buccal sulcus

Based on her history and exam, what would be the most likely diagnosis?

What further tools or investigations would be helpful in establishing the cause of her oral burning?

Further investigations

- Serology and saliva testing (with limitations).
- Is there objective salivary gland hypofunction?

Consider:

- nutritional abnormalities (e.g vitamin B12, folic acid or iron
- deficiencies)
- Diabetes mellitus
- Hormonal deficiencies

Blood Tests

"Send to GP for blood tests"

FBC, iron studies, serum folate and vitamin B12 levels

- Vitamins B1, B2 and B6 and zinc, although a strong association has not been shown.
- *Serum zinc: not always useful
- Thyroid function test (if patient has other symptoms that support this suspicion.
- HbA1c

Other serology: Autoimmune investigations

- Sjogren's syndrome and systemic lupus erythematosus

- Based on Jane's history, I order a FBC, iron studies and tests for vitamin B12, serum folate and glycated haemoglobin. All serological tests are within normal limits.

- Assuming there are no signs of other systemic conditions, no cranial nerve abnormalities, and no oral pathology or mucosal lesions, what could her diagnosis be?

Burning Mouth Syndrome

- BMS
  - oral dysaesthesia or complex oral sensitivity disorder. Older terminology includes ‘stomatodynia’, ‘glossopyrosis’ or ‘glossodynia’.
  - Other “classifications”: Types 1,2,3. primary and secondary

- It is a <u>diagnosis of exclusion</u>
- Not actually a syndrome
- BMS is defined as ‘a chronic intraoral burning sensation that has no identifiable cause – either local or systemic condition
- “Normal” clinical signs and laboratory findings
- Intensity can fluctuate

Epidemiology

- Affects between 0.1% and 3.9% of the general population
- Can be seen in anyone, more commonly in postmenopausal women.
- The cause of BMS is poorly understood, but hypotheses include peripheral neuropathy or neuropathic pain, with central sensitisation.
- Varying levels of changes in somatosensory function in patients with this condition.

ICOP definition

6.1 Burning mouth syndrome (BMS)

An intraoral burning or dysaesthetic sensation, recurring daily for more than 2 hours per day for more than 3 months, without evident causative lesions on clinical examination and investigation.

Diagnostic criteria:

A. Oral pain fulfilling criteria B and C

B. Recurring daily for >2 hours per day for >3 months *if less than, probable BMS

C. Pain has both of the following characteristics:

- burning quality
- felt superficially in the oral mucosa

D. Oral mucosa is of normal appearance, and local or systemic causes have been excluded

E. Not better accounted for by another ICOP or ICHD-3 diagnosis.

- 6.1 implies that quantitative sensory testing has not been performed.

How is burning mouth syndrome (BMS) treated?

Management

- Need to be conscious of expectations and effect on quality of life.
- Chronic
- Management may be difficult
- Needs consideration of any perpetuating psychosocial factors.
- Typically referred to oral medicine specialist or other appropriate specialist
  - Multidisciplinary management considered e.g psychological support

Pharmacotherapy

Many pharmacological treatments have been trialled, including topical or systemic clonazepam, gabapentinoids, tricyclic antidepressants and antispasmodics.

- Success rates vary considerably.

Other

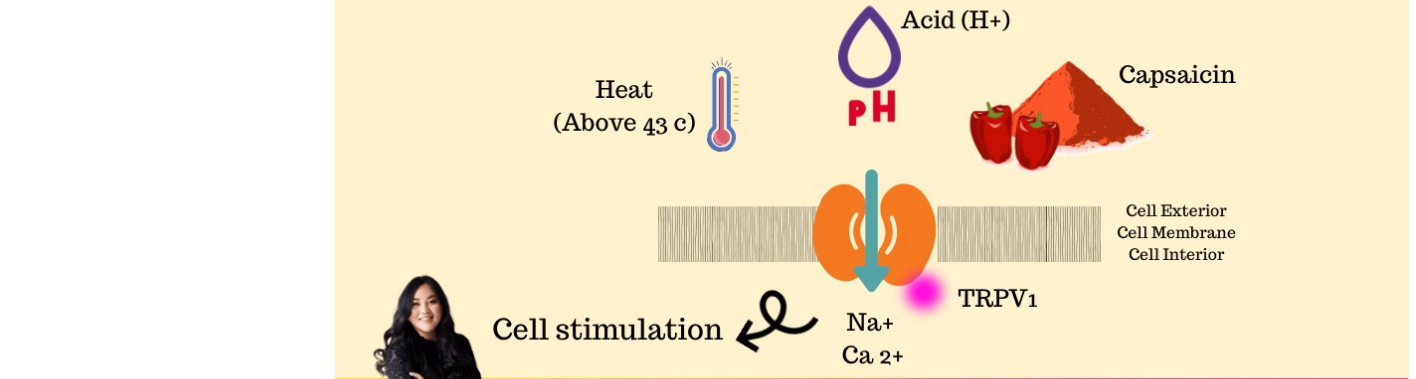
- Vitamin B12 or zinc supplementation
- Alpha-lipoic acid
- Palmitoylethanolamide
- Low-level laser therapy
- Capsaicin mouthwashes

To date, few effective treatments are available, and management of BMS can be challenging.

Studies have shown that there is up-regulation of TRPV1-positive nerve fibres in tongue mucosa in patients with Burning Mouth Syndrome (also known as oral dysaesthesia).

The vanilloid receptor-1 (TRPV1) is a voltage-dependent cation channel expressed by the unmyelinated C-nociceptive nerve fibres. The receptor may be activated by capsaicin (from chili peppers), heat and H+ (see image below)

Capsaicin binds to the TRPV1 receptor causing depolarization of the C-nociceptors. Prolonged activation of these neurons by capsaicin depletes pre-synaptic substance P and makes them less likely to to report pain.



Oral Dysaesthesia!

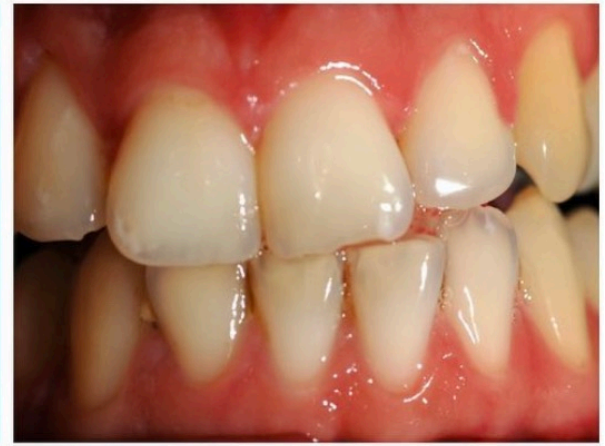
Dysperceptions in Patients with BMS

Adamo et al. 2023

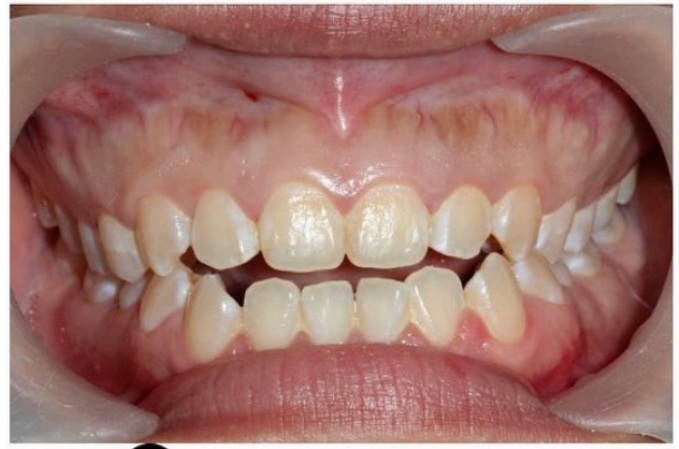
Burning
Intraoral Foreign Body Sensation
Xerostomia
Dysgeusia
Globus pharyngeus
Subjective change in tongue morphology
Sialorrhea
Itching
Tingling sensation
Occlusal Dysesthesia
Oral dyskinesia
Dysosmia
Subjective Halitosis

Originally described by Marbach in 1976 as a "mono-symptomatic hypochondriacal syndrome", more recently known as ‘Somatic Symptom Disorder". May have overlapping features similar to those with body dysmorphic disorder (BDD)

American Psychiatric Association's DSM V (2013)



WOULD YOU RECOGNISE OCCLUSAL DYSAESTHESIA OR PHANTOM BITE SYNDROME?



Unknown prevalence or incidence of this condition, where patients complain of bite discomfort without evident occlusal abnormalities

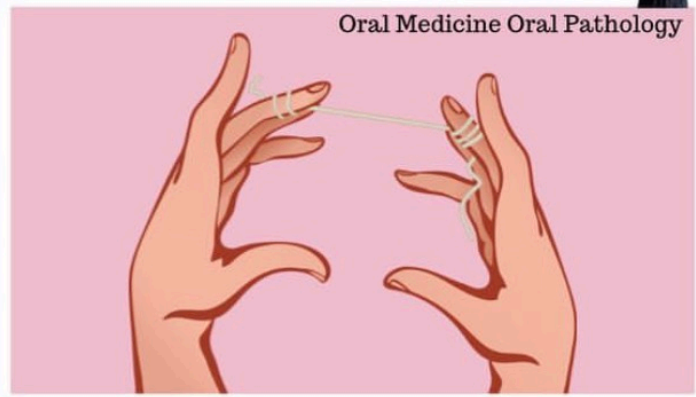
Can present at any age, in any gender, with the condition often lasting decades

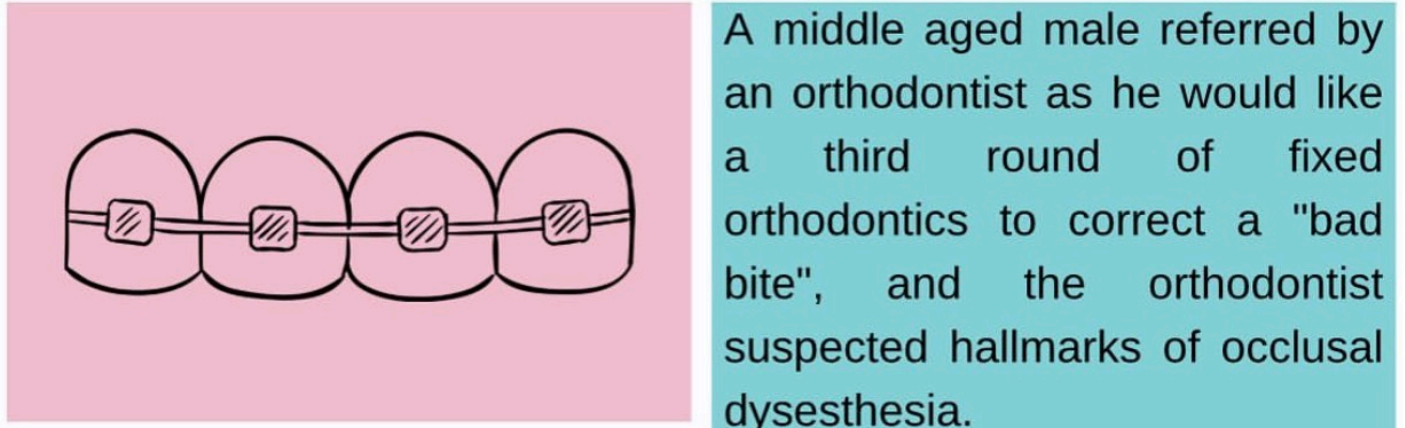
Oral Medicine Oral Pathology

A Spoonful of Oral Medicine

EXAMPLES: SOME OF MY CASES

A middle aged female referred to me as she has had something stuck in between her teeth for 5 years and cannot floss it out. She has seen multiple dentists and no one can reach it.





A middle aged male referred by an orthodontist as he would like a third round of fixed orthodontics to correct a "bad bite", and the orthodontist suspected hallmarks of occlusal dysesthesia.

A middle aged female seen as she had many complaints about her multiple dentures, and felt that the poor bite of her dentures were causing body asymmetry, with her clothes no longer fitting her well.

MARBACH'S DIAGNOSTIC INDICATORS OF PBS

Belief that severe symptoms all being due to their occlusion

Perception of a serious bite or cosmetic defect, with frustration that multiple clinicians cannot find the problem.

Perceived dental knowledge

-Often know dental jargon
-Will talk about their 'bite' or 'occlusal' problems, and suggest how they should be changed, or altered, to correct their problems.

Have study casts and detailed clinical records

May have numerous diagnostic casts that they have accumulated over the years.

Many photos and documents in attempt to explain the problem

Sustained delusion

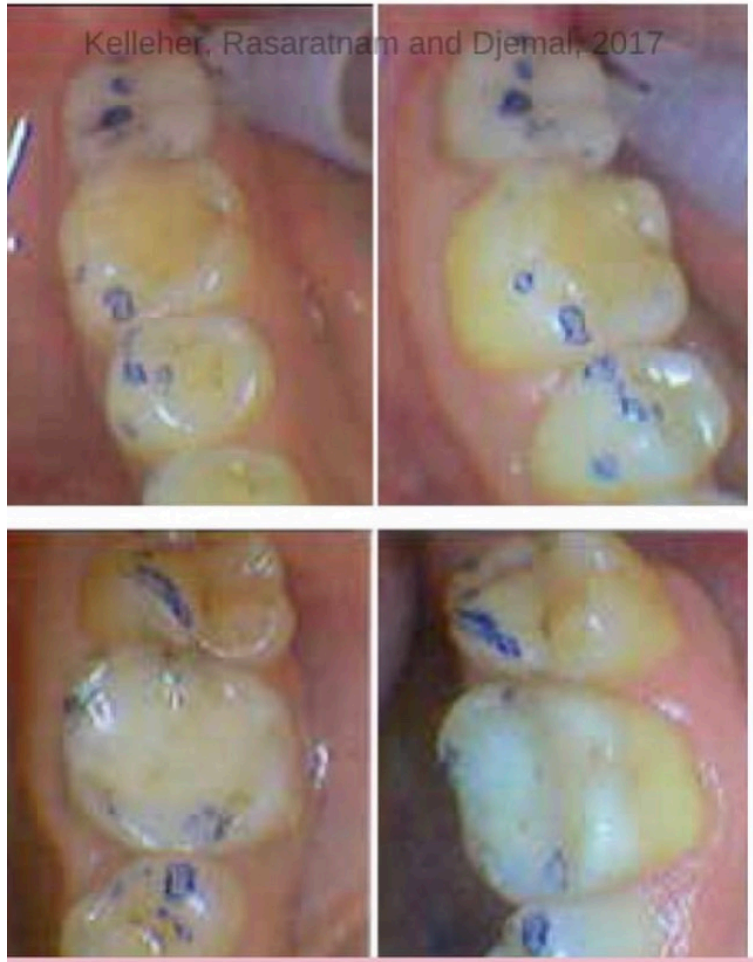
This condition usually lasts between 10-20 years.

While there may be some initial placebo effect, the symptoms are rarely improved by occlusal splint therapy, orthodontics, occlusal adjustments or 'equilibration', or prosthodontic interventions of different types by different dentists or various specialists.

May be seen more commonly in high socio-economic status patients (as they can afford to undergo repeated and extensive treatments to solve the problems), with above average intelligence who are often very articulate about what needs to be done.

Difficulty accepting diagnosis or accepting referral to psychiatry

(Adapted from Kelleher, Rasaratnam and Djemal, 2017)



Case: Photographs taken by the patient herself, highlighting the occlusal contacts that she had marked herself and that she 'knew needed to be ground down'. Apparently she did this with a Dremel DIY drill because 'no dentist could see what needed to be done'.

(Kelleher, Rasaratnam and Djemal, 2017)

FURTHER READING

Kelleher, M., Rasaratnam, L. and Djemal, S., 2017. The paradoxes of phantom bite syndrome or occlusal dysaesthesia ('dysesthesia'). Dental Update, 44(1), pp.8-32.

Tsukiyama Y, Yamada A, Kuwatsuru R, Koyano, K, 2012. Biopsychosocial assessment of occlusal dysaesthesia patients. Journal of Oral Rehabilitation, 39(8), pp.623-629.

MANAGEMENT

- Difficult as patients usually remain resolutely convinced that if they could only get someone competent enough to get their 'bite right' then all their problems would be solved.

- Multidisciplinary
- Medical specialty care


Questions?