# Saliva Hypernatrium: An Exploratory Scoping Review

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#### **PREFACE**

This report is an exploratory scoping review prepared for Dr. Alex Stockman, Rheumatology Clinic Footscray, Victoria at the request of Mr. Peter Racovalis (RACV Club, Melbourne, Victoria), and as a general public submission for the World Health Organization International Statistical Classification of Diseases and Related Health Problems, Volume 10:11<sup>th</sup> Edition, Australian Modification (ICD-10-AM)ICD-10-AM/ACHI/ACS Eleventh Edition). Support for this report was provided by the Public Health Palliative Care Unit, La Trobe University, and the Public Health Participatory Field Placement (PHE3PFP) Internship Program, La Trobe University, which is a capstone subject for all Public Health and Rehabilitation Counselling Students within the Bachelor of Health Sciences program, School of Psychology and Public Health, La Trobe University (Melbourne, Victoria, Australia).

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#### **ABSTRACT**

**Purpose:** This scoping review explored the available peer-reviewed literature, medical/health information management records, case studies, expert opinions in the field of otolaryngology, and other relevant resources relating to the condition of idiopathic persistent and excessive salty tasting saliva, labelled by the authors as 'Saliva Hypernatrium'. Method: An exploratory scoping review was conducted using the Arksey and O'Malley (2005) method to source key literature and other resources. **Results:** A total of 684 articles were initially identified using search terms derived from conditions relating to taste, salt and saliva. A total of 12 articles were found to be specifically relevant. Six key themes were discernible from the 12 articles which identified possible causes for salty saliva having no currently known/associated medical cause. **Discussion & Conclusion:** The overall findings identified numerous conditions which may cause persistent and excessive salty taste abnormalities and various possible treatment options. Given this review it is recommended that the term <u>Saliva Hypernatrium</u> is a more appropriate and specialist classification to be utilised for individuals experiencing an idiopathic and continuously salty taste, rather than current conventional generic terms that are potentially misleading. It is also recommended that further research be conducted in this field.

**Keywords:** Saliva, salty saliva, dysgeusia, taste disorder, phantogeusia, zinc, depression

#### INTRODUCTION

The sense of taste is important for physical and psychological health and quality of life. Human saliva comprised inorganic substances, proteins and water. It plays a role in lubrication, sensory perception of food, speech and digestion (Humphrey & Williamson, 2001). Taste (gustation) constitutes bitter, sweet, umami, sour and salty flavours. The tongue, epiglottis and soft palate are covered in taste buds or *lingual papillae* which allows humans to perceive different tastes. The principle fluid component of the taste receptor cells is saliva, and this plays a key role in taste perception/sensitivity (Matsuo, 2000). Another key role of saliva is to transport taste

substances and protect taste receptors. Any disturbances of saliva can change an individual's ability to perceive taste (Matsuo, 2000).

Whilst saliva and lingual papillae play an important role in the activation of taste receptors and ion channels, the fundamental understanding of how saliva exactly affects taste sensitivity is still largely unknown. The first process of taste perception is when saliva chemically interacts with substances within the mouth to produce a taste sensation (Purves, 1997). When disturbances in taste occur, and specifically with the salt taste, there are implications for the individual's quality of life, food choices and nutritional intake which can lead to secondary factors such as weight loss, impaired immunity, malnutrition and a decline in overall health (Boyce & Shone, 2006). It is expected that individuals experiencing taste aberrations will often wait before seeking medical advice and therefore a decrease in psychological health can also be observed in individuals due to the isolating nature of this condition.

There have been several popular quasi remedies which have gained traction in the public domain in recent times such as the miracle fruit *snsepalum dulcificum*, as seen via ABC news broadcasts (ABC News, 2017). The pulp of the miracle fruit contains *miraculin* which is a glycoprotein that binds to and activates sweet taste receptors — as a result, this berry has seen an increase in popularity due to its ability to change the perception of sour foods to sweet. Lipatova and Campolattaro (2016) discussed the reliability of such a miracle berry also being used for individuals with salt taste sensitivity. Whilst there appeared some possible benefits with this treatment, the findings were not sufficiently conclusive for consideration within this report.

#### **PURPOSE**

This project sought to identify, from the currently available scientific literature, possible causes and proposed remedies for persistent salt taste in human saliva. To date, excess sodium, the major component of salt in human saliva, is rarely reported in the medical literature unless associated with another known condition (e.g., Sjogren syndrome, dehydration, hypersalivation, bacteria, chemotherapy, nutritional deficiency, dry mouth, oral infection/oral bleeding, acid or bile reflux). The research question for this report is to discover what causes salty saliva (that is not the by-product of any other known medical conditions listed in this

report) and to identify what can remediate the condition which the authors have termed *Saliva Hypernatrium*. A case study example of the condition is presented at Appendix A.

#### **METHOD**

The scoping review framework developed by Arksey and O'Malley (2005) was utilised to retrieve key articles using a predetermined process of: (i) identifying the research question; (ii) identifying relevant articles; (iii) developing an inclusion/exclusion criterion for study selection; (iv) charting the data, and (v) collating, summarising and reporting the results.

The research question – "What are the potential causes of idiopathic persistent sodium in human saliva?" – identified the primary purpose of the research into the aetiology of saliva hypernatrium with no previously identified cause. By utilising the PICO (Population, Intervention, Comparison, Outcome) technique (Miller & Forrest, 2001). This enabled a thorough search strategy of available literature. The population studied for this current research was taste disorder, specifically individuals with a salt taste disorder (refer to Table 1 and Table 2). Remediation was investigated as the intervention. There were no comparative agents used in this study. Truncation and Boolean operators were used to incorporate all synonyms relating to the keywords searched.

**Table 1** *PICO research question* 

Population	Intervention/ Exposure	Intervention/ Exposure	Comparison	Outcome
"Tast*		Remediation	No comparison	All possible
Disorder*"				outcomes of taste
"Salt Tast*				remediation
Disorder*"				identified in the
				literature.

**Table 2**Database search terms and related synonyms

Database search terms	Synonyms
Tast* Palata* Flavo?r* OR Flav\$rr* (wild card symbol dependent on database search) Taste Bud* Taste Perception*	<ul> <li>Taste, tastes, tasting, tastes, tasty,</li> <li>Palate, palatable, palatableness</li> <li>Flavour, flavours, flavours, flavouring, flavouring, flavourless, flavorless</li> <li>Taste buds, taste bud</li> <li>Taste perception, taste perceptions</li> </ul>
Salt* "Sodium Chloride*" Sodium*  Saliva* OR Slobber*	- Salt, salty, salts - Sodium - Sodium chloride, sodium chlorides - Saliva, salivating, salivas - Slobbers, slobber,
OR Spittle*	slobbering - Spittle, spittling, spittles

The following databases utilised for searching and retrieving literature were: EMBASE (OVID), La Trobe Library Data Base, Proquest Central, MedLine. Cochrane Library, PubMed and Google Scholar. The appropriate search term was used depending on the database protocols (e.g., flavo?r\* was used for Medline database and flav\$rr\* was used for EMBASE [OVID] database). Duplicates and articles that were irrelevant to the research topic were removed (refer to Appendix A). The key articles that were identified contained different levels of relevance to the research topic which assisted with the identification and documentation of common themes found within each article.

Consultation with expert medical and allied health professionals in the field assisted in decisions about search terms and article relevance. Secondary searches were conducted in order to capture all relevant resources. The population studied for this supplementary research was patients identified with a *taste disorder* (refer to Table 3) with the additional medical conditions applied as the intervention. The databases utilised for searching and retrieving literature in the secondary search were: Medline, La Trobe Library and EMBASE (OVID).

 Table 3

 PICO terms for secondary search

Population	Intervention/ Exposure	Comparison	Outcome
"Tast* Disorder*" "Salt Tast* Disorder*"	Titanium plate in jaw	No comparison	This review of the literature is seeking to determine the taste complications of the diagnosable conditions.
"Tast* Disorder*" "Salt Tast* Disorder*"	Uric acid	No comparison	This review of the literature is seeking to determine the taste complications of the diagnosable conditions.
"Tast* Disorder*" "Salt Tast* Disorder*"	Gout	No comparison	This review of the literature is seeking to determine the taste complications of the diagnosable conditions.
"Tast* Disorder*" "Salt Tast* Disorder*"	Inflamed spleen	No comparison	This review of the literature is seeking to determine the taste complications of the diagnosable conditions.
"Tast* Disorder*" "Salt Tast* Disorder*"	Hydrocephalus	No comparison	This review of the literature is seeking to determine the taste complications of the diagnosable conditions.

#### **RESULTS**

A total of 684 articles were initially identified but many of these were not directly related to the specific topic regarding the causes of excessive sodium in human saliva. Nevertheless, 12 key articles (n = 12) were identified and considered to be relevant to the research topic (refer to Appendix B). These key articles enabled the identification and documentation of themes that could be used to categories the relevant literature being identified (refer to Table 3).

#### **Key themes**

Six main themes were identified within the literature review: (1) Idiopathic salt taste, (2) Phantogeusia, (3) Taste Disorder and/or Dysgeusia (4) Salt Taste sensitivity and/or perception (5) Zinc Deficiency and/or Supplements and (6) Depression. Table 4 lists the research authors and the associated themes identified within their work. Appendix B provides additional detail.

**Table 4** *Author research and associated identified themes* 

Author Research & Themes	1	2	3	4	5	6
Nagraj et al (2013)	✓	✓	✓	$\checkmark$	$\checkmark$	$\checkmark$
Ambaldhage et al (2014)	$\checkmark$	✓	$\checkmark$		<b>✓</b>	✓
Fark et al (2012)	✓	✓	<b>✓</b>			$\checkmark$
Henkin (1981)	✓	<b>✓</b>	<b>✓</b>	<b>✓</b>		
Hirai et al (2012)		<b>✓</b>	<b>✓</b>	<b>✓</b>	<b>✓</b>	
Maheswaran et al. (2014)		<b>✓</b>	<b>✓</b>		<b>✓</b>	$\checkmark$
Scully (2013)		<b>✓</b>	<b>✓</b>		<b>✓</b>	✓
Yagi et al. (2013)	<b>✓</b>		<b>✓</b>	<b>✓</b>		✓
Heinzerling et al (2011)			$\checkmark$	$\checkmark$	<b>✓</b>	
Hershkovich/Nagler(2004)	<b>✓</b>		$\checkmark$	<b>✓</b>		
Barasch & Epstein, J (2018)		$\checkmark$	$\checkmark$			
Henkin (1989)		$\checkmark$				
Total:	6	9	11	6	6	6

*Note*: Themes are: (1) Idiopathic salt taste, (2) Phantogeusia, (3) Taste Disorder and/or Dysgeusia, (4) Salt taste sensitivity and perception, (5) Zinc Deficiency and/or Supplements and (6) Depression. Abstracts for each article provided at Appendix C.

#### Theme 1: Idiopathic Salt Taste

Idiopathic indicates that the aetiology and pathogenesis of the condition is unknown. Numerous studies contained within this report discuss idiopathic taste disturbances as a key characteristic. In particular a study by Fark, Hummel, Haeher, Hummel and Nin (2012) discussed the three most frequent causes of taste disorders. The researchers identified that 34% of taste disorders resulted from idiopathic disturbances. Considering this, there have been few studies that reported the possible biological causes of the idiopathic taste disturbance and even fewer studies have reported on effective treatments. Ambaldhage, Puttabuddi, Nunsavath and Tummuru (2014) are one of the few that provide statistically significant data about effective treatments. The positive correlations between idiopathic or persistent taste disturbances and zinc deficiencies in some patients leads the authors to recommend patients take 50 mgs of zinc gluconate three times a day until the abnoral taste subsided or was relieved. This study also investigated the use of a-lipoic acid (200mg every eight hours) as a successful treatment option of idiopathic taste disorders. A number of other articles reviewed discuss the existence of

idiopathic taste disorders within their broader discussion and suggest the pathophysiology which may have led to the taste disturbance.

It is worth noting that these are contained within articles by Henkin (1981), Hershkovich and Naglet (2004) and Kumbargere et al. (2013) and all also discuss potential remedies for this presentation, however, most with little scientific evidence.

#### Theme 2: Phantogeusia

Phantogeusia (phanto / hallucination + geusis /taste) is a medical term used to describe a taste distortion when there is no external stimulus evident. There is very little scientifically known about the aetiology or treatments of phantogeusia. Barasch and Epstein (2018), Henkin (1989), Hirai et al (2012), Maheswaran (2014) and Scully (2013) are all authors identified in this report and all note phantogeusia. Three of these articles identify the possible role of the T2R taste receptor gene in identifying taste distortions in patients with no known cause. Further research would be required to identify similar patterns or homology, amongst the T2R genes in the tongue of patients with diagnosed phantogeusia. Such information could identify the pathogenesis of phantogeusia.

One purpose of this report is to identify the possible causes of an idiopathic salt taste. Phantogeusia by medical definition is an often metallic or salty taste in the mouth with no external stimulus found. Whilst a salt taste is the <u>least</u> common of taste disturbances (as observed through this report), it was discovered by Fark, Hummel, Haeher, Hummel and Nin (2012) that 38% of patients who presented with phantogeuia had a salt taste disturbance that was either an absent (lack of ability) of heightened sense of taste in any of the five tastes.

Other possible explanations for sporadic onset of phantogeusia could be multiple sclerosis and depression. Ambaldhage, Puttabuddy, Nunsavath and Tummuru (2014) discuss that given presentations of phantom taste complaints. The authors also noted that it is paramount to rule out any oral cavity problems and this may be an underlying cause. They also recommend an oral examination to be to determine any abnormalities in the microbial flora in the oral cavity.

#### Theme 3: Taste disorder and dysgeusia

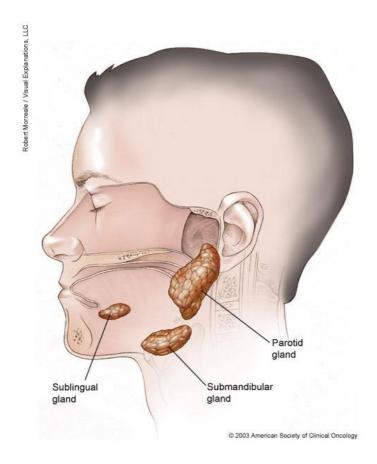
Taste disorder and dysgeusia is the most common theme across the majority of articles. Dysgeusia is a subcategory of a taste disorder and describes the symptom of distorted taste. An exploratory study by Kukbargere et al. (2013) only included studies in their report that identified taste disturbances of an idiopathic nature. Of the eleven articles in which taste disorders/dysgeusia occurred as a prominent theme, eight of these discuss the prevalence and incidence rate of taste disturbances within the community of their focus and categories this into which taste is altered (Table 4).

Yagi et al (2013) determines that a salt taste disturbance or dysgeusia affecting the salt taste perception is the least common of the possible disturbances. Of the eleven articles, three mention the correlation between drug use or drug cessation in drug-induced dysgeusia and the difficulty of treating this potential condition. Drug-induced dysgeusia is outside of the scope of this report on Saliva Hypernatirum, therefore, will not be explored in further detail.

One out of the eleven articles identified possible treatment options with 140 mg/day of zinc gluconate recommended for the treatment of idiopathic dysgeusia (as previously mentioned above in this report). This method as identified by Yagi et al (2013), found that within three months of continuous treatment, there may be an improvement to saliva flow and taste disorders. There was also a note made regarding the role of mood in the success of treatment; a decrease in mood was likely to lessen the outcome.

#### Theme 4: Salt taste sensitivity and perception

There is significant differentiation between an individual's perception and anatomical sensitivity to taste substances. There are differentiations in the anatomical role of saliva depending on taste buds, salivary glands and oral openings of the ducts (Hershkovich & Nagler, 2013).



**Figure 1**: Diagram of salivary glands. Reprinted from "Patient Care and Health Information" by American Society of Clinical Oncology, 2003, Copyright 1998-2019.

Three of the articles included in this report discuss the role of oral sensitivity in an individual's perception of the intensity of a particular taste. There are potential links between a persistent salty taste and sensitivity of taste buds. Kumbargere et al. (2013), found a way in which to identify an individual's sensitivity to salt taste by the sip and spit method where a concentration of either sweet, salty, butter or sour substances are gargled and then discarded. The patient is asked to identify the taste substance and then a threshold of taste is identified via a questionnaire.

Disturbances to an individual's taste sensitivity should be considered if the primary concern is an overwhelming/persistent taste. There is little-to-no substantial research done in this field in terms of the treatment options for individuals experiencing taste bud sensitivity for substances. Only one of the six articles to contain salt taste sensitivity as a theme mentions the suspected success of zinc supplements (zinc gluconate) for individual with increased salt taste sensitivity but more research is needed in this field in order for it to be conclusive (Yagi et al, 2013).

#### Theme 5: Zinc deficiency and/or zinc supplements

Six articles within this report have the theme of zinc supplements for treating an array of taste disturbances. Of the six articles (Table 4), zinc supplements were found to be successful in the treatment of taste disturbances regardless of the aetiology or trigger (cause), however, authors admit more research is needed in the field to be conclusive. Barasch and Epstein (2018) and Kumbargere et al. (2013) conclude that it is unclear as to what extent zinc deficiency affects taste but there is a correlation evident. At the present time there is insufficient data highlighting what leads to taste disorders and there is insufficient evidence showing whether supplements improve taste acuity. However, there was a strong correlation between idiopathic persistent salt taste and zinc treatment

The actual role of zinc benefits for taste disturbances was evaluated by Ambaldhage, Puttabuddi, Nunsavath and Tummuru (2014) in order to further the research in this field. It is known that zinc plays a vital role in the synthesis of the protein *gustin* which is linked to the building of taste buds. Biologically, a deficiency of zinc results in damaged gustatory papillae, that is, raised tongue structures that contain the taste buds) (Medical Dictionary, 2012)) and taste buds. This report acknowledges that there may be significant benefits of zinc supplements for a salt taste, however, whilst the research is strong when discussing the role zinc plays on the ability to taste, there needs to be more research for zinc and taste disorders specifically.

#### Theme 6: Depression

A discussed topic within the medical field is that there may be various causes of taste disturbances. This can include altered threshold of taste and sensory pathways or may also be as a result of various mental and physical disorders including depression. Of the twelve articles included in this report, six mention depression being an uncommon but significant cause of taste disturbances. Within these articles, there was no discussion regarding the exact reason as to why depression may cause taste disorders.

Of these six articles, three suggest the potential benefits of zinc supplements, especially in the instance when the depression symptoms are no longer present, but the taste disturbance persists. It is important to note that taste abnormalities that are caused by depression can occur during depressive episodes, whilst being treated or after the depression symptoms are no longer prominent.

#### **DISCUSSION AND RECOMMENDATIONS**

The current scoping review aimed to investigate *Saliva Hypernatirum* and the potential causes and current available remedies for a persistent salt taste not caused by any other medical diagnoses. The literature sources explored in this review, aimed to identify other known causes for excessive sodium in saliva and what has been proven to alleviate this sensation. Each source demonstrated that there are several possible medical reasons and potential treatments for *Saliva Hypernatrium*.

However, among all twelve key articles identified within this review, there were no results that could be considered absolute, because within every main theme identified (refer Table 4), there was little in-depth research into the correlation between the identified theme and taste disturbances. It is therefore recommended that further research should be conducted to investigate the broader causes of taste abnormalities and more clinical trials are needed to evaluate the effectiveness of treatments noted in this report particularly in relation to zinc supplements.

A second recommendation affirms the use of the term 'Salvia Hypernatrium'. Saliva Hypernatrium was uniquely developed by the current authors as there was no identified literature within the various databases regarding this specific condition nor utilisation of this specific term. The authors propose that this term Saliva Hypernatrium should be used in the future to describe idiopathic persistent salty saliva rather than a generic (and potentially misleading) broad term such as 'Dysgeusia', which broadly and rather crudely refers to any and various type of distortion of taste sensation, and thus insufficiently diagnostic for clinical nor research purposes.

Saliva Hypernatrium should also be used in preference to 'phantogeusia' meaning any hallucination in the sense of taste that is not produced by an external stimulus. 'Phantogeusia' is also a very broad term that may refer to any heightened salty saliva taste or no salty taste whatsoever — which again is insufficiently diagnostic for clinical or research purposes. Saliva Hypernatrium would appropriately form a specific and unique subcategory descriptor of 'dysgeusia' and/or 'phanotgeusia', however salvia hypernatrium would refer specifically to the presence of an idiopathic persistent and excessive salty saliva taste.

#### Limitations

The Arksey and O'Maley (2005) scoping review framework proved to be a key strength of the current scoping review. This strategy allowed for relevant articles to be searched, retrieved and effective inclusion/exclusion criteria to be applied that could assess the level of suitability and relevance of each publication. The main limitation for a more extensive report was the lack of available scientifically significant literature and search time restrictions. Time restrictions during this review meant that there was an inability to conduct third and fourth round database searches.

#### **CONCLUSION**

This project sought to identify from the currently available scientific literature, possible causes and proposed remedies for persistent salt taste in human saliva distinct from other known conditions/causes of salt taste disturbances. This article identified five possible causes (i) phantogeusia, (ii) taste disorders, (iii) dysgeusia, (iv) depression and (v) salt taste sensitivity. Salt taste disturbances are a seemingly rare occurrence but within the articles included in this report, there are noted chances of recovery/termination of symptoms given the right treatment.

Whilst the data concerned with the success of these treatments is scarce, most of the articles in this report have completed trials of exploratory reviews and purposeful treatment recommendations with high levels of success, including zink supplements and a-lipoic acid. Zinc supplements were highlighted in half of the articles within this report (Table 4) as a seemly effective treatment for salty saliva. It is recommended by the authors however that further research and case studies need to be identified to determine the success of zinc remediating taste disorders. Overall, a review of the twelve articles in this report provides an in-depth analysis and possible avenues of further exploration regarding taste disturbances, but collectively there is clearly a need for a more specific term to be utilised such as 'Saliva Hypernatrium,' so as to better label, more accurately describe and research this condition for the benefit of researchers, clinicians and patients.

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#### **APPENDIX A**

#### **Case Study Example:**

A 55-year-old male ("Peter") began, for no apparent reason, to have an increased salty taste in his mouth which has continued to persist beyond 12 months. The excessive sodium in his saliva is present in his mouth all day, every day, some days the taste is stronger than others and often overpowers all other taste sensations (e.g., "... a sweet lolly actually tastes salty"). Peter has an extensive medical history in which he has numerous active diagnoses. These include an inflamed spleen, history of depression, hydrocephalies, uric acid and gout, but none of these previous conditions appear to have any medical links to his <u>Saliva Hypernatrium</u>. He was initially treated with Nexium by his GP for gastroesophageal reflux. There was no change in the salty taste of his saliva. He subsequently underwent various assessments which included testing for bacterium *helicobacter pylori* and Sjogren syndrome's, but all results were negative. To date autoimmune specialists have not been able to determine the cause.

#### **APPENDIX B**

Search Strategy

#### Electronic databses searched utilising keywords and search terms (Table 1 & 2)

Embase (OVID), Proquest Central, MedLine, PubMed, La Trobe Research, SCOPUS, Cochrane Library and Google Scholar

N= 684 papers retrieved; articles screened by one author

N= 644 rejected after abstract appraisal

N= 27 rejected after papers critiqued

Articles that did not specifically address the potential causes of an idiopathic salt taste where rejected.

**Total results** 

N = 12

# APPENDIX C

# Literature and Thematic Coding

Article no.	Author/ Year / Title	Brief summary	Thematic coding
1	Ambaldhage et al (2014)  Taste disorders a review.	"For maintenance of the health of an individual, taste sensation is very important. It is an important sensation that serves to assess the nutritious content of food, support oral intake, and prevent ingestion of potentially toxic substances. Disturbances in the perception of taste can lead to loss of appetite, causing malnutrition and thus distressing both the physical and psychological well-being of the patient. Oral physicians are often the first clinicians who hear complaints about alteration in taste from the patients. In spite of the effect of taste changes on health, literature on the diagnosis, pathogenesis, and precise treatment of taste disorders are less. Taste changes may lead patients to seek inappropriate dental treatments. Proper diagnosis of the aetiology is the foremost step in the treatment of taste disorders. Thus, it is important that dental clinicians to be familiar with the various causes and proper management of taste changes. In this article, we have reviewed related articles focusing on taste disorders and their management, to provide a quick sketch for the clinicians. A detailed search was performed to identify the systematic reviews and research articles on taste disorders, using PUBMED and Cochrane. All the authors independently extracted data for analysis and review. Ultimately, 26 articles underwent a full text review. In conclusion, the research to date certainly offers us valid management strategies for taste disorders. Meanwhile, practical strategies with the highest success are needed for further intervention." (p.1)	1, 2, 3, 5, 6
2	Barasch, A., Epstein, J (2018) BMJ Best Practise: Evaluation of taste disorders	"Taste (gustation) is attributed to sensory information received from the oral cavity and oropharynx and is the perception accompanying oral intake. Taste comprises five basic taste qualities: sweet, bitter, salty, sour, and umami. Umami (pleasant, good, desirable taste), identified a decade ago, is what the Japanese call the perception for monosodium glutamate; its taste resembles that of chicken bouillon. Additional taste functions have been identified, with fat "taste" that may be mediated by receptor transduction and nonspecific transport across the cell membrane and spicy "sensation" (e.g., capsaicin, ginger) mediated by small nerve fibers. However, the common sense of the word "taste" often means "flavor," which in turn is a composite of several (nongustatory) chemosensory afferents including taste, spice, texture, and temperature (both mediated by the trigeminal nerve - i.e., cranial nerve V) and, importantly, olfaction (more precisely, retro-olfaction) perceived while eating. As such, a patient's complaints about taste loss do not always reflect the underlying pathology. Taste testing is mandatory to exclude a primary olfactory or trigeminal nerve pathology that manifests clinically to the patient as a problem with taste. According to testing with taste strips, 5.3% of the people considered as healthy have hypogeusia although very few have complete ageusia. The evaluation of a patient presenting with taste dysfunction comprises the patient's history (including drug intake and nutritional elements), a detailed clinical exam (including oral and dental exam), and investigations to determine the underlying aetiology."	2, 3
3	Fark, Hummel, Hummel, Haeher & Nin (2012)	"Aim of this retrospective study was to obtain information about the frequency of taste disorders, their most frequent causes, and typical symptoms. A total of 491 out of 4,680 patients (presenting for the first time between 1998 and 2011) exhibited taste disorders (10.5 %). All patients underwent a thorough physical otorhinolaryngological examination including detailed assessment of smell and taste functions. The three most	1, 2, 3, 6

	Characteristics of taste disorder	frequent causes of disorders were idiopathic (34 %), posttraumatic (24 %), and postoperative (15 %). Patients with idiopathic and postoperative taste disorders complained mainly about hypogeusia and parageusia; in comparison, patients with posttraumatic taste disorders exhibited a relatively higher degree of partial, local, or complete ageusia. Among patients with phantogeusia and parageusia, 38 % reported salty, and 22 % mixed sensations like bitter–salty or sour– sweet. In approximately 1/3 of this group of patients the cause of dysgeusia is unknown. Twenty-one percent of the patients complained of qualitative rather than quantitative taste problems."	
4	Heinzerling, Stieger, Bult & Smit (2011)  Individually Modified Saliva Delivery Changes the Perceived Intensity of Saltiness and Sourness	"Individuals vary largely in their salivary flow and composition and given the importance of saliva on perception of taste, this might influence how the tastant stimuli are perceived. We therefore hypothesise that altering the individual salivary flow rates has an impact on the perceived taste intensity. In this study, we investigated the role of saliva amount on the perceived taste intensity by excluding parotid saliva and adding artificial saliva close to the parotid duct at pre-set flow rates. Significant decreases in perception with increasing salivary flow rates were observed for citric acid and sodium chloride. This can partially be explained by a dilution effect which is in line with previous studies on detectable concentration differences. However, since the bitterness and sweetness remained unaffected by the salivary flow conditions and the dilution effect was comparable to that of saltiness, further explanation is needed. Furthermore, we investigated whether the suppression of taste intensity in binary mixtures (taste—taste interactions) could possibly be caused by the increased salivary flow rate induced by an additional taste attribute. The results show, however, that suppression of taste intensity in binary mixtures was not affected by the rate of salivation. This was more likely to be explained by psychophysics. "	3, 4, 5
5	Henkin (1981)  Taste Disorder- Questions and Answers	"This article is a review of all medical forums in which individuals have asked online doctors about their symptoms of excessive salt taste in their mouth. A doctor has responded and provided insight into the potential causes and remedies for their concerns. The medical professionals discussed idiopathic phantogeusia and the primary cause for their symptoms with small doses of dopamine inhibitors, thioridazine (Mallari) hydrochloride or haloperidol (Haldol) being successful in treatment in small doses."	1, 2, 3, 4
6	Henkin (1989) Finding the cause of taste disorder	"The main discussion of this document is a presentation of idiopathic taste disorder. The identified explanation for this symptom were phantogeusia or zinc deficiency with the best treatment options being Haloperidol, thioridazine and pimozide."	2
7	Hershkovich & Nagler (2004)  Biochemical analysis of saliva and taste acuity evaluation in patients with burning mouth syndrome, xerostamia and/or gustatory disturbances	"Objective: In the current study, we performed taste and salivary analysis on patients suffering from burning mouth syndrome and xerostomia or taste disturbances. Study design: A total of 180 patients who complained of idiopathic burning mouth syndrome (BMS) and taste aberrations and/or xerostomia that may accompany BMS were evaluated. These patients were compared with 90 healthy, age- and sex-matched controls. Salivary flow rate, biochemical and immunological analysis and taste acuity by the forced-choice drop technique were performed for all subjects. These analyses were found to be conclusive in distinguishing controls from patients with complaints. Results: The great similarity of both salivary and taste analysis in the BMS, taste aberration and xerostomia groups, which were significantly different from the results obtained in the control group, was found to be the most striking result. Higher salivary concentrations in the experimental group were consistent with a lower saliva (water) flow rate. Conclusion: An oral neuropathy and/or neurological transduction interruption induced by salivary compositional alterations is suggested as the possible aetiology for the complaints. "	1, 3, 4

8 Hirai, Takoa, Onoda, Kokubun & Ikeda (2012)

"Objectives: The taste receptor gene family T2R has been implicated in the sensation of bitter taste. Phantogeusia is a spontaneous abnormal taste with no external stimulus. We analyzed the expression of T2R taste receptor genes in the tongues of patients with phantogeusia to assess their role in the pathogenesis of phantogeusia Methods: We obtained specimens from 43 patients with phantogeusia and 24 normal volunteers by scraping the foliate papillae and examined these specimens for the expression of 10 T2R taste receptor genes using reverse transcription-polymerase chain reaction and electrophoresis. Results: The expression rate (subjects with detectable expression) of the 10 taste receptor genes in the healthy subjects ranged from 16.7% to 100%; 3 receptor genes were found in 50% or fewer of these subjects. In the patients with phantogeusia, the expression rate was increased significantly compared to that in the healthy control subjects for 3 of the 10 receptor genes examined. Conclusions: Our results show that the expression rate of some of the T2R taste receptor genes was increased significantly in patients with phantogeusia. These results suggest that increased expression of taste receptor genes is involved in the pathogenesis of phantogeusia; this finding may contribute to elucidation of the mechanism of this disorder."

2, 3, 4, 5

9 Nagraj, Puttabuddi, Nunsavath & Tummuru (2013)

> Taste Disorders: A Review

"Background: The sense of taste is very much essential to the overall health of the individual. It is a necessary component to enjoying one's food, which in turn provides nutrition to an individual. Any disturbance in taste perception can hamper the quality of life in such patients by influencing their appetite, body weight and psychological well-being. Taste disorders have been treated using different modalities of treatment and there is no consensus for the best intervention. Hence this Cochrane systematic review was undertaken. Objectives To assess the effects of interventions for the management of patients with taste disturbances. Search methods We searched the Cochrane Oral Health Group Trials Register (to 5 March 2014), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 1, 2014), MEDLINE via OVID (1948 to 5 March 2014), EMBASE via OVID (1980 to 5 March 2014), CINAHL via EBSCO (1980 to 5 March 2014) and AMED via OVID (1985 to 5 March 2014). We also searched the relevant clinical trial registries and conference of proceedings fromthe International Association Dental Research/American Association of Dental Research (to 5 March 2014), Association for Research in Otolaryngology (to 5 March 2014), the US National Institutes of Health Trials Register (to 5 March 2014), metaRegister of Controlled Trials (mRCT) (to 5March 2014), World Health Organization's International Clinical Trials Registry Platform (WHO ICTRP) (to 5 March 2014) and International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Clinical Trials Portal (to 5 March 2014). Selection criteria We included all randomised controlled trials (RCTs) comparing any pharmacological agent with a control intervention or any nonpharmacological agent with a control intervention. We also included cross-over trials in the review. Data collection and analysis: Two authors independently, and in duplicate, assessed the quality of trials and extracted data. Wherever possible, we contacted study authors for additional information. We collected adverse events information from the trials."

1, 2, 3, 4, 5, 6

**10.** Maheswaran et al. (2014)

Gustory Dysfunction "Tastes in humans provide a vital tool for screening soluble chemicals for food evaluation, selection, and avoidance of potentially toxic substances. Taste or gustatory dysfunctions are implicated in loss of appetite, unintended weight loss, malnutrition, and reduced quality of life. Dental practitioners are often the first clinicians to be presented with complaints about taste dysfunction. This brief review provides a summary of the common causes of taste disorders, problems associated with assessing taste function in a clinical setting and management options available to the dental practitioner. The chemosensory functions of taste and smell play a vital role in human physiology. They determine the flavor and palatability of foods and beverages, the selection of nutrients essential for life, and the warning

2, 3, 5, 6

of toxic vapors, fire, and spoiled foodstuffs. Chemosensory dysfunctions have serious implications for the preservation of oral and systemic health, with dramatic effects on quality-of-life. [sup][1] Patients frequently report increased use of sugar and salt to compensate for diminished sense of taste, a practice that is detrimental to those with diabetes mellitus or hypertension."

**11** Scully (2013)

Learn more about taste disorder

Frequently, when individuals say they cannot taste, the problem is that they cannot appreciate the flavour of food. As the aroma of food contributes to about 75% of its flavour, these individuals have often suffered a loss of smell ability only. True taste disorders are uncommon, but may present as a loss of taste, or as an abnormal taste in the mouth, an unpleasant taste, or even an electrical sensation. Taste impairment ranges from distorted taste to a complete loss of taste – ageusia, hypogeusia (partial taste loss), and dysgeusia (persistent abnormal taste). Some have termed the phantom sensation of bitterness as 'phantogeusia' (Table 22.1). Disorders of taste sense can be distressing and sometimes incapacitating, and can even cause anorexia and depression.

2, 3, 5, 6

Yagi et al. (2013)

The use of Zinc in the Treatment of Taste Disorders

"Although in 1990s the number of patients with taste disorders in USA and Japan was over 1 million people each year, it is annually increasing. Taste disorders are caused by several factors such as genetic disease, head trauma, structural changes, glossodynia, cancer, lifestyle, and others. The role of zinc in the treatment of taste disorders has been studied since the oral administration of zinc by patients was reported to improve their taste disorders. Carbonic anhydrase (CA), a zinc metalloenzyme, has also been studied in association with taste disorders, since the regulation of serum CA levels was shown to influence the effect of orally administrated zinc in the treatment of taste disorders. Zinc is an essential trace element that contributes to the active centre of approximately 300 enzymes. Studies have revealed that zinc is involved in various physiological functions. Moreover, some medications have been shown to induce a zinc deficiency, which has been associated with a variety of clinical conditions. Hence, since the relationship between taste disorder and serum zinc concentration have been discussed for long time, taste disorder may be useful in diagnosing zinc deficiency. Moreover, the appearance of the medicine of the zinc-containing supplement type contributes to the treatment of taste disorders due to zinc deficiency. Orally administered zinc has been shown to directly stimulate food intake via neuropeptide in the hypothalamus. Therefore, zinc administration may be potentially used to treat taste disorders as well as several other diseases by stimulating feeding."

1, 3, 4, 6

*Note*: Thematic Codes: (1) Idiopathic salt taste, (2) Phantogeusia, (3) Taste Disorder and/or Dysgeusia, (4) Salt Taste sensitivity and/or perception, (5) Zinc Deficiency and/or Supplements, and (6) Depression.

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