All environmental nutrients and airborne chemicals required for life enter the human body by means of the nose and the mouth. Olfaction and taste monitor the intake of such materials and determine the flavor and palatability of foods and beverages. In addition, these primary senses warn of toxins, such as spoiled food, leaking natural gas, polluted air, and smoke, and serve as diagnostic indicators for a number of serious diseases, including Alzheimer's disease and some forms of parkinsonism. Despite such important functions, however, the chemical senses have been generally disregarded from a medical perspective and are often not tested. Such neglect does not stem from a want of patients experiencing chemosensory problems; for example, data from the National Ambulatory Medical Care Survey suggest that, for 1975 and 1976 combined, 435,000 visits to physicians' offices occurred in which a major presenting complaint was chemosensory in nature (Report of the Panel on Communicative Disorders to the National Advisory Neurological and Communicative Disorders and Stroke Council, 1979).

This chapter summarizes key aspects of the anatomy and physiology of the olfactory and gustatory systems and presents techniques for their clinical assessment. Emphasis is placed on the sensory evaluation of olfactory function and on the pathophysiology of this system, because olfactory disorders are much more common than gustatory ones, and most complaints of taste dysfunction are in fact due to olfactory anomalies.

**OLFACTION**

**Anatomy and Physiology of Olfaction**

Odorants are detected intranasally by specialized receptor cells in the olfactory epithelium and, in some cases, by free nerve endings from the opththalmic and maxillary divisions of the trigeminal nerve within the nasal epithelium. In addition, some inhaled chemicals are detected by nerve endings within the pharynx and the oral cavity, such as those associated with the glossopharyngeal and vagal nerves. Qualitative odor sensations are mediated by the cranial nerve I receptors; the sensations mediated by the other nerves are primarily those of the common chemical sense, such as warmth/coolness, sharpness, and irritation (Doty et al., 1978; Silver and Moulton, 1982).

The human olfactory neuroepithelium is located in the superior nasal cavity and encompasses a portion...
of the superior turbinate, the superior nasal septum, and the region of the cribriform plate. Contrary to textbook descriptions, this 2- to 5-cm² region is rarely visually distinct from the surrounding respiratory epithelium. At least four main cell types are found in this region: bipolar olfactory receptor cells, microvillar cells, sustentacular or supporting cells, and basal cells (Moran et al., 1982b) (Fig. 27-1).

The first of these cell types—the primary olfactory receptor cell—numbers approximately 6 million in humans. Each of these bipolar flask-shaped neurons bears a slender rod, which enlarges at the surface of the epithelium into the olfactory knob or vesicle, from which 10–30 cilia project (Fig. 27-2). Odorant receptor sites are found on these hair-like processes. The cilia often have the standard 9 + 2 arrangement of microtubules in their basal segments, although variations occur (e.g., 9 + 3 and 9 + 4). Because they generally lack dynein arms, active motility is believed to be absent (Moran et al., 1982b).

The second of these cell types—the microvillar cell—contains microvilli that project into the mucus. These rotund cells are located adjacent to the primary bipolar cells in a 1:10 ratio and bear no cilia (Moran et al., 1982a) (see Fig. 27-1). The function of these cells is unknown, although a study using horseradish peroxidase tracer indicates that they send axons into the olfactory bulb, suggesting a sensory function (Rowley et al., 1989).

The third of these cell types—the sustentacular cell—is distributed throughout the olfactory region in contact with the other cell types and with one another, forming the matrix of the epithelium. These cells contribute to the production of mucus and may serve pinocytotic uptake and enzymatic degradation functions. In addition, they probably insulate the primary olfactory receptor cells from one another and may regulate the potassium concentration in the extracellular space near the receptor cells (Walz and Hertz, 1983).

The last of these four cell types—the basal cell—serves as the stem cell for the other cells in the olfactory epithelium, including the bipolar receptor cells. These cells are located near the lamina propria during their resting stage (see Fig. 27-1) and undergo major morphologic and functional changes during differentiation. The capacity of the bipolar receptor cell neuron to regenerate continuously from the basal cells or from cells in a compartment immediately above them (e.g., see Yamagishi et al., 1989) is a unique property of the olfactory neuroepithelium.
Glomeruli (Fig. 27-3). These complex structures consist of interwoven processes of the receptor cell axons with mitral, tufted, and periglomerular cell dendrites or processes. Because many more neurons enter glomeruli than leave them, they are a focus of a high degree of convergence of information (A.C. Allison and Warwick, 1949). These spheric structures are a key component of all olfactory systems, being present even in insects (MacLeod, 1971; Shepherd, 1972).

As can be seen in Figure 27-3, the mitral and tufted cells are large second-order neurons with primary dendrites entering the glomeruli and with secondary dendrites terminating in various regions of the bulb. These cells give off collaterals along their centrally directed course that interact with granule cells and cells within the periglomerular and external plexiform layer regions. The mitral and tufted cell axons form the lateral olfactory tract, which projects to more central brain regions, including the anterior olfactory nucleus, the prepiriform cortex, the periamygdaloid cortex, the olfactory tubercle, the nucleus of the lateral olfactory tract, and the corticomedial nucleus of the amygdala (for details on central projections, see Brodal, 1981; Haberly and Price, 1977; Krettek and Price, 1977a, 1978; MacLeod, 1971; Powell et al., 1965).

The mitral and tufted cells are involved in complex reverberating circuits in which negative feedback and positive feedback occur. For example, mitral cells can modulate their own output via the stimulation of granule cells (which are inhibitory to them) or via stimulation of excitatory inputs within the external plexiform layer. Reciprocal inhibition between neighboring mitral or tufted cells presumably results in sharpening the contrast between adjacent channels, similar to that seen in visual and tactile pathways (MacLeod, 1971).

Although the manner in which specific olfactory information is conveyed via the first-order neurons is not well understood, the initial component of the olfactory code is mediated by a large ensemble of sensory cells, each of which conveys a fraction of the information that signifies the nature of the odorant (Lancet, 1986). Odorants absorb into the mucus covering the olfactory epithelium and diffuse (alone or in conjunction with carrier proteins) to the cilia and terminal processes of olfactory receptor cells, where they bind to proteinaceous receptor sites located on one or both of these structures (Rhein and Cagan, 1981). This process leads, at least for some odorants, to the activation of a membrane-bound protein, which in turn induces an adenylate cyclase–mediated increase in intracellular cyclic AMP (cAMP) (Jones and Reed, 1989; Menevse et al., 1977; Pace et al., 1985). As in other senses, intensity is coded, in part, by the relative frequency of firing in the afferent neurons (cf. Drake et al., 1969; Osterhammel et al., 1969). Interestingly, and as would be expected from the aforementioned observations, the perceived intensity of some odors to humans is correlated with the degree to which they induce adenylate cyclase activity in ciliary preparations (Doty et al., 1990). Odor quality is presumably coded via some type of a cross-fiber pattern, because individual olfactory receptor cells respond to a wide range of odorants, have response spectra that do not completely overlap, exhibit different types of responses to applied stimulants (e.g., although most receptor cells evidence excitatory responses, some evidence inhibitory responses, and others, on-off responses), and have highly overlapping response spectra (Mair and Gesteland, 1980; Sicard and Holley, 1984).

Clinical Evaluation of Olfactory Function

Olfactory distortion or loss arises from a number of causes, including intranasal pathologic conditions...
(e.g., sinusitis, rhinitis), mechanical obstruction of the nasal airways, environmental or industrial pollutants, aging, and various medical and psychologic conditions (e.g., Alzheimer's disease, Parkinson's disease, Korsakoff's psychosis, and cystic fibrosis) (Amoore, 1986; 1988a,b; 1989b; Doty, 1979; Doty and Frye, 1989; Doty et al., 1984b; Schiffman, 1983; Schwartz et al., 1989) (Table 27-1). Overall incidence of smell loss after head injuries is approximately 7%, although this figure is much higher in cases of severe injury (ranging from 30 to 80% [cf. Sumner, 1976]). In the past, olfactory disorders were rarely examined quantitatively, largely because of the lack of standardized assessment procedures. Fortunately, significant progress has been made in the area of clinical measurement of olfactory function, permitting more detailed clinical discription of olfactory disturbances.

**Classification of Olfactory Disorders**

Both the patient's complaint and the objective sensory diagnosis can be adequately classified within the following schema:

Table 27-1. EXAMPLES OF DISORDERS REPORTED TO BE ASSOCIATED WITH OLFACTORY DYSFUNCTION

<table>
<thead>
<tr>
<th>Endocrine</th>
<th>Nutritional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenocortical insufficiency</td>
<td>Chronic renal failure</td>
</tr>
<tr>
<td>Cushing's syndrome</td>
<td>Cyanocobalamin (vitamin B₁₂) deficiency</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Korsakoff's psychosis</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>Kallmann's syndrome</td>
<td>Depression</td>
</tr>
<tr>
<td>Primary amenorrhea</td>
<td>Olfactory reference syndrome</td>
</tr>
<tr>
<td>Pseudohypoparathyroidism</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td>Turner's syndrome</td>
<td>Tumors</td>
</tr>
<tr>
<td>Local Diseases and Mechanical Obstruction of Airways</td>
<td>Intracranial</td>
</tr>
<tr>
<td>Adenoid hypertrophy</td>
<td>Aneurysms of the anterior communicating bifurcation</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>Frontal lobe glioma</td>
</tr>
<tr>
<td>Atrophic rhinitis (ozena)</td>
<td>Hydrocephalus</td>
</tr>
<tr>
<td>Bronchial asthma</td>
<td>Internal carotid aneurysms extending over the pituitary fossa</td>
</tr>
<tr>
<td>Deformity caused by trauma</td>
<td>Neuroblastoma</td>
</tr>
<tr>
<td>Exposure to toxic chemicals</td>
<td>Suprasellar meningioma</td>
</tr>
<tr>
<td>Leprosy</td>
<td>Sphenoid ridge meningioma</td>
</tr>
<tr>
<td>Malignant disease of paranasal sinuses with extension into nasal cavities</td>
<td>Other meningiomas</td>
</tr>
<tr>
<td>Nasal polypsis</td>
<td>Intranasal</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Sjogren's syndrome</td>
<td>Inverted papilloma</td>
</tr>
<tr>
<td>Tumors of nasopharynx with extension into nasal cavities</td>
<td>Melanoma</td>
</tr>
<tr>
<td>Vasomotor rhinitis</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Viral and infectious</td>
</tr>
<tr>
<td>Alzheimer's disease</td>
<td>Acute viral hepatitis</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>Herpes simplex</td>
</tr>
<tr>
<td>Head trauma</td>
<td>Influenza-like infections</td>
</tr>
<tr>
<td>Huntington's chorea</td>
<td>Parkinson's disease</td>
</tr>
<tr>
<td>Intracranial surgery</td>
<td>Korsakoff's psychosis</td>
</tr>
<tr>
<td>Korsakoff's psychosis</td>
<td>Multiple sclerosis</td>
</tr>
</tbody>
</table>

Separate determination of the patient's complaint and the objectively determined sensory disorder is important, because the two do not always coincide. Although other classification schemes are utilized in the literature (e.g., dysosmia is sometimes used as a generic term under which the other classes fall), the terminology just given suffices to categorize the vast majority of olfactory complaints and dysfunctions.

**Sensory Assessment of Olfactory Function**

Quantitative assessment of olfactory function is essential for a number of reasons: first, to establish the validity of the patient's complaint; second, to characterize the exact nature of the problem (which is critical for establishing a diagnosis); and third, to monitor objectively the efficacy of any interventions or treatments. In addition, some tests of smell function provide means for detecting malingering (cf. Doty, 1989; Doty et al., 1984a,b). Such detection is particularly important in litigation cases, as a number of courts have awarded sizable sums of money for loss of olfactory function.

Psychophysical procedures remain the primary means by which olfactory function is assessed in the clinic, even though certain electrophysiologic techniques offer the theoretic advantage of not being dependent on a patient's verbal response (e.g., averaged evoked potentials) (for review, see Doty, 1991). Controversy surrounds the validity of olfactory evoked potentials and other odorant-induced changes in electrophysiologic measures (e.g., heart rate changes), as they are highly variable and their neural origin is difficult to determine (cf. T. Allison and Goff, 1967; Lorig, 1989; Plattig and Kobal, 1979;
D.B. Smith et al., 1971). Although psychophysical responses can be obtained from subjects injected intravenously with an odorant (a potentially useful means of assessing the presence of intact cranial nerve I function in persons with nasal diseases that prevent testing with airborne odorants), the physiologic basis of this phenomenon is controversial (Maruniak et al., 1983), and sound normative data are not available for the interpretation of such tests.

The first step in assessing olfactory function is to determine the degree to which qualitative olfactory sensations are present. For this assessment, we routinely use a 40-item microencapsulated ("scratch 'n sniff") smell test (termed the University of Pennsylvania Smell Identification Test; commercially available from Sensonics, Inc., Haddonfield, NJ). This test is highly reliable (test-retest reliability is .95 [cf. Doty et al., 1984a, 1989b]), allows the classification of patients into discrete categories of dysfunction, provides a percentile score of a patient’s performance relative to age- and sex-matched controls, and has procedures for detecting malingering. Scores on this test reflect both gross and subtle olfactory problems associated with current and previous smoking behavior (Frye et al., 1990) and numerous neurologic diseases (e.g., Alzheimer’s disease, Korsakoff’s psychosis, and Parkinson’s disease [Fig. 27-4]) and correlate highly with the levels of certain catecholamine metabolites in the cerebrospinal fluid of some patient groups (e.g., \( r = .90 \) with the lumbar levels of 3-methoxy-4-hydroxyphenylglycol in patients with Korsakoff’s psychosis [cf. Mair et al., 1983]). The relationship between age and the scores on this standardized test is presented in Figure 27-5, which shows the pattern of smell loss in the elderly (Doty et al., 1984b). It is also apparent from this illustration that, on the average, women score higher on this test than men.

A second step in assessing smell function is to determine the absolute level of an odorant that the patient can detect. Although air-dilution olfactometry is the method of choice in presenting stimuli for such an assessment, it is not practical in the typical clinical setting. An alternative approach is to present odorants diluted in a liquid diluent (e.g., odorless mineral oil) via small vessels held over the nose (i.e., “sniff bottles”). We most commonly use the rose-like odorant phenyl ethyl alcohol for such a test, because it is pleasant smelling at higher concentrations, elicits relatively little trigeminal activity, and is easily dissolved in most diluents (Doty et al., 1978; 1984a). Although several psychophysical procedures can be used to establish a threshold estimate, a modified ascending single staircase procedure is preferable, because higher concentrations are initially avoided (minimizing adaptation effects) and a stable measure can be established with a minimal number of trials (see Cornsweet, 1962; Doty et al., 1984a; Ghorbanian et al., 1983).

Although detection threshold values typically agree with results obtained from smell identification tests, in some instances patients who fail identification tests perform normally on detection tests. However, the reverse rarely occurs. Because some patients can use subtle non–cranial nerve I cues to obtain low detection thresholds, the results of the identification test are weighted more heavily in ascertaining a sensory diagnosis than are those from the threshold test. Care must be taken in making this judgment, however, because an odor identification test can be sensitive to distortions of smell function that are unaccompanied by changes in the detection threshold, including some forms of agnosia. Even though such conditions are rare compared with uncomplicated smell losses caused by viruses and nasal obstruction, they must be kept in mind in cases in which central nervous system damage is known or suspected.

On rare occasion, it is useful to evaluate unilateral olfactory function by occluding each nostril. However, the patency of the nasal airways cyclically fluctuates in most persons (the so-called nasal cycle) and the majority of olfactory disorders occur bilaterally, including the dysfunction associated with Parkinson’s disease (Doty et al., 1991c).

Although a number of other procedures are avail-
SMELL IDENTIFICATION TEST SCORES

<table>
<thead>
<tr>
<th>AGE GROUP (YEARS)</th>
<th>MEDIAN UPSET VALUE (WITH INTERQUARTILE RANGE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-9</td>
<td>10-19</td>
</tr>
<tr>
<td>20-29</td>
<td>30-39</td>
</tr>
<tr>
<td>40-49</td>
<td>50-59</td>
</tr>
<tr>
<td>60-69</td>
<td>70-79</td>
</tr>
<tr>
<td>80-89</td>
<td>90-99</td>
</tr>
</tbody>
</table>

- **FEMALES** (n = 1158)
- **MALES** (n = 797)
- **TOTAL GROUP** (N = 1955)


able for assessing olfactory function, such as magnitude estimation and multidimensional scaling, more research is needed to determine whether they contribute substantially to the clinical information obtained by the aforementioned tests. Procedures such as magnitude estimation, although quite economical of time, share with thresholds the problem of marked between-subject variability, and—depending on the odorant used—may not be as sensitive to a number of subject-related variables as detection threshold measures (cf. Berglund et al., 1971; R.L. Doty, unpublished observations).

During the physical examination, the physician should pay special attention to the nose and the upper respiratory tract. This necessitates endoscopic examination of the nasal cavity, the meati, the septum, and the sinus ostia. Small polyps may be found, which otherwise would have gone undetected. A nasopharyngeal neoplasm or its metastasis to the neck may be discovered. Neurologic examination of the orbital contents and the cranial nerves may direct attention to a lesion of the skull base. Although a severely deviated nasal septum may play a role in olfactory dysfunction (Leopold, 1988), most septal deviations are unrelated to the ability to smell.

The following laboratory studies are recommended when clinically indicated: complete blood count with white blood cell differential count, serum levels of calcium and angiotensin-converting enzyme (may be elevated in sarcoidosis), erythrocyte sedimentation rate (may be elevated in inflammatory disorders, such as Wegener’s granulomatosis), serologic tests for syphilis, and serum levels of glucose and creatinine. Imaging studies of the nose, paranasal sinuses, and cranial contents are critical to the evaluation. This is best done with computed tomography or magnetic resonance imaging in the axial, coronal and/or sagittal planes. Biopsy of the olfactory neuroepithelium has been performed in the research setting but is not done routinely in the clinic (Lovell et al., 1982).

After all information is gathered, a diagnosis is reached. Usually, the cause of the olfactory dysfunction is (1) obstruction of odorant access to the neuroepithelium by inflammation or, rarely, neoplasm; (2) damage to the olfactory neuroepithelium; or (3) damage to the central olfactory pathways. Obstructive problems can result from allergic rhinitis, nasal polyps, chronic rhinosinusitis, and benign or malig-
nant nasal neoplasms. Overuse and abuse of topical nasal sprays (as in rhinitis medicamentosa) is also seen. Direct injury to the neuroepithelium can be caused by nasal or skull base surgery, external trauma, topical or systemic effects of drugs (cocaine, aminoglycoside antibiotics), and most commonly, viruses, such as herpes simplex and influenza.

Trauma, although capable of shearing the fine nerve filaments of cranial nerve I from the olfactory bulb at the cribiform plate, can also have central causes (Sumner, 1976), and animal research has revealed that intracranial hemorrhage can lead to degeneration of the olfactory epithelium without transection of the olfactory nerve (Nakashima et al., 1984b). It is generally believed that long-standing cases of anosmia not caused by intranasal disease or blockage are likely permanent and untreatable with current therapies.

Of considerable significance to the neurologist are the findings that Alzheimer's disease, Korsakoff's psychosis, Huntington's chorea, idiopathic Parkinson's disease, and the parkinsonism-dementia complex of Guam are accompanied by clear-cut alterations in smell function (Doty et al., 1987, 1988b, 1989a, 1991a,b,c; Mair et al., 1983; Moberg et al., 1987; Peabody and Tinklenberg, 1985; Ward et al., 1983). Such alterations are consistent, in several of these conditions, with known biochemical and morphologic anomalies in brain regions associated with olfaction, including the primary and secondary olfactory pathways (Esiri and Wilcock, 1984; Reyes et al., 1986). Indeed, lesions within the olfactory system appear to be among the first pathologic changes to occur in Alzheimer's disease (Hyman et al., 1984), and punctate lesions in monoamine-rich regions of the brain stem and diencephalon of patients with Korsakoff's psychosis likely relate to the previously noted correlation between their smell identification test scores and lumbar cerebrospinal fluid levels of 3-methoxy-4-hydroxyphenylglycol (Mair et al., 1983). Interestingly, MPTP-induced parkinsonism is accompanied by major olfactory dysfunction (Doty et al., 1991b).

It is also significant that a variety of intracranial tumors can influence smell function (for review see Doty, 1979). For example, it has been estimated that 20% of the tumors of the temporal lobe or lesions of the uncinate convolution produce olfactory disturbances, usually in the form of unpleasant smell hallucinations (e.g., Furstenberg et al., 1943).

Most authors believe that olfactory auras occur in association with temporal lobe seizures (Daly, 1958b; Holmes, 1927; Jackson, 1869, 1880; Penfield and Kristiansen, 1951; Weiser et al., 1985). Gloor et al. (1982), elaborating on this, suggested that the mesiotemporal limbic structures, but not the temporal neocortex, were essential for such symptoms. Auras have been variously described and include smells resembling burning oil (Penfield and Kristiansen, 1951), peaches, lemons (Daly, 1975), blood (Daly, 1958a), and "something to do with animals" (Gloor et al., 1982).

Howe and Gibson (1982) reviewed 273 patients with complex partial seizures. Only 22 had olfactory and 9 had gustatory hallucinations with their seizures. Six had both. Three of these were proved to have gliomas, and one, an arteriovenous malformation. These authors pointed out that, overall, the frequency of tumors in this group was not higher than would be expected in patients with temporal lobe epilepsy.

Studies of patients undergoing surgical treatment of intractable psychomotor seizures suggested that the amygdala is an essential element for the elaboration of olfactory auras and that amygdalotomy can eliminate such hallucinatory phenomena (Andy et al., 1975). For example, Chitanondh (1966) reported successful treatment of seven patients with seizure disorders, olfactory hallucinations, and psychiatric problems by stereotactically placed amygdalotomies and that "stereotaxic amygdalotomy has a dramatic effect upon olfactory seizures, auras and hallucinations. It is a safe surgical procedure and can be done without neurological deficit."

Although few detailed psychophysical studies of olfactory function have been performed in patients receiving amygdalotomies, there is some indication that bilateral amygdaloid lesions have at least some adverse effect on odor differentiation and identification (Andy et al., 1975). Clearly, unilateral excision of 5–7 cm of the anterior temporal lobe for intractable epilepsy has detrimental effects on odor quality discrimination, immediate and delayed recognition memory, ability to match an odor to its visually or haptically presented source, and the verbal identification of odors (Eskenazi et al., 1983). However, odor detection ability per se appears to be unimpaired, and the benefits derived from the elimination of olfactory hallucinations and seizure activity by such procedures appear considerable.

It is possible to characterize routinely most olfactory problems quantitatively and to use this information, along with that obtained from the history and the physical examination, to determine the cause of the dysfunction. Unfortunately, with the exception of odorant access problems within the nose and those rare cases in which dysosmia is associated with clear-cut seizure disorders, meaningful treatments are not available for most olfactory problems. Although zinc and vitamin therapies have been suggested in the literature, there is no compelling evidence that these therapies are effective, except in cases in which frank zinc or vitamin deficiencies exist. Even though some dysosmias are reportedly cured by periodic anesthetization of the olfactory receptor region, most dysosmias remit spontaneously, and such treatment often provides only temporary relief. Extremely debilitating, long-standing, severe dysosmia may be amenable to treatment either by resection of one or both olfactory bulbs (Kaufman et al., 1988) or by operative destruction of segments of the olfactory neuroepithelium (Leopold et al., 1990).
GUSTATION

Patients commonly fail to distinguish between flavor and taste and often report loss of taste sensation in the presence of normal sweet, sour, bitter, and salty responsiveness. Although true loss of gustatory function exists, it is rare, as taste responsiveness is mediated bilaterally by four nerves within the oral cavity, as indicated in the next section. Thus, a number of studies report that less than 1% of head injury patients exhibit true taste loss, as compared with more than 7% overall for loss of olfactory function (Sumner, 1976). In our experience, strange taste sensations (i.e., dysgeusias) are much more common than taste losses or decrements per se.

Anatomy and Physiology of Taste

The peripheral receptors for taste—the taste buds—are round epithelial structures consisting of slender cells arranged like the segments of a grapefruit (Fig. 27-6C). The long axis of the taste bud is perpendicular to the surface of the epithelium. The superficial portion of the bud is marked by an excavation, the taste pit, into which the microvilli of the sensory cells project. Several cell types are discernible within the taste bud. There is also a light cell with a club-like ending, as well as basal cells (Murray, 1973). These different cell types are presumed to represent different stages of generation and degeneration of the sensory taste cells. Cell turnover is thought to occur during a 10-day interval, at least in the rat (Beidler and Smallman, 1965).

As in the olfactory system, somatosensory sensations (e.g., stinging, burning, cooling, and sharpness) can be induced by some oral stimulants via trigeminal afferents located on the tongue and throughout the oral cavity. Although, in a strict sense, one cannot view this type of stimulation as being taste, such stimulation is critical in determining the overall gestalt of flavor, such as that experienced when eating spicy foods like chili.

Taste buds are located in the oral cavity on the soft palate and tongue, the pharynx, the larynx, and the esophagus. The largest number are on the surface of the tongue, being associated with visible protuberances termed papillae. Of the four types of papillae—fungiform, foliate, circumvallate, and filiform—only the first three harbor taste buds. The location of these types of papillae varies, with the circumvallate papillae being arranged in an inverted V at the border between the anterior two-thirds and the posterior one-third of the tongue. The club-like fungiform papillae are scattered on the anterior two-thirds of the tongue, and the foliate papillae are located on the lateral border of the posterior middle third of the tongue (Fig. 27-6A).

Up to 200 taste buds are present in each circumvallate papilla, whereas far fewer buds are present in each of the other types. The pores of the circumvallate taste buds open into a furrow or moat, separating each papilla from the surrounding tissue. Secretions from the glands of von Ebner enter this moat, which acts as a container for the taste solutions. Secretions from the glands of von Ebner enter this moat, which acts as a container for the taste solutions. Taste buds associated with the foliate papillae are similarly positioned within the walls of furrows, unlike the taste buds in the fungiform papillae, which are positioned within a small opening at their top (Fig. 27-6B).

The innervation of the taste buds is complex. The afferent fibers from the buds within the fungiform papillae and from trigeminal nerve endings enter the lingual nerve. The taste fibers subsequently join the chorda tympani nerve, which merges with the facial nerve in the temporal bone. These fibers enter the brain stem with the nervus intermedius. The taste buds of the circumvallate and foliate papillae are subserved by fibers traveling directly to the brain stem with the glossopharyngeal nerve, although the anterior folds of the foliate papillae may be inner-
CRANIAL NERVES AND THEIR DISORDERS

by Penfield and Faulck (1955) reported resolution of taste hallucinations. Although little is known about these pathways in the human, there is physiologic evidence that the primary cortical area for taste in other primates is located deep in the parietal operculum and adjacent parainsular cortex (see Norgren, 1984).

Hausser-Hauw and Bancaud (1987) provided clinical evidence that supports this conclusion in a group of 30 patients who manifested gustatory hallucinations during epileptic seizures. Such symptoms could have resulted from seizures of parietal or temporal origin or occur after electrical stimulation of the hippocampus, the amygdala, the Rolandic or parietal operculum, or the first or second temporal convolutions. However, whereas they were intermixed with other symptoms in the case of temporal lobe seizures, they occurred as isolated or prominent symptoms in the case of parietal seizures or parietal or Rolandic stimulation. One of their patients and one described by Penfield and Faulck (1955) reported resolution of gustatory symptoms after resections of the parietal operculum. However, Hausser-Hauw and Bancaud (1987) noted that 4% of 305 patients with temporal lobe seizures, but only 2% of 309 patients with suprasylvian seizures and 3% of 102 patients with suprasylvian and infrasylvian seizures, reported gustatory symptoms; they suggested that reorganization of cortical pathways in patients with temporal lobe epilepsy accounted for the discrepancy. An alternative possibility, suggested by Gloor et al. (1982), is that activation of mesiotemporal structures is necessary before symptoms such as taste achieve experiential immediacy. Hausser-Hauw and Bancaud (1987) reviewed the physiologic and anatomic evidence, which supports the presence of taste pathway projections to the amygdala, particularly its central nucleus. Such a pathway might provide an additional explanation for the observations of Gloor et al. (1982).

As in the case of olfaction, taste intensity in humans has been shown to correlate with the magnitude of the neural response (as measured electrophysiologically from the chorda tympani nerve bundle as it crosses the tympanic membrane) (Diamant et al., 1965). The nature of quality coding is more complex, and there are proponents of both labeled line and cross-fiber patterning theories. Other investigators believe that this distinction is artificial and subsume labeled line theory within a cross-fiber patterning theory. Regardless of such theoretic distinctions, there is evidence at the level of the first-order neuron for reasonably discrete classes of neurons (within a broadly tuned population of cells) that can be identified as responding best to specific tastants. For example, there are sweet-sensitive fibers in the hamster chorda tympani nerve that increase their firing rates more vigorously to sucrose than to other tastants (Frank, 1973). Analogous cell types are seen for stimulants representing nonsweet taste categories. However, recordings in taste-related neurons in the brain stem suggest that the central fibers are much more broadly tuned than are the first-order neurons (D.V. Smith et al., 1983). It is noteworthy that substances have been discovered that selectively alter taste perceptions. For example, miraculin, a glycoprotein from the berry of the African shrub Synsepalum dulcificum, produces an alteration of all sour tastes to a sucrose-like sweetness. Gymnemic acid, an extract from the leaves of the Indian plant Gymnema sylvestre, can block the perception of sweet sensation (and the corresponding electrophysiologic activity) without significantly altering the perception of the other taste qualities (for review of taste modifiers, see Kurihara, 1971).

Clinical Evaluation of Taste Function

Numerous factors influence normal gustatory function. It should be re-emphasized, however, that most patients with the complaint of loss of taste evidence, on psychophysical examination, normal taste function and abnormal smell function. For this reason, it is useful to use the term flavor in describing the complex synthesis of gustatory, olfactory, and somatosensory sensations. Whole-mouth taste deficits are uncommon.

Many of the same conditions that are associated with olfactory disturbances are also reported to influence taste function. For example, taste disorders have been reported after head trauma, zinc deficiency, adrenocortical insufficiency, and viral infections (Table 27-2). In addition, however, taste disturbances appear to be present much more frequently than olfactory ones as a result of the use of pharmacologic agents, such as antirheumatic drugs, antiproliferative drugs, and substances bearing a sulphydryl group (e.g., penicillamine and captopril). Although the
mechanisms responsible for such phenomena are poorly understood, a number of taste stimuli can elicit taste perceptions when injected into the bloodstream, analogous to the intravascular olfaction phenomenon discussed earlier (Bradley, 1973).

Deficiency (as in Sjögren's syndrome) or hyperviscosity of saliva leads, in time, to lessened taste acuity, presumably as the result of accompanying decreases in the number of papillae and taste buds and possible functional alteration in the remaining taste buds (Brightman, 1977). Whether such morphologic alterations in humans are due to the elimination of lubricating or trophic activity from the saliva is not known. In our experience, neither artificial saliva nor water mouthwashes have proved successful in restoring normal taste function in patients with xerostomia. However, systematic research is needed to ascertain whether such materials can improve taste function in certain types of xerostomia.

Post-traumatic ageusia is much less common than post-traumatic anosmia. Ageusia to one or more of the primary taste modalities is believed to occur in less than 1% of persons with major head injury (Sumner, 1976). Although the literature is scant, the prognosis for post-traumatic ageusia is far better than for post-traumatic anosmia. Considerable controversy exists regarding the underlying cause of most head trauma–related cases of ageusia, because general ageusia should theoretically be nearly impossible to induce. Unfortunately, many of the reports of ageusia in the literature are based on the patient’s report rather than on the results of sound psychophysical testing, so they may not reflect the true incidence of this problem and, in some instances, may actually be mislabeled cases of anosmia (Deems et al., 1991).

Complaints of taste loss or distortion are commonly reported in various carcinomas. For example, squamous cell carcinoma of the mucous membranes of the upper aerodigestive tract can interfere with taste by direct destruction of receptors and neural pathways. Malnutrition associated with these tumors can also lead to ageusia. Significant increases in recognition thresholds for bitter in patients with metastatic carcinomas and decreases in such thresholds for sour in breast cancer patients were reported (Settle et al., 1979). Radiation therapy alters taste bud cell turnover and can affect taste function, although return after radiation treatment has been observed (Conger, 1973).

Gustatory symptoms have been reported in association with epileptic seizures for more than a century (Daly, 1958a; Gowers, 1909; Holmes, 1927; Jackson, 1990; Wieser et al., 1985). Daly (1975) suggested that such sensations reflect those basic to taste (sweet, acid, bitter, and salty), although sweet tastes seem to occur less frequently. Tastes have been described as peculiar, rotten (Penfield and Kristiansen 1951), sweet—along with a pungent odor (Daly, 1958b), or like a cigarette, rotten apples, or vomitus (Hauser-Hauw and Bancaud, 1987). However, as noted earlier, many of the latter tastes likely represent smell sensations that are misclassified as tastes by both the patients and their physicians.

Although taste acuity declines with age, the perceptual decrease is not as marked as that seen for olfaction (Cowart, 1981; Weiffenbach, 1984; Weiffenbach et al., 1982). Nonetheless, in conjunction with the loss seen in the sense of smell, such decrements may lead to anorexia, weight loss, and malnutrition in some of the elderly.

**Classification of Taste Disorders**

As for olfactory disorders, we classify the patient’s complaint and the results of sensory tests separately. The terms we use for such classification are as follows:

- **Total ageusia**—lack of taste sensation to all tastants
- **Partial ageusia**—lack of taste sensation to some tastants

### Table 27-2. Examples of Disorders Reported to Be Associated with Gustatory Dysfunction

<table>
<thead>
<tr>
<th>Endocrine</th>
<th>Autoimmune</th>
<th>Nutritional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenocortical insufficiency</td>
<td>Pemphigus</td>
<td>Cachexia</td>
</tr>
<tr>
<td>Congenital adrenal hyperplasia</td>
<td>Sjögren’s syndrome</td>
<td>Chronic renal failure</td>
</tr>
<tr>
<td>Panhypopituitarism</td>
<td>Local Alterations of Taste Buds or Papillae</td>
<td>Cirrhosis of the liver</td>
</tr>
<tr>
<td>Cushing’s syndrome</td>
<td>Chemicals, drugs</td>
<td>Niacin (vitamin B1) deficiency</td>
</tr>
<tr>
<td>Cretinism</td>
<td>Xerostomia</td>
<td>Zinc deficiency</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Neurologic</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Bell’s palsy</td>
<td>Depression</td>
</tr>
<tr>
<td>Turner’s syndrome</td>
<td>Epilepsy</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td>Pseudohypoparathyroidism</td>
<td>Familial dysautonomia</td>
<td>Tumors</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Head trauma</td>
<td>Oral cavity cancer</td>
</tr>
<tr>
<td>Infections</td>
<td>Middle ear operations with manipulation or damage to chorda tympani</td>
<td>Base of skull neoplasia</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>Multiple sclerosis</td>
<td></td>
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<tr>
<td>Gingivitis</td>
<td>Raeder’s paratrigeminal syndrome</td>
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<tr>
<td>Herpes simplex</td>
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<tr>
<td>Periodontitis</td>
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<tr>
<td>Sialadenitis</td>
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</tbody>
</table>

Total hypogeusia—lessened sensation to all tastants
Partial hypogeusia—lessened sensation to tastants representing one to three of the four major taste qualities
Hypergeusia—heightened smell ability
Dysgeusia—the presence of a strange or distorted taste sensation

Sensory Assessment of Taste Function

Numerous procedures have been developed for evaluating gustatory function, although few data are available concerning their reliability or validity. We find that taste tests in which drops of stimulus are applied to the tongue are less than satisfactory in some instances, because the area stimulated is difficult to control and often the stimulus volume is not large enough to induce a reliable response. Although electrogustometric procedures can be of use in establishing gross neural deficit, they have limited use in the clinic, as the results obtained are dependent on the electrodes selected (electrical taste may be an iontophoretic phenomenon) and not all taste qualities can be reliably elicited. Furthermore, subtle alterations in taste function cannot be measured by these techniques. In general, when direct current is used, a sour taste is evoked if the anode is applied to the tongue, it is sometimes difficult to deposit a taste stimulus accurately on the back of the tongue, given its depth within the oral cavity and the stimulation of the gag reflex. In most cases, tastants can be micropipetted into the region, although stimulus spread can be a problem. Although it is possible to confine the stimulus spread by using small pieces of filter paper soaked in the taste solution, stimulus contact is not always adequate and difficulties are encountered in retrieving the small pieces of filter paper. For such regional testing, it is useful to employ an automated micropipette to present suprathreshold concentrations of the four target tastants in a forced-choice paradigm with deionized water rinsing between trials.

Medical Examination and Treatment of Patients with Gustatory Disorders

Dysfunction of the taste system can be due to one or more causes, including the following:

1. Oral medical problems that release bad-tasting materials (e.g., gingivitis and sialadenitis)
2. The use of different types of metals in fillings and dental appliances, which results in intraoral current gradients sensed by the taste system
3. Transport problems of tastants to the taste buds (e.g., caused by dryness of the oral cavity and by damage of the taste pores or the papillae)
4. Destruction or loss of the taste buds themselves
5. Damage to one or more of the neural pathways innervating the taste buds
6. Central neural factors

In addition to performing the standard history and physical examination mentioned under Medical Examination and Treatment of Patients with Olfactory Disorders, we palpate and examine the tongue carefully to detect signs of scarring, inflammation, atrophy of papillae, or neoplasm. Although not done routinely, biopsy of circumvallate or fungiform papillae for detailed microscopic examination has proved useful in determining whether pathologic changes are present in taste bud tissue. In cases of suspected salivary gland disease, we obtain a biopsy specimen of minor salivary gland tissue in the lower lip to determine the presence of lymphoepithelial lesion (indicative of Sjögren’s syndrome). In cases in which
the basis of the dysfunction cannot be ascribed to peripheral factors, we obtain appropriate radiographs to rule out central nervous system tumors or lesions.

Treatment is straightforward in cases in which decreased salivation or local oral pathologic alteration caused by dental factors is the basis of a dysgeusia or hypogeusia. Saliva can be supplemented by various salivary substitutes. Nutritional deficiencies can be corrected. Radiation-induced xerostomia may improve with time. In some cases, flavor enhancers can be of at least some benefit.

CONCLUDING REMARKS

The chemical senses of taste and smell determine, in large part, the flavor of foods and beverages and warn of fire, dangerous fumes, leaking gas, spoiled foods, and polluted environments. Disorders of these senses often result from accidents, disease states, medical interventions, aging, and exposure to a number of environmental pollutants and can serve as important indicators of a number of diseases. This chapter briefly reviewed the anatomy and physiology of these senses, some etiologic factors responsible for their dysfunction, and information regarding their evaluation and management. It was specifically noted that most patients with complaints of taste loss have, in fact, olfactory dysfunction and that true taste loss is relatively rare.

References

(Key references are designated with an asterisk.)


Jackson J.H. (1880) On right or left-side spasm at the onset of epileptic fits and the connection of the convulsions with the brain. Lancet 1:175–178, 1880.


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