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# Dysgeusia

## A review in the context of COVID-19



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### ABSTRACT

**Background.** Taste disorders in general, and dysgeusia in particular, are relatively common disorders that may be a sign of a more complex acute or chronic medical condition. During the COVID-19 pandemic, taste disorders have found their way into the realm of general as well as specialty dentistry, with significance in screening for patients who potentially may have the virus.

**Types of Studies Reviewed.** The authors searched electronic databases (PubMed, Embase, Web of Science, Google Scholar) for studies focused on dysgeusia, ageusia, and other taste disorders and their relationship to local and systemic causes.

**Results.** The authors found pertinent literature explaining the normal physiology of taste sensation, proposals for suggested new tastes, presence of gustatory receptors in remote tissues of the body, and etiology and pathophysiology of taste disorders, in addition to the valuable knowledge gained about gustatory disorders in the context of COVID-19. Along with olfactory disorders, taste disorders are one of the earliest suggestive symptoms of COVID-19 infection.

**Conclusions.** Gustatory disorders are the result of local or systemic etiology or both. Newer taste sensations, such as calcium and fat tastes, have been discovered, as well as taste receptors that are remote from the oropharyngeal area. Literature published during the COVID-19 pandemic to date reinforces the significance of early detection of potential patients with COVID-19 by means of screening for recent-onset taste disorders.

**Practical Implications.** Timely screening and identification of potential gustatory disorders are paramount for the dental care practitioner to aid in the early diagnosis of COVID-19 and other serious systemic disorders.

**Key Words.** Dysgeusia; gustation; virus; taste disorders; infections; burning mouth syndrome; COVID-19; drug-induced; taste receptors; newer tastes.

JADA 2022;153(3):251-264

<https://doi.org/10.1016/j.adaj.2021.08.009>

The 5 special senses described in the literature are taste, smell, vision, hearing, and equilibrium.<sup>1-3</sup> Taste is proposed to be guiding an organism toward appropriate recognition and consumption of nutrients. It also helps the organism in the prevention of consumption of materials that are toxic or difficult to digest. In humans, 5 types of basic tastes have been identified, namely sour, salt, sweet, bitter, and umami.<sup>4</sup> Newer tastes, such as metallic, fatty, and calcium, have also been identified.<sup>5</sup> Each taste sensation supposedly gravitates people toward specific foods. For example, sweet-tasting foods inherently announce the carbohydrate content that then could serve as an energy source. The sensation of salt controls sodium intake and aids in the maintenance of water and electrolyte content. Although bitter is supposed to warn against poisonous food content, there are several cultures and nations in the world that savor a bitter taste in foods that are not poisonous. It would be interesting to see why bitter tastants (any chemical that elicits a taste sensation) form a substantial component of traditional medicines, such as those used in Ayurveda, the Indian medical science. Differences in taste perceptions and preferences are seen as resulting from genetic variations, personal experiences, cultural diversity, psychology, personality traits, and, of course, pathologic changes in taste sensations. The physiology of gustation is complex, involving multiple receptors, pathways, and brain centers. In our comprehensive review, we summarized the

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various subtopics under which the sensation of gustation is discussed and the possible mechanisms of gustatory disorders. In the context of the COVID-19 pandemic, the topic of dysgeusia assumes paramount importance, especially because it is one of the first symptoms of COVID-19 to appear. The astute and educated dental care practitioner is one of the earliest to pick up symptoms of dysgeusia.

## NEUROANATOMY AND PHYSIOLOGY OF GUSTATION

The transmission of taste signals from various sites in the oral cavity to the brain stem is believed to occur through cranial nerves, namely, facial, glossopharyngeal, and vagus.<sup>6</sup> The location and course of the first-, second-, and third-order neurons, their corresponding ganglia and nuclei, and the cortical centers of taste have been well elucidated (Figure 1).<sup>7</sup> Third-order neurons carrying the taste sensations from the thalamus also project into the orbitofrontal cortex, termed the *secondary taste cortex*, which is responsible for the reward value of taste.<sup>8-10</sup> The difficulty in pinpointing a single cortical area as responsible for taste comes from the varied results that functional imaging studies have yielded in the past few decades.<sup>11-13</sup>

The functional unit of taste is the taste bud, located on the various tongue papillae. The relative location of the taste buds on these papillae are shown in Figure 2. Taste buds have receptors, which are the biological transducers that convert chemical energy from tastants into electrical energy, facilitating the transmission of these taste impulses.<sup>7,14,15</sup>

Taste buds are present on the tongue, palate, pharynx, epiglottis, and esophagus.<sup>7</sup> Remote taste receptors have been reported in tissues from the gastrointestinal tract, bladder, brain, respiratory tract, heart, buccal mucosa, sinuses, white blood cells, bone marrow, thyroid, keratinocytes, and testicles.<sup>16-24</sup> The functional specificity of taste cells has prompted researchers to divide them into the following 5 types: type I (glialike), type II (bitter, sweet, umami), type III (sour), type IV (pluripotent), and type V (marginal cells).<sup>25,26</sup> The older concept of “taste mapping”—representing the tongue diagrammatically and showing the relative concentrations of specific taste sensations—has been replaced largely with the newer concept that all areas of the tongue represent the different tastes almost equally (Figure 3).<sup>27</sup> A similar topographic arrangement in the cerebral cortex has also been proposed.<sup>28</sup>

## GUSTATION AS RELATED TO OLFACTION: THE CONCEPT OF FLAVOR

Flavor is defined as a blend of taste, smell, and touch, acting as a premonition on the safety and quality of the food being consumed.<sup>29-31</sup> It is a perception with multiple inputs from additional sensations, including vision and hearing.<sup>32,33</sup> The robust interaction between the gustatory and olfactory areas of the brain is well known.<sup>34-37</sup> There is a blend of olfaction, gustation, and texture in most of the taste perception (Figure 4).<sup>38,39</sup> The orbitofrontal cortex, the basolateral amygdala, and the insular cortex have been reported to be associated with interactions among odor, taste, and flavor.<sup>40,41</sup> Odors conditioning and enhancing specific tastes, such as saltiness, have been reported in studies during the past few decades.<sup>42,43</sup>

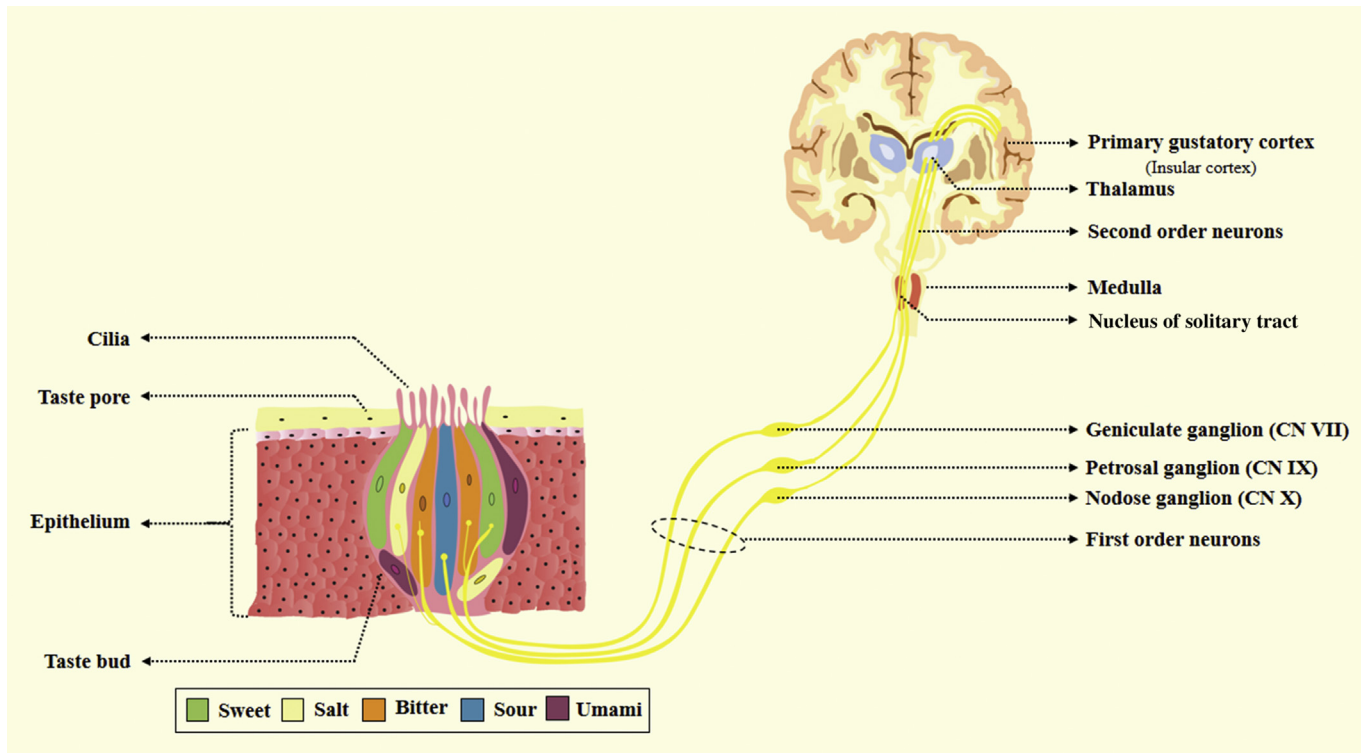
## INDIVIDUAL TASTE SENSATIONS

The analgesic effect of sweet sensation may have a role in activating the endogenous opioid system; in addition, endocannabinoids have been reported to change taste perception by means of modulating sweet receptors.<sup>44</sup> This might explain the preference for sweet foods in patients with chronic pain syndromes, such as burning mouth syndrome (BMS). The role of sweet sensation in regulating food intake, glucose homeostasis, and energy balance may be instrumental in the discovery of newer drugs for diseases such as diabetes and obesity.<sup>45-47</sup> Sour taste is generally considered to be an indicator of acid (hydrogen ions). The presence of salt-sensing cells in the taste buds in fungiform papillae and their absence in the circumvallate papillae, has been confirmed.<sup>48-50</sup> Salt sensation has a crucial role to play in the normal development of the gustatory circuits in the central nervous system.<sup>51</sup> The role of tongue cleaning and its positive effect on the identification of salt sensation has been well known.<sup>52,53</sup> Researchers have proposed that salt sensitivity in people with normal blood pressure could predict their susceptibility to hypertension.<sup>54-56</sup>

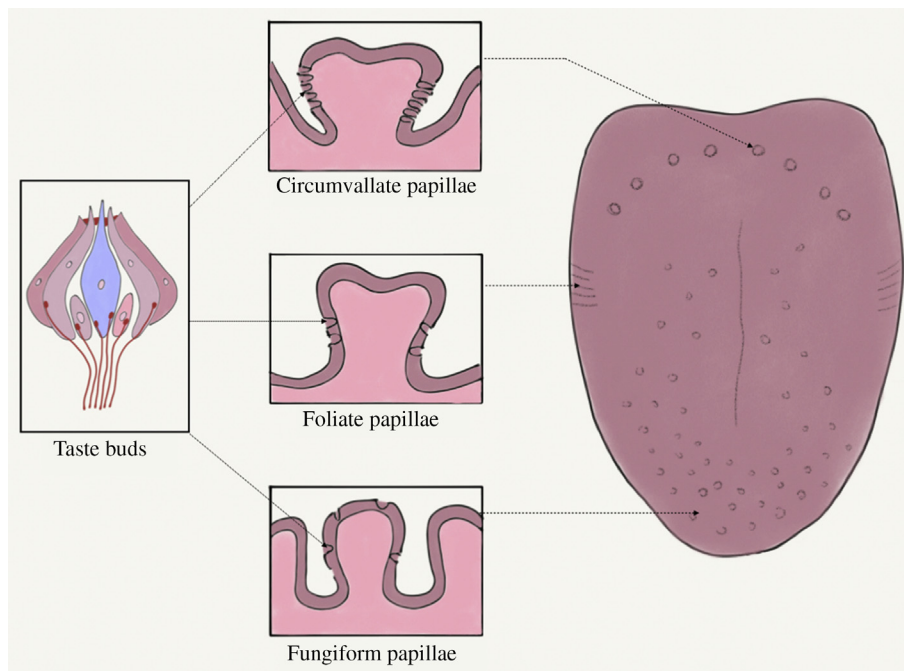
Umami (glutamic acid) occurs naturally in a variety of foods, including tomatoes, seafood, and egg yolks.<sup>57,58</sup> Multiple umami receptors have been identified in rodents in the past 2 decades, and the taste is mediated through glossopharyngeal nerve.<sup>59-64</sup> Certain published articles refer to a

### ABBREVIATION KEY

- BMS:** Burning mouth syndrome.
- SARS-CoV-2:** Severe acute respiratory syndrome coronavirus 2.
- SS:** Sjögren syndrome.

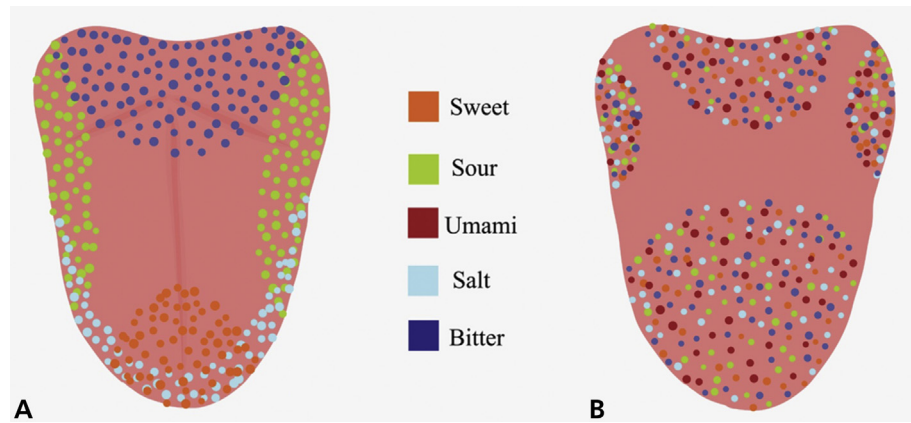


**Figure 1.** Neuroanatomy of the taste pathway. CN: Cranial nerve. Figure courtesy of Swetha Kannan and Dr. Sita Mahalakshmi Baddireddy.

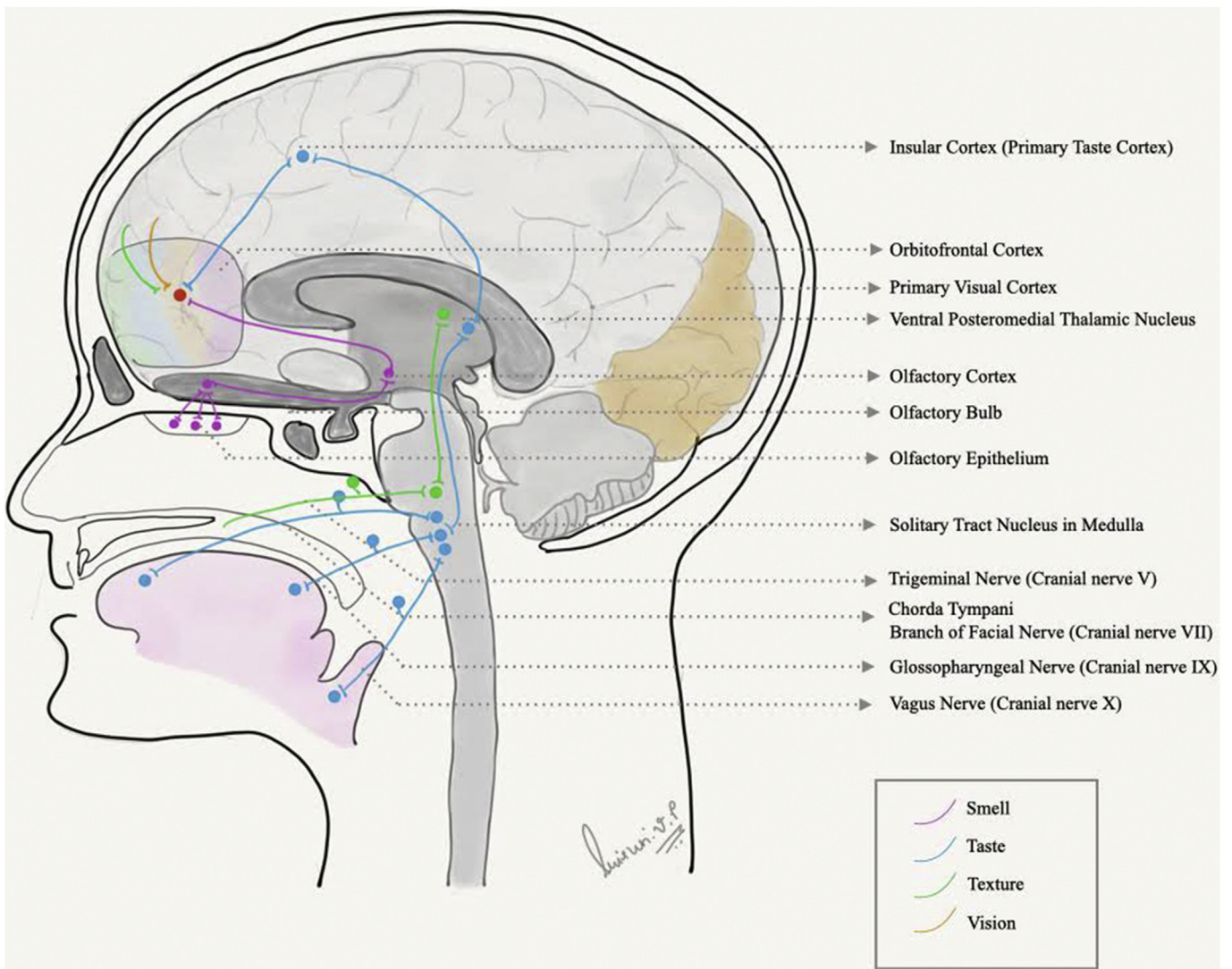


**Figure 2.** Location of taste buds within various papillae. Figure courtesy of Dr. Srishti Parekh.

positive aspect of umami taste in terms of improvement of nutritional intake, enhancement of habitual choice of healthy foods, and improvement of food flavor.<sup>65-69</sup> The proposed negative effects of umami include hepatotoxicity, asthma, migraine headache, and central nervous system damage.<sup>70-73</sup> Owing to the finding that a reduction in umami taste perception may trigger loss of appetite, subsequent health issues, and reduction in the quality of life, testing for this taste has been proposed to be one of the key tools for managing the treatment of patients with dysgeusia.<sup>74</sup>



**Figure 3.** Anatomic distribution of specific taste receptors. **A.** Older concept of concentration of specific taste receptors at specific sites of the tongue (taste mapping). **B.** Newer concept of clusters of blends of taste receptors localizing at specific anatomic areas of the tongue. Figure courtesy of Swetha Kannan and Dr. Sita Mahalakshmi Baddireddy.



**Figure 4.** Pathways of olfaction, gustation, and the concept of flavor. Figure courtesy of Dr. Srishti Parekh.

The bitter taste receptors that are present in the respiratory tract have been proposed to have crucial roles in the body's defense mechanism against possible invading microbes.<sup>16</sup> Their role in the possible detection of certain bacteria and in the process of bronchodilation has also been proposed

and could become a novel target for therapy. Through the research of the previous 2 decades, we have come to know that approximately 30 taste receptor genes code for the bitter taste.<sup>17,75</sup> Fat taste (oleogustus) is one of the newer described taste sensations and is proposed to be carried via the glossopharyngeal and chorda tympani nerves.<sup>76-78</sup> Calcium taste has been found to help modulate calcium metabolism, intake, and homeostasis in mammals and has specific receptors coded via multiple genes.<sup>79-84</sup>

## EPIDEMIOLOGY OF GUSTATORY DISORDERS

Prevalence rates for taste disorders have been reported as ranging from 0.6% through 20% in the literature.<sup>85-87</sup> Researchers have found that, in general, women perceive taste better.<sup>88</sup> Researchers from multiple studies have reported that there is a decline in taste perception with increasing age.<sup>88,89</sup> There is a reported reduction in prevalence of taste dysfunctions with aging in women compared with men.<sup>85</sup> Researchers reported a strange association of taste disorders with educational attainment, in that the higher the level of education, the lower the incidence of taste disorders.<sup>85</sup> There was similar association reported with olfactory disorders; however, the researchers failed to provide a plausible explanation for this phenomena. Sour tasting ability was consistently found to be most affected with aging.<sup>90</sup> Liu and colleagues<sup>85</sup> found that Black participants in their study had a higher prevalence of taste disorders, suggesting an association between ethnicity and taste disorders.

## ETIOPATHOLOGY OF GUSTATORY DISORDERS

Taste disorders can range from dysgeusia (abnormal taste sensation) to ageusia (complete loss of taste sensation), depending on the degree of severity of the taste abnormality. The various terms used for the types of taste disorders are provided in Table 1. The total experience of taste has olfaction as a major component.<sup>91,92</sup> Most apparent gustatory dysfunctions (such as dysgeusia) are the result of impaired olfaction (for example, allergies) rather than gustation.<sup>91-94</sup> Abnormalities in transport (inability of the tastant to reach the receptor), gustatory unit (abnormality of peripheral sensory organs), and neuronal unit (such as damage to the peripheral or central nervous system) are the mechanisms of such gustatory dysfunctions.<sup>92,95-97</sup> In the oral cavity, the gustatory receptors can be exposed to pathologies (such as inflammation) or artificial restorative dental materials (such as acrylic) and can thereby affect gustation.<sup>92,98-100</sup>

Several genes and their associated receptors (for example, *ENaC*, *T1R*, *T2R*, *TAS2R*, and *TRPV1*) have been identified as coding for specific taste sensations.<sup>25,45,108-114</sup> Conceivably, any sequence variation in these receptors and genes can cause a taste disorder. Researchers have reported that more than 50% of the drugs prescribed routinely in the United States cause some level of a taste disorder.<sup>115</sup> The various medications that can cause dysgeusia are summarized in Table 2. Aging is also a factor for reduction in taste sensation.<sup>92</sup>

## RELEVANCE IN MEDICINE AND DENTISTRY

As alluded to earlier, multiple cranial nerves are involved in the sensation of taste, including trigeminal, facial, glossopharyngeal, and vagus. Mediators of chemosensation of taste include, but are not limited to, the tongue (factors are health of the tongue and papillae of the tongue), saliva (quality, quantity), oral mucous membrane, nerves, and neurotransmitters.<sup>95</sup> Consequently, any alterations in these factors can contribute to a change in taste perception. As would be expected, dentists are among the first clinicians that patients approach with taste disorders. The most common symptoms in these patients include dysgeusia, phantogeusia, or an accompanying burning sensation.<sup>121</sup> Many dental-related factors have been hypothesized to cause taste alterations, including local trauma, medications, infections, dental restorations, and salivary gland dysfunctions.<sup>95</sup> Radiation therapy of the head and neck area have also been found to result in dysgeusia.<sup>122</sup> Dysgeusia is also associated with several orofacial pain conditions, such as BMS and temporomandibular disorders.<sup>123-126</sup> Researchers have also reported an association between dysgeusia and other conditions, such as Bell palsy and Guillain-Barré syndrome.<sup>127-129</sup> The relevance of dysgeusia in the context of the COVID-19 pandemic is explained below.

**Table 1.** Taste terminology.

TASTE TERMINOLOGY	DESCRIPTION
<b>Ageusia</b>	Complete loss of taste sensation <sup>38,102</sup>
<b>Aliageusia</b>	Bad taste to normally considered “good” taste <sup>105</sup>
<b>Dysgeusia</b>	General term used for any abnormal taste sensation <sup>104</sup>
<b>Gustation</b>	The scientific term given for the process of taste sensation <sup>95</sup>
<b>Hypergeusia</b>	Increased sense of taste <sup>38</sup>
<b>Hypogeusia</b>	Diminished sense of taste <sup>38</sup>
<b>Parageusia</b>	Altered taste sensation in the presence of a tastant <sup>103</sup>
<b>Phantogeusia</b>	Taste sensation in the absence of a tastant <sup>103</sup>
<b>Presbygeusia</b>	An alteration in taste sensation considered as a result of aging <sup>106</sup>
<b>Tastant</b>	Any chemical that elicits taste sensation <sup>101</sup>
<b>Taste Agnosia</b>	A term used when a person cannot recognize a taste sensation, independent of normalcy in intellect, sensory processing, and linguistic abilities <sup>107</sup>

### Systemic conditions affecting taste

Dysgeusia has been found to be associated with several systemic medical conditions, however, the mechanisms contributing to it are diverse. Systemic diseases commonly exhibiting taste dysfunction include, but are not limited to, Sjögren syndrome (SS), chronic renal failure, end-stage liver disease, endocrine disturbances (such as diabetes mellitus and thyroid disorders), genetic disorders (familial dysautonomia), neurologic disorders, and psychiatric conditions. Alterations in taste function have also been found in pregnant and postmenopausal women.<sup>99</sup> The conditions that are related to taste disorders etiopathologically and their proposed mechanisms are summarized in [Table 3](#).

### Dysgeusia in autoimmune disorders

There are contradicting reports on the association between reduced salivary flow and taste disorders.<sup>171-173</sup> SS, an autoimmune disorder with associated xerostomia, has been reported to include taste disorders as well.<sup>174</sup> The mechanisms proposed to explain dysgeusia associated with SS include systemic inflammation, interaction with genetic pathways that influence gustation, an increase in the taste threshold, and small fiber neuropathy.<sup>175,176</sup> Possibly due to the fact that sweet taste is independent of salivation, there was minimal alteration of the sweet taste in patients with SS.<sup>177,178</sup> Other dysgeusia-associated disorders include autoimmune encephalitis, myasthenia gravis, systemic lupus erythematosus, multiple sclerosis, and Parkinson disease.<sup>132,179-182</sup>

### Dysgeusia associated with BMS

Taste alterations accompany BMS.<sup>183-185</sup> These include phantogeusia (bitter, metallic, burning quality).<sup>186-189</sup> The qualities of bitter and metallic that patients report as being associated with BMS are thought to be from cranial nerve IX being disinhibited subsequent to possible damage or hypofunction of the chorda tympani nerve.<sup>185,187,189</sup> Consequently, it has been reported in the literature that patients with BMS find relief from symptoms when consuming sugary or sweet foods, which possibly stimulate a hypofunctioning chorda tympani nerve.<sup>188,190,191</sup> There is a reported increase in taste threshold (that is, decreased taste sensitivity) of all tastes except umami.<sup>187,192-194</sup> An increased fungiform papillae count has been proposed to be associated with “supertasters,” who are apparently at a higher risk of having BMS.<sup>195,196</sup> Psychological factors have also been implicated in dysgeusia related to BMS.<sup>197,198</sup>

### Dysgeusia associated with infections

Diseases such as upper respiratory infections, viral hepatitis, and oral cavity infections have been associated with an increase in the detection and identification of individual taste stimuli via taste buds, thereby causing dysgeusia.<sup>132,199-203</sup> Inflammation has been found to disrupt normal cell turnover of taste buds, leading to dysgeusia.<sup>132</sup> HIV infections and subsequent therapies have been reported to be associated with dysgeusia.<sup>155,204,205</sup> Other infections reportedly associated with

**Table 2.** Types of medications causing dysgeusia.

TYPE OF DRUGS	REPRESENTATIVE DRUGS
Antianemic	Ferric carboxymaltose <sup>116-118</sup>
Antibacterial	Ampicillin, ciprofloxacin, metronidazole <sup>116-118</sup>
Anticholinergic	Atropine <sup>116-118</sup>
Antidepressant	Amitriptyline, clomipramine, desipramine <sup>116-118</sup>
Antiepileptic	Carbamazepine, phenytoin <sup>116-118</sup>
Antifungal	Griseofulvin <sup>116-118</sup>
Antihistamine and Decongestant	Chlorphenamine, loratadine <sup>116-118</sup>
Antihypertensive and Cardiac Medications	Acetazolamide, amiodarone, propranolol, nitroglycerine <sup>116-120</sup>
Anti-inflammatory	Dexamethasone <sup>116-118</sup>
Antimanic	Lithium <sup>116-118</sup>
Antimigraine	Dihydroergotamine, sumatriptan <sup>116-118</sup>
Antineoplastic	Cisplatin, methotrexate, vincristine <sup>116-118</sup>
Antiparkinsonian	Levodopa <sup>116-118</sup>
Antipsychotic	Clozapine, trifluoperazine <sup>116-118</sup>
Antiviral	Aciclovir, interferon <sup>116-118</sup>
Anxiolytic	Alprazolam, buspirone <sup>116-118</sup>
Bronchodilator	Bitolterol <sup>116-118</sup>
Central Nervous System Stimulant	Amphetamine <sup>116-118</sup>
Drugs for Peptic Ulcer and Gastroesophageal Reflux Disease	Esomeprazole <sup>116-118</sup>
Hypnotic	Eszopiclone, zolpidem <sup>116-118</sup>
Hypoglycemic	Metformin <sup>116-118</sup>
Intestinal Anti-infective	Miconazole <sup>116-118</sup>
Intestinal Anti-inflammatory	Budesonide <sup>116-118</sup>
Lipid-Lowering	Atorvastatin <sup>116-118</sup>
Muscle Relaxant	Baclofen, dantrolene <sup>116-118</sup>
Pancreatic Enzyme Preparation	Pancrelipase <sup>116-118</sup>
Stomatologic Preparation	Hydrogen peroxide <sup>116-118</sup>
Smoking-Cessation Aids	Nicotine <sup>116-118</sup>
Thyroid	Levothyroxine sodium, propylthiouracil <sup>116-118</sup>

dysgeusia include, but are not limited to, rhinosinusitis, hepatitis E, *Helicobacter pylori*, Lyme disease, leprosy, syphilis, and cytomegalovirus.<sup>99,136,206,207</sup>

## COVID-19 AND DYSGEUSIA

Although the COVID-19 pandemic began in early 2020, the data regarding anosmia and dysgeusia in the context of the association, pathogenesis, diagnosis, and prognosis of the disease are limited.<sup>208</sup> A change in taste sensation is one of the earliest symptoms of COVID-19 and many times precedes the actual respiratory manifestation of the disease.<sup>209-213</sup> Multiple hypotheses have been proposed in an attempt to explain the mechanistic pathway of how the COVID-19 organism affects gustatory senses.<sup>209,214</sup> These include, but are not limited to, damage to the central nervous system, abnormal zinc homeostasis, angiotensin-converting enzyme 2 receptor manifestation, and increased proinflammatory cytokines.<sup>14,139-143</sup> There is a high rate of sensation recovery rate in patients with COVID-19; however, whether more permanent loss of taste sensation occurs with COVID-19 infection is still unclear.<sup>215,216</sup> The higher prevalence of taste alterations associated with the pandemic has prompted organizations, such as the European Centre for Disease Prevention and



**Table 3.** Etiology of gustatory disorders: proposed mechanisms of action.

DISORDER	PROPOSED MECHANISM OF ACTION
<b>Aging and Cognition</b> <sup>130,131</sup>	Cognitive processes like language and memory involved in taste recognition impaired in older adults
	Increased bitterness threshold in older adults
<b>Bacterial Infections</b> <sup>132</sup>	Alteration of gene expression by stimulation of Toll-like receptors
<b>Cancer Treatment</b> <sup>97</sup>	Damage to and reduced turnover of taste receptor cells
	Loss of connectivity between receptor cells and neurons
	Direct neuronal damage
<b>Chronic Kidney Disease</b> <sup>96,133,134</sup>	Raised salivary sodium, salivary urea, salivary bicarbonate
	Reduced salivary zinc
	Uremic toxins
	Altered axon conduction
	Impaired cognitive status
<b>Chronic Rhinosinusitis</b> <sup>135,136</sup>	Altered functionality of T2R38 bitter taste receptor
<b>Chemotherapy</b> <sup>137</sup>	Alteration in zinc metabolism
	Carbonic anhydrase VI deficiency
<b>Consumption of Ethyl Alcohol</b> <sup>14,138</sup>	Change in taste receptor sensitivity
	Abnormalities in micronutrient absorption
	Changes in saliva
	Alterations in taste buds
<b>COVID-19 (Severe Acute Respiratory Syndrome Coronavirus 2)</b> <sup>14,139-144</sup>	Damage to the central nervous system by the virus attaching to the angiotensin-converting enzyme 2 receptors in glial cells and spinal neurons
	Abnormal zinc homeostasis
	Increased proinflammatory cytokines
	Direct infection of cells in the tongue
	Consequences of obstruction of taste cells chemesthesis due to inflammation and damage to cranial nerves VII, IX, and X
<b>Diabetes Mellitus</b> <sup>145-147</sup>	Xerostomia secondary to diabetes mellitus
	Diabetic neuropathy
	Reduction in innervation of taste buds
	Increased apoptosis of taste buds
	Lower density of the fungiform papillae
<b>Drug Induced</b> <sup>14,99,148-150</sup>	Hyposalivation
	Adverse effects on taste receptors
	Adverse effects on taste neural pathway
	Abnormalities in neurotransmitter function
<b>Fungal Infection, <i>Candida albicans</i></b> <sup>99,151</sup>	Mechanical barrier by formation of pseudomembrane due to disproportional overgrowth
<b>Genetic Disorders</b> <sup>14,152-154</sup>	Reduced number of taste papillae
	Changes in taste phenotypes
<b>HIV and AIDS</b> <sup>99,155,156</sup>	Directly affects gustatory neurons
	Development of local lesions
	Xerostomia
	Chemosensory alterations secondary to antiretroviral therapy
	Neuronal degeneration secondary to HIV leukoencephalopathy
<b>Liver Failure</b> <sup>99</sup>	Deficiency of vitamins B and C, zinc, and copper

**Table 3.** Continued

DISORDER	PROPOSED MECHANISM OF ACTION
<b>Multiple Sclerosis</b> <sup>99,157</sup>	Central demyelination
<b>Neurodegenerative Disorders (Dementia, Alzheimer, and Others)</b> <sup>147,158,159</sup>	Insular atrophy
	Secondary to effect of medications used for management
	Amyloid deposition in the insula and amygdala
<b>Parkinson Disease</b> <sup>147,160-162</sup>	Neurodegenerative changes of the frontal operculum or orbitofrontal cortex
	Other concomitant factors: depression, poor oral hygiene, gastrointestinal disease, and zinc deficiency
<b>Rheumatoid Arthritis</b> <sup>163</sup>	Neuropathy of terminal nerve fibers
	Neuropathy secondary to rheumatoid arthritis drugs
<b>Sjögren Syndrome</b> <sup>99</sup>	Excessive dryness of the oral cavity and hyperviscosity of saliva
<b>Stroke</b> <sup>99,164</sup>	Injury to the insula, pons, thalamus, midbrain, and internal capsule
<b>Systemic Lupus Erythematosus</b> <sup>165,166</sup>	Proinflammatory cytokines
	Inhibition of turnover of taste bud cells by inflammation
<b>Thyroid Disorder</b> <sup>167,168</sup>	Zinc deficiency secondary to thyroid disease
	Reduced cognitive functions
<b>Toxins: Environmental</b> <sup>169,170</sup>	Chemosensory dysfunction
	Disruption of the cell membrane resulting in alteration in energy production by the chemosensory cells
	Modification of channels and secondary messenger system in chemosensory receptor cells
	Affecting blood flow to tongue
	Direct interaction with saliva
	Heavy metals concentration in saliva producing harmful changes in taste receptors
<b>Viral Diseases</b> <sup>14,132</sup>	Nasal blockage; increased mucus production
	Changes in olfaction
	Inflammation affecting gene expression in taste bud cells

Control, the American Academy of Otolaryngology—Head and Neck Surgery, and the World Health Organization, to recommend using taste alterations as a screening test and, when screening is positive, advise the clinician to test the patient for COVID-19.<sup>215,217,218</sup> Identification of gustatory disturbances in the absence of concomitant symptoms of COVID-19 is of paramount importance to alerting physicians about the possibility of COVID-19, thereby aiding in self-isolating and testing the people affected.<sup>219</sup>

### DIAGNOSTIC TESTING FOR GUSTATION

Various taste-testing measures have been used, ranging from simple chairside testing to objective and measured research-level testing for gustation. In a clinical setup, a clinician may use such tastants as a dilute aqueous solution of sugar, salt, sour, and bitter, although this method is subjective and lacks sufficient sensitivity and specificity. Objective testing can be done using electrogustometry, filter paper disk method, whole mouth method, taste strip method, and e-tongue method. The electrogustometry method tests the taste sensory nerves by means of measuring the electrical taste threshold in the soft-tissue areas supplied via the chorda tympani, greater petrosal, and glossopharyngeal nerves.<sup>220,221</sup> In the filter paper disk method, test disks soaked in different taste solutions are placed on selected parts of the oral cavity.<sup>220,221</sup> These tastes are applied in increasing concentration grades from the lowest to a point at which the participant identifies the correct taste. In the whole mouth method, participants rinse their mouths with multiple taste solutions with various molarities and identify the taste. This method also tests for taste threshold.<sup>220</sup>

In the taste strip method, filter paper strips embedded with the 4 basic tastes are used and placed in successive graded concentrations at the center of the anterior one-third of the tongue when the tongue is protruded.<sup>220,222</sup> The e-tongue method is used mostly in pharmaceutical research and uses an analytical instrument that helps interpret the data from a sensor that records electrical signals from the taste fibers.<sup>223</sup>

### **EFFECT OF TASTE AND SMELL DISORDERS ON NUTRITION**

Taste and smell sensations are closely interrelated when it comes to motivation to eat, enjoyment of food, and activation of the satiety centers of the brain.<sup>224</sup> Induction of abnormal eating habits by means of olfactory disorders has been documented in the literature.<sup>29</sup> Although taste disorders have been reported to affect body weight, evidence is lacking to link the former to an abnormal nutritional status.<sup>224,225</sup> Patients with dysgeusia do not have a substantial change in their nutrition.<sup>226,227</sup> Systemic diseases, such as diabetes and hypertension, have been reported to be associated with changes in the chemosensory function.<sup>224</sup> There have also been several researchers who have linked ageusia to weight loss and even to anorexia.<sup>228-234</sup> Substantial taste disturbances, such as reduction in taste acuity, abnormal salt taste, and metallic taste, have been proposed to cause noncompliance with recommended renal diets in patients with chronic kidney disease, thereby culminating in nutritional deficiencies.<sup>235-237</sup> The effect of dysgeusia on quality of life has been reported as varied in the literature, however, most researchers report considerable reductions in quality of life.<sup>238,239</sup>

### **CLINICAL PEARLS**

Taste alterations, as one of the earliest symptoms of COVID-19, can be used as a simple, early screening tool for detection of the infection. The simplest tool for testing olfaction is to have the patient respond to smelling small amounts of odorants that are easily identifiable, such as coffee, fragrant soap, or other nonpungent material. Care must be taken to ascertain that the patient is not experiencing any nasal blockage, such as would occur with a common cold. In conjunction, the sense of taste can be checked easily by means of simply having the patient taste (sip and spit) dilute aqueous solutions of sugar, salt, sour, and bitter, as we mentioned above. The use of commercially available, more sophisticated kits is not usually warranted, as these techniques, such as electro-gustometry, may be beyond the purview of a routine dental practice setup. Clinicians should understand that it is unlikely the patient will pick up minimal alterations of gustation unless prompted by the screening dentist. In the era of COVID-19, it may be prudent for dental clinicians to screen every patient routinely for olfactory and gustatory changes using a simple questionnaire with yes or no answers. The clinician should keep in mind that, in addition to COVID-19, several other conditions, including systemic diseases and medications, may be related etiologically to gustatory disorders. In the event that gustatory screening is positive for dysgeusia, the patient should be referred promptly for COVID-19 screening. If the patient is negative for COVID-19 and dysgeusia continues, the patient should be referred to a special senses clinic, possibly working together with the patient's primary care physician.

Also, we should understand that taste disorders contribute considerably to reduced quality of life in patients. Screening for taste alterations can form the foundation for an early warning and detection system that a dentist can use to attempt to quell the spread and effects of COVID.

### **CONCLUSIONS**

Gustatory disturbances are prevalent in several systemic disorders and infections, including COVID-19. Taste disorders, regardless of the etiologic factor, affect the quality of life of patients in general and of patients with COVID-19 in particular. Screening and identification of possible taste disorders should form the standard of care for dental clinicians, especially in the context of the COVID-19 pandemic. Early recognition of gustatory disorders may be crucial in identifying possible infection with the COVID-19 virus in the dental patient population. Dental clinicians must be aware of the fact that multiple factors (in addition to COVID-19) may be instrumental in the etiology and pathophysiology of dysgeusia, and a comprehensive workup of the case is needed to reach a conclusion about etiology. Knowing the short- and long-term consequences of COVID-19

infection, early screening, and identification are instrumental in potentially changing the life of a patient for the better. ■

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**Disclosures.** None of the authors reported any disclosures.

The authors acknowledge Swetha Kannan and Dr. Sita Mahalakshmi Baddireddy for designing and digitizing [Figures 1 and 3](#) and Dr. Srishti Parekh for designing and digitizing [Figures 2 and 4](#).

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