Chapter 65: Physiology

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The oral cavity is a complex organ comprising muscle, glands, teeth, and specialized sensory receptors. For most animals, the orosensory and oromotor apparatus is critical for successful defense, reproduction, exploration, and vocalization (Darian-Smith, 1973). In humans, vocalization has evolved into complex speech production, but other human behaviors depend less on the mouth and tongue than on the eye and hand. In all animals, however, the mouth is essential for the ingestion of nutrients. The incorporation of nutrients by mastication and drinking involves a high degree of coordination both within and between different oral motor systems. Chewing requires both the reciprocal activation of antagonist trigeminal muscles to open and close the jaws and the tongue to position food between the teeth. A diverse array of highly specialized sensory systems guide these complex oromotor responses. Mechanoreceptors on the tongue, palate, and periodontal ligament all contribute to a three-dimensional (stereognosic) perception of the oral cavity (Bosma, 1970). The sense of taste serves both in food selection and protection from ingesting potentially toxic substances.

Recent reviews provide comprehensive coverage of specific aspects of oral function, including mastication (Hiiemae and Crompton, 1985; Lund, 1991; Lund and Enomoto, 1988; Luschei and Goldberg, 1981; Rossignol et al, 1988), swallowing (Jean, 1990; Miller, 1982), dental mechanoreception (Byers, 1984), and the sense of taste (Cagan, 1989; Finger, 1987; Meiselman and Rivlin, 1986; Travers et al, 1987b). In addition, several recent papers have reviewed oral pain (Sessle, 1987) and taste dysfunction (Schiffman, 1983a, 1983b; Smith, 1988).

This chapter provides a concise overview of orosensory and oromotor function. A brief synopsis of orosensory function describes the innervation and sensitivity of the oral cavity and a summary or central pathways. A section on sensorimotor function includes a discussion of masticatory, lingual, and autonomic reflexes followed by a discussion of mastication and the oral phase of deglutition. The sense of taste is treated separately.

Sensory Function

Oral sensitivity

Somatosensory innervation of the oral cavity is provided by the maxillary and mandibular branches of the trigeminal nerve and by the glossopharyngeal nerve. The mandibular nerve branches to innervate the oral mucosa of the cheek, anterior two thirds of the tongue, mandibular dentition, periodontal ligament, gingiva, and anterior mandibular vestibule. Branches of the maxillary nerve innervate the hard and soft palate, the oral mucosa of the maxillary vestibule, and the maxillary dentition, gingiva, and periodontal ligament. Somatosensory innervation of the back of the tongue and oropharynx is provided by the glossopharyngeal nerve. Although the entire oral cavity is densely innervated with sensory fibers, considerable evidence indicates that the innervation is not uniform. Specialized oral tissues, including the lips, teeth, periodontal ligament, tongue, and palate, each display specific patterns of sensitivity. In some instances these sensitivities are associated with specific oral functions.

Overall, the anterior oral cavity displays greater tactile sensitivity than posterior oral structures (Darian-Smith, 1973). The tip of the tongue is particularly sensitive, with a discriminative capability equivalent to that of the digits. Using a two-point discrimination test, Ringel (1967) determined that two-point discrimination was greatest for the tongue tip (1.75 mm), followed by the finertip (2.09 mm), lip (2.42 mm), soft palate (2.88 mm), alveolar ridge (3.02 mm), and thenar region (5.6 mm). The midlines of the palate and tongue were more sensitive than lateral regions. A similar pattern of sensitivity to mechanical stimulation applied to the teeth has also been reported (Manly et al, 1952). Adults with complete dentition could detect a 1 g von Frey hair applied to the anterior (midline) teeth but required nearly 10 g to detect stimulation of the first molar. The tearing and piercing functions of anterior teeth require greater sensory control than does the crushing or grinding associated with molar function.

The high degree of sensitivity from structures anterior in the mouth correlates with the physiologic properties of the afferent fibers innervating these structures. Neural responses from afferent fibers innervating the human perioral region had small oval receptive fields (median - 8 sq mm) and low-threshold, slowly adapting responses (Johansson and Olsson, 1976; Johansson et al, 1988). Two additional cells with receptive fields restricted to a single tooth were directionally sensitive. Maximal response rates and the lowest threshold responses were obtained by forces directed distally and labially. Similar response properties to dental stimulation have been obtained from experimental animals. A study of mechanoreceptors in the lower cat canine revealed that forces applied in the distolingual direction were generally the most effective and that 81% of the responses were slowly adapting (Loescher and Robinson, 1989). Numerous studies have determined that low-threshold mechanical stimulation directed at the teeth stimulates receptors in the supporting periodontal ligament (Dubner et al, 1978; Linden, 1975). The preponderance of experimental data indicates that sensations resulting from stimulation of the C- and A-delta fibers innervating the tooth pulp are nociceptive. Sessle (1987), however, points out that small-diameter fibers found elsewhere in the body may mediate touch or temperature sensations.

Studies in experimental animals suggest that specific regions of the perioral and intraoral receptor surface sequentially contribute to oromotor function associated with ingestion. Denervation studies in rats, for example, indicate that cutting trigeminal nerve branches that innervate the perioral region decreases the appetitive response to food (Zeigler et al, 1985). Animals can still chew and swallow if food is placed in their mouths, but they do not actively ingest food. Other trigeminally innervated regions, those of the palate, for example, are low-threshold sites for eliciting the rhythmic oral movements of chewing and drinking (van Willigen and Weijs-Boot, 1984). Neither the front of the mouth nor the palate, however, is a particularly sensitive region for eliciting swallowing, the last stage of the ingestive consumatory response. Rather, the posterior aspect of the tongue, fauces, and epiglottis, innervated by the glossopharyngeal and vagus nerves, are low-threshold sites for eliciting a swallow.

A variety of chronic pain syndromes are associated with trigeminal nerve complications of the perioral region associated with maxillofacial surgery, but feeding disorders appear secondary to the loss of masticatory proprioception (Donoff and Colin, 1990; Gregg, 1990). Nevertheless, experimental animal studies provide insight into the anatomic and physiologic response of the trigeminal nerve to injury.

Trigeminal response to injury

Several studies by Robinson have examined the recovery of function and reinnervation of the teeth following injury to the inferior alveolar nerves in the cat (Robinson, 1981, 1986). Reinnervation of the teeth was assessed by monitoring the return of a jaw-opening reflex to pulpal stimulation and by recording antidromic responses from the tooth pulp in response to more proximal nerve stimulation.

Evidence for reinnervation and collateral sprouting was clearly evident. Compared to intact animals, the ipsilateral mental nerve and the contralateral inferior alveolar, mental, and lingual nerves all innervated teeth on the side of the severed inferior alveolar nerve. A progressive decrease in both the threshold and latency of the jaw-opening reflex over a 12-week period suggested progressive remyelination of the reinnervating fibers.

A more recent study by Loescher and Robinson (1989(showed how the receptive field characteristics of single periodontal mechanoreceptors recovered following crush or section of the cat inferior alveolar nerve. Twelve weeks after nerve damage, periodontal ligament mechanoreceptors responded to stimulation directed at the tooth but were generally less sensitive; that is, they had similar receptive fields and lower response rates. The response properties of recovering afferent fibers also depended on whether the nerve was crushed or severed. Nerve secion resulted in greater response thresholds and decreased conduction velocities as compared with animals sustaining the nerve crush.

There is also evidence for changes in the central trigeminal pathway in response to peripheral nerve damage. Damage to the trigeminal nerve in which peripheral reinnervation is blocked can result in transganglionic degeneration of first-order afferent fibers (Aldskogius et al, 1985; Westrum et al, 1976). Moreover, following tooth pulp deafferentation in the cat, neurons in the subnucleus oralis had significantly larger receptive fields and responded atypically to stimulation of more than one division of the trigeminal nerve (Hu et al, 1986). These central changes may be associated with the pathophysiology of chronic pain after damage to trigeminal nerves (Gregg, 1990).

Central projections of trigeminal system

Afferent fibers of the trigeminal nerve enter the brainstem in the pons, bifurcate, and terminate in either the principal sensory nucleus in the pons or descend to terminate in the spinal trigeminal complex in the medulla. The bifurcation of the trigeminal nerve at the level of the pons reflects a tendecy toward a segregation of function (Kelly, 1985). In general, low-threshold mechanoreceptors predominate in the principal trigeminal sensory nucleus, indicative of a tactile discriminative function. In contrast, considerable evidence implicates the subnucleus caudalis in orofacial pain mechanisms, and many neurons in the subnucleus caudalis respond to noxious stimuli applied to the head and neck (reviewed in Sessle, 1987). These neurons include those specifically activated by noxious stimuli (nociceptive-specific neurons) and wide dynamic range neurons, responsive to both low- and high-intensity stimulation (Fig. 65-1).

Because the receptive fields for many nociceptive neurons in the subnucleus caudalis are large and include responses to nociceptive stimuli applied to the masticatory muscles, tooth pulp, and temporomandibular joint, a role for these neurons in referred pain has been suggested (Sessle et al, 1986). Anatomic studies confirm that afferent fibers innervating the oral cavity, tooth pulp, oropharynx, temporomandibular joint, masticatory muscles, and superficial skin all converge in the subnucleus caudalis (Beckstead and Norgren, 1979; Capra, 1987; Shigenaga et al, 1986; Westrum et al, 1976). Other parts of the sensory trigeminal complex, however, also are involved in trigeminal pain. Nociceptive responses have been obtained from extensive areas of the sensory trigeminal complex, and destruction of the subnucleus caudalis does not prevent all trigeminal pain unction (Sessle, 1987). Lesions in the subnucleus caudalis, for example, did not interfere with the jaw-opening reflex to pulpal stimulation (Azerad et al, 1982).

Somatosensory information reaches the ventrobasal complex of the thalamus from all major subdivisions of the trigeminal sensory complex (Sessle, 1987). Many cells in the ventrobasal complex respond to low-intensity stimulation, indicative of a tactile discriminatory function; however, other neurons require high-intensity stimulation. The small receptive fields of both these types of neurons suggest a role in localization. Other nuclei, including the posterior thalamic nuclei and the nucleus submedius, respond preferentially to high-intensity stimulation and may be involved in affective components of pain (Craig and Burton, 1981; Sessle, 1987).

Motor Function

Much of what we know about orosensory and motor function has come from the study of oral reflexes and ingestive function in experimental animals. Although a great deal is known of the synaptic basis for oral reflexes, the role of oral reflexes in complex, integrated oral behavior including either feeding or vocalization remains obscure (Dubner et al, 1978; Rossignol et al, 1988). Oral stimuli not only affect the masticatory, lingual, palatal, and facial muscles, but also elicit autonomic responses involved in chemical digestion. These responses, collectively referred to as the cephalic phase response (Powley, 1977), include salivation, the relase of digestive enzymes (amylase), and the pancreatic release of insulin (Gjorstrup, 1980; Grill et al, 1984; Naim et al, 1978).

Oral (masticatory muscle) reflexes

A jaw-closing reflex, initiated by stretching muscle spindle afferents in jaw-closing muscles, monosynaptically excites ipsilateral jaw-closing motoneurons (Lund and Olsson, 1983). Unlike spinal stretch reflexes, however, there is no corresponding inhibition of antagonist (jaw-opener) motoneurons. The cell bodies for the muscle spindle afferent fibers are located centrally in the mesencephalic trigeminal nucleus. In humans the masseteric reflex is differentially modulated by stimulation of different sites in the oral cavity. Stimulation of the palate decreased masseteric force, but stimulation of the tongue increased it (Smith et al, 1985).

The jaw-opening reflex is mediated by a different set of pathways (reviewed in Lund and Olsson, 1983). Although the jaw-opening reflex can be elicited by nonpainful stimuli, it has been used widely in the study of pain mechanisms (Mason et al, 1985). There are few, if any, muscle spindles in the jaw-opening muscles (Dugner et al, 1978). Thus, during jaw closure when considerable force can be generated to crush objects between the teeth, the corresponding lengthening of the jaw-opener muscles does not provide the afferent signal for a reciprocal reflex. Stimulation of mechanoreceptors located in the periodontal ligament, tongue, and other soft tissues of the mouth, however, initiates reflex jaw opening. The cell bodies for these mechanoreceptors are located both in the mesencephalic trigeminal nucleus and in the trigeminal ganglion. The central processes of primary afferent fibers terminate in the supratrigeminal area and in the principal trigeminal sensory nucleus, which in turn inhibit jaw-closer motoneurons and excite jaw openers. Thus the soft tissues of the mouth are protected against potentially damaging objects through dysynaptic reflex pathways.

Lingual reflexes

Lingual reflexes can be elicited by stimulation of virtually any of the afferent nerves innervating the oral cavity. Depending on the site of stimulation, either a protrusive or a retractive movement of the tongue is produced. An overview by Lowe (1984) on the functional significance of lingual reflexes ephasizes a protective role, either for the tongue itself during mastication or for the airway during swallowing.

Compounding the complexity of interpreting lingual reflexes are observations that reflex excitation of the tongue rarely influences a single lungual muscle, and contraction of a single lingual muscle can move the tongue in more than one plane (Lowe, 1981). For example, although a primarily retrusive movement of the tongue is produced by electrical stimulation of the lingual nerve, both protruder and retractor hypoglossal motoneurons are excited (Lowe, 1981).

Electrical stimulation of the glossopharyngeal nerve that innervates mechanoreceptors on the posterior aspected of the tongue and oropharynx also elicits tongue movement. Similar to the lingual nerve, stimulation of the glossopharyngeal nerve excites both protruder and retractor motoneurons, and the movement of the tongue is primarily retrusive. The simultaneous activation of the glossopharyngeal nerve afferent fibers by electrical stimulation, however, may mask a more complex reflex organization. Lowe (1984) has suggested that stimulation of lingual receptors innervated by the glossopharyngeal nerve elicits a primarily retrusive movement of the tongue, in contrast to lingual protrusion produced by stimulating pharyngeal regions innervated by the glossopharyngeal nerve. Thus both lingual and glossopharyngeal nerve fibers innervating different regions of the tongue may reflexly protect the tongue during the occlusal phase of mastication with a retrusive movement.

In contrast, electrical stimulation of the superior laryngeal nerve that innervates laryngeal mechanoreceptors produces a protrusive action of the tongue, and protruder motoneurons show depolarizing potentials during this reflex. Mechanoreceptors in the oropharynx and larynx innervated by the superior laryngeal and glossopharyngeal nerves thus preserve airway patency during a swallow with a protrusive tongue movement.

Complex oral reflexes

Oromotor reflexes often involve several motor systems. Electrical stimulation of either the masseteric or anterior digastric nerves, for example, suppressed genioglossus activity, suggesting that proprioceptive or nociceptive signals from the trigeminal musculature inhibited lingual protrusion (Sauerland and Mizuno, 1970). In contrast, passively depressing the mandible (in cats) excited the genioglossus muscle, suggesting that lingual protrusion may be reflexly facilitated during jaw opening when the tongue is not subject to occlusal forces (Hellstrand, 1982). Similarly, stimulation of the hypoglossal nerve, which contains some afferent fibers, inhibited the masseteric (jaw-closing) reflex (Nakamura et al, 1978). Thus there appears to be a tendency for an oral reflex organization that facilitates certain oromotor combinations, that is, jaw opening with tongue protrusion and jaw closing with tongue retraction.

Autonomic reflexes

Studies in both humans and experimental animals indicate that gustatory and mechanical stimuli are effective in eliciting the flow of saliva during mastication (Anderson and Hector, 1987). Stimulation of receptors in the periodontal ligament may be one source for reflex salivation. In both rabbits and humans, there is a high correlation between parotid flow and mandibular movement, especially on the working, ipsilateral side (Fig. 65-2). In humans, selective anesthetization of the nerves innervating the periodontal ligament significantly reduced the amount of saliva elicited from crushing a "Grape Nut" stimulus (Anderson and Hector, 1987).

Both location and stimulus modality influence the release of saliva (reviewed in Travers et al, 1987a). Stimulating the anterior part of the tongue is most effective for evoking salivation from the sublingual and submandibular glands, but posterior tongue stimulation is more effective for producing parotid gland flow. Aversive gustatory stimuli such as (sour) acids or (bitter) quinine hydrochloride are more effective for eliciting saliva than is stimulation with weak salt or sucrose solutions. Nevertheless, in experimental animals, sweet stimuli were the most effective stimuli for the release of the enzyme amylase from the parotid gland (Gjorstrup, 1980).

Gustatory receptos also trigger the release of insulin in response to glucose stimulation (Goldfine et al, 1969; Grill et al, 1984). Oropharyngeal receptors innervated by the superior laryngeal nerve may influence other metabolic or digestive functions (Shingai et al, 1988). There is increased diuresis in response to drinking a saline solution as compared with the intragastric infusion of the same volume of fluid (Gebruers et al, 1985).

Ingestion

The orosensory apparatus of the mouth and perioral region is an integral part of the regulation of food and fluid intake. In general, the sensory receptors in the mouth are specialized for the consummatory phase of ingestion and play an important role both in the sensory evaluation of food and in the sensory control of mastication and deglutition.

Food consumption through the oral cavity can be characterized as a series of stages or phases (Fig. 65-3). Different stages of ingestion have been defined by placing small metal markers in the jaws, hyoid, and tongue of experimental animals. These markers can be detected with high-speed cinefluorographic techniques, allowing the movements of the internal oral apparatus to be monitored during the entire ingestive sequence of the awake preparation (Hiiemae and Crompton, 1985). The division of feeding into five dynamic stages by Hiiemae and Crompton is indicated on the second tier of Fig. 65-3.

The first stage of putting food into the mouth (ingestion) is followed by intraoral transport and the positioning of food between the molars (second stage) for mastication (third stage). Intraoral transport to the back of the tongue (fourth stage) initiates deglutition (fifth stage). The duration of each stage of feeding is both species specific and variable, depending on what is being ingested (Hiiemae and Crompton, 1985). Fluid consumption does not require mechanical breakdown by mastication and thus has only three stages. In humans, drinking uses the same muscles as mastication, but the coupling among the facial, trigeminal, and lingual muscles is different (Lund and Enomoto, 1988). The orbicularis oris muscle contracts to form a tight seal during human drinking (sucking) but relaxes during mastication.

Mastication

The movements of mastication can be further subdivided. Kinematic measurements during mastication indicate that rhythmic masticatory movements o solid food typically involve several distinct components (Hiiemae, 1976; Luschei and Goldberg, 1981). Beginning the masticatory cycle with an open mandible, the jaw closes rapidly and then more slowly. The transition from fast closure to slow closure occurs when the teeth make contact with solid food and is thought to involve sensory feedback from the periodontal ligament (Lund and Enomoto, 1988). More detailed analysis of the opening phase of mastication indicates additional complexity. Following the slow-closure phase, during which time the teeth make maximal intercuspation, the masticatory cycle continues with a slow-opening phase followed by a fast-opening phase. A recent review of mastication suggests a transition phase between slow and fast opening (Lund and Enomoto, 1988). Pauses during rhythmic mastication are frequent during this tansition phase. When mastication commences, it starts with the rapid opening phase, followed by fast and slow closure, and ends with a slow opening.

Electromyography. Although mastication involves coordinated activity of the jaws, hyoid apparatus, and tongue (Hiiemae and Crompton, 1985), the majority of electromyographic studies of mastication have focused on the jaw musculature. Jaw opening during mastication is associated with activity in the anterior digastric muscles and the inferior head of the lateral pterygoid muscle (Lund and Enomoto, 1988; Luschei and Goldberg, 1981). The closing phase of mastication begins with contraction of the masseter muscle, followed by the temporalis, medial pterygoid, and superior head of the pterygoid, which are recruited during the power stroke (slow closure). Food is typically chewed unilaterally. Although the trigeminal musculature is bilaterally activated during mastication, the ipsilateral (working) side is active earlier (Luschei and Goldberg, 1981).

Food consistency is one factor affecting the masticatory rhythm (Ahlgren, 1976; Thexton et al, 1980). In a study of the effects of hardness on chewing, Plesh and colleagues (1986) observed that most subjects chewed hard gum at a slightly slower rate than soft gum.

The decreased frequency of chewing was associated with significantly longer opening and occlusal phases of chewing rather than with the closing phase, despite the significantly greater electromyographic (EMG) activity in the masseter muscle.

Age is another factor that affects the masticatory rhythm (Karlsson and Carlsson, 1990). Older subjects chewed chisp bread at the same frequency as younger subjects (approximately 1.4 Hz), but the structure of the rhythm was different. The older subjects opened and closed their mouths at a slower velocity but achieved the same overall chewing rate by not opening their mouths as far. Movement irregularities during chewing were also observed during the jaw-opening and jaw-closing phases of mastication in patients diagnosed with temporomandibular pain (Stohler and Ash, 1985). Unlike the smooth, uninterrupted alteration between opening and closing seen in normal individuals, patients with temporomandibular pain frequently started reopening their mouths during the closing phase of mastication or reclosed during the opening phase.

Central control. Experimental studies indicate that the masticatory rhythm is centrally programmed; that is, a peripheral stimulus is not necessary to initiate the masticatory rhythm nor is feedback from the active muscles necessary to sustain the response (reviewed in Lund and Enomoto, 1988). Fictive mastication evoked by central stimulation in a paralyzed experimental preparation indicates that neither the afferent limb of the jaw-opening reflex nor that of the jaw-closing reflex is necessary to generate the masticatory rhythm. Thus the alternating activation of a jaw-opening reflex followed by a jaw-closing reflex does not explain the origins of the masticatory rhythm.

Nevertheless, both the jaw-opening and jaw-closing reflexes are functionally entwined in rhythmic oral behavior, and the excitability of these reflexes varies as a unction of jaw position during rhythmic opening and closing (Lund and Olsson, 1983; reviewed in Rossignol et al, 1988). In general, the jaw-opening reflex is attenuated during rhythmic masticatory movements as compared with a stationary mandible. In particular, low-threshold mechanical stimuli are less efective than high-threshold stimuli in producing a jaw-opening reflex when applied during rhythmic masticatory movements (Fig. 65-4). Thus during the occlusal phase of mastication, a protective jaw-opening reflex can be initiated in the presence of unexpected mechanical forces directed against the teeth or soft tissues, but innocuous mechanical stimulation associated with chewing will not interrupt the masticatory rhythm. Recent studies implicate secondary sensory neurons in the sensory trigeminal complex in jaw-opening reflex modulation (Olsson et al, 1986). Low-threshold mechanoreceptors in the rostral sensory trigeminal complex had depressed excitability during cortically evoked mastication. High-threshold neuron excitability, in contrast, was clearly phase modulated, with the greatest excitability during the occlusal phase of mastication. The significance of this reflex modulation is still the subject of debate. Are the oral reflexes inhibited to allow voluntary or rhythmic behavior via a central pattern generator, or does reflex modulation reflect the involvement of reflex circuits in the generation of the motor behavior itself?

Transection studies have localized the central pattern generator for mastication to the pontomedullary reticular formation (Chandler and Tal, 1986; Nozaki et al, 1986), and anatomic and neurophysiologic studies indicate that the medial reticular formation at the pontomedullaryjunction receives projections from the masticatory cortex (reviewed in Lund, 1991). The basic neural circuitry necessary for the rhythmic alternating contraction of jaw-

opening and jaw-closing muscles do not require sensory input. Nevertheless, intraoral sensory receptors are critical for regulating bite force during mastication.

Sensory control. Efficient eating requires that food be reduced in size or swallowing. This requires determining both the hardness and size of the food and correctly positioning food between the occlusal surfaces of teeth. Psychophysical studies in humans indicate that receptors in both the periodontal ligament and temporomandibular joint contribute to the interdental discrimination required during eating (reviewed in Dubner et al, 1978). The loss of periodontal ligament receptors associated with complete dentures results in impaired interdental discrimination, as does anesthetization of the dentition in individuals with natural teeth. Receptors in the temporomandibular joint also contribute to size discrimination in the mouth. When the temporomandibular joint is anesthetized, interdental discrimination decreases.

Recent studies have reexamined the morphology, distribution, and innervation of receptors within the periodontal ligament (Byers, 1985; Byers and Dong, 1989). As many as six varieties of receptor morphology were described, ranging from complex Ruffini-like branched endings to free nerve endings. The cell bodies for periodontal ligament receptors were located peripherally in the trigeminal ganglion and centrally in the mesencephalic trigeminal nucleus (Jerge, 1963). Mesencephalic trigeminal innervation of the periodontal ligament was primarily in the apical region near the root and consisted of mostly small myelinated Ruffini-like endings (Byers et al, 1986). Trigeminal ganglion innervation extended from the apical region to the more superficial region and included small unmyelinated nerve endings.

The differential innervation of the periodontal ligament by both the trigeminal ganglion and mesencephalic trigeminal nucleus has functional significance. Mesencephalic receptors are primarily medium and rapidly adapting receptor types, many with directional sensitivity. The central termination of these mesencephalic force detectors includes inhibitory connections to trigeminal jaw closer motoneurons via the supratrigeminal area (Kidokoro et al, 1968). Thus these receptors serve a protective role in preventing potentially damaging tooth contact during mastication. In contrast, trigeminal ganglion receptors include slowly adapting mechanoreceptors (position detectors) and high-threshold C fibers (nociceptors) in addition to rapidly adapting mechanoreceptors. Moreover, periodontal receptors from the trigeminal ganglion terminate centrally in the sensory trigeminal complex, the source for the ascending (lemniscal) sensory pathway to the thalamus and cortex. Thus tooth displacement and dental pain information from the periodontal ligament originates from the sensory trigeminal complex via the trigeminal ganglion pathway.

Although mechanoreceptors in the periodontal ligament are not encapsulated, their response characteristics may be influenced by the elastic properties of the ligament (Byers and Dong, 1989). When the attachment of the ligament is compromised, for example, during periodontitis that looses the connective attachments of the ligament, a corresponding loss in interdental force discrimination is observed (van Steenberghe et al, 1981). Periodontal receptors also contribute to the regulation of bite force. Individuals with dentures could not bite as hard as normal dentulous subjects and could not perceive variations in their own bite force (Williams et al, 1985). Similar results were obtained by anesthetizing the inferior alveolar nerve (Williams et al, 1984). In contrast, anesthetizing the temporomandibular joint

does not affect bite force discrimination but does impair jaw-positioning performance. Thus sensing jaw position and controlling bite force during mastication may be regulated by different populations of oral receptors.

Oral phase of deglutition

Following mastication and the intraoral transport of food to the back of the tongue, deglutition consists of an upward movement of the tongue against the soft palate to force the bolus in the direction of the pharynx (Miller, 1982). The precise nature of the stimulus that triggers the pharyngeal stage of deglutition is unknown. Both the volume and the rate of bolus accumulation interact to trigger swallows in experimental animals (Weijnen et al, 1984). When the rate of licking (intraoral transport) increased in response to increased stimulus delivery, the volume per swallow also increased. Moreover, the physical nature of the bolus can influence both the sequence and recruitment of individual muscles involved in the buccal phase of swallowing. In monkeys the masseter muscle was recruited with the suprahyoid muscles (the anterior digastric, geniohyoid, and mylohyoid) during swallows of solid food in contrast to fluid swallows (McNamara and Moyers, 1973). Similarly, there is individual variation in the activation sequence of the suprahyoid muscles and genioglossus muscle during voluntary swallows in humans (Hrycyshyn and Basmajian, 1972). In summary, the oral phase of swallowing is characterized by the overall movement of a bolus from the dorsal surface of the posterior tongue to the pharynx. The precise motor sequence of individual muscles during the oral phase of deglutition can vary, depending both on the individual and the sensory characteristics of the bolus. Contact of thebolus with sensory receptors in the oropharynx triggers peristaltic contractions of the pharyngeal musculature.

Like mastication, swallowing can be evoked from electrical stimulation of central structures in the absence of peripheral (muscular) feedback and is thus thought to be controlled by a central pattern generator (Miller, 1982). The location of the central pattern generator for swallowing involves the caudal region of the nucleus of the solitary tract and the medullary reticular formation adjacent to the nucleus ambiguus. Voluntary swallowing is mediated by cortical pathways that reach these medullary regions through descending pathways.

Specialized Sensory Systems: Taste

Oral sensitivity to chemical stimuli

The oral cavity is sensitive to a wide range of chemical stimuli. Stimulation of the oral cavity with high concentrations of salts, acids, alkaloids, and other compounds elicits sensations ranging from stinging and burning to warm, cool, and painful. This sensitivity of the oral cavity, mediated by nonspecialized free nerve endings and shared by all mucosal membranes, is referred to as the common chemical sense and should not be confused with taste. Free nerve endings respond to many traditional gustatory stimuli but typically display a much lower sensitivity. Electrophysiologic recordings from the lingual nerve, for example, indicate that single fibers require concentrations of sodium chloride 1000 times higher than those necessary to elicit a response from a gustatory fiber in the chorda tympani nerve (Silver, 1987). Much lower concentrations of other types o chemical stimuli, for example, menthol (10^{-4}), however, are adequate to elicit a response in trigeminal nerve fibers. The types of

chemical stimuli that elicit low-threshold responses in trigeminal fibers suggest that one function of the common chemical sense is to protect the oral cavity (reviewed in Silver, 1987). Responses to common chemical stimuli such as salivation and coughing diffuse and remove offending stimuli from the mouth. The common chemical sense is not purely protective, however. Spices such as horseradish, ginger, and red pepper are effective stimuli for trigeminal afferent fibers and contribute to the flavor of food.

In contrast to the common chemical sense, taste sensations are evoked by relative low concentrations of chemical stimuli when applied to the specialized gustatory receptor cells. Most investigators agree that there are a discrete number of taste sensations; the most common and easily recognizable are sweet, salty, sour, and bitter. The Japanese frequently include a fifth taste, "umami" (heavenly), associated with the taste of monosodium glutamate (Kawamura and Kare, 1987). The sensations of flavor while eating are more diverse than those of pure taste and result from the interaction of taste with the smell and texture of food. The confusion between taste and flavor is well documented in taste and smell clinics (Bartoshuk et al, 1983; Smith, 1988). Self reports of chemosensory dysfunction are highly unreliable; on testing, many individuals reporting loss of taste are frequently found to have impaired olfactory function with no loss in taste sensitivity.

In addition to a sensory-quality dimension with four distinct tastes, taste stimuli can be categorized on a hedonic dimension with stimuli divided into those that are preferred and those that are disliked. The hedonic attribute of taste is concentration dependent and spans the different submodalities of sweet, sour, salty, and bitter. Low and medium concentrations of salt are preferred, but salt becomes aversive at high concentrations. Although there is a strong genetic component to the hedonic values associated with gustatory stimuli, taste preferences are clearly modifiable by experience (Cowart and Beauchamp, 1986). Human neonates find bitter solutions strongly aversive, but adults learn to enjoy coffee, alcohol, and other bitter-tasting substances. The hedonic attributes of taste are also subject to metabolic state (discussed below).

Gustatory structures

Approximately 7900 gustatory receptos in the human mouth are grouped into distinct subpopulations, defined by their intraoral location, gross morphology, and innervation (reviewed in Travers and Nicklas, 1990). Gustatory subpopulations differ in sensitivity to chemical stimuli; however, the overal morphology of the taste bud structure within each subpopulation is very similar (reviewed in Kinnamon, 1987). Each taste bud contains 50 to 150 neuroepithelial cells arranged in spindlelike clusters. Some of the cells within the taste bud extent microvilli into a nonkeratinized "pore" region on the apical surface of the bud. Taste bud cells without microvilli are designated supporting (or basal) cells and may represent a developing receptor cell. Receptor cells die and are replaced over a 10- to 14-day period (Beidler and Smallman, 1965); however, the lineage of replacement receptor cells within the taste bud remains controversial. Because taste cells undergo continuous differentiation, disruption of cell division by radiation or other agents can disrupt the sense of taste.

The chorda tympani branch of the facial nerve innervates two to five taste buds on each of approximately 400 fungiform papillae on the anterior aspect of the tongue (Miller, 1986). Fungiform papillae density is greatest at the tip of the tongue and decreases along the dorsal and dorsolateral edges of the tongue. No fungiform papillae are found along the midline. Taste buds on the posterior aspect of the tongue are innervated by the glossopharyngeal nerve and located either in tightly packed clusters distributed along the walls of the trenches surrounding seven to ten circumvallate papillae or in the inner folds of the folate papillae located along the lateral edges of the posterior part of the tongue. The 2400 taste buds in the circumvallate papillae and 1300 in the foliate papillae constitute the largest percentage in the human oral cavity. A third large subpopulation of gustatory receptors located in the pharynx and larynx numbers approximately 2400 in humans. These taste buds are not associated with distinct papillae; however, the bud morphology is similar to that found on the tongue. Taste buds of the pharynx are innervated by the glossopharyngeal nerve, and those in the larynx are innervated by the superior laryngeal nerve branch of the vagus. A smaller subpopulation of taste budes (approximately 400 in humans) is found on the soft palate. These taste receptors, also not associated with distinct papillae, are probably innervated by the greater superficial petrosal nerve branch of the facial nerve. In rodent species, small populations of taste buds are also ound on the buccal wall and sublingual organ, but these have yet to be characterized in humans.

The specific pattern of innervation of taste buds by a peripheral nerve has been characterized for the fungiform papillae on the front of the tongue. Single fibers of the chorda tympani nerve synapse on multiple receptor cells within a single taste bud and on receptor cells in adjacent taste buds (Miller, 1971). Likewise, each receptor cell is innervated by more than one fiber of the chorda tympani nerve. Each fiber of the chorda tympani thus receives input from multiple receptor cells, and each bud is innervated by more than one fiber. This pattern of convergence of multiple receptor cells from adjacent taste buds onto a single afferent fiber provides an anatomic substrate for spatial interactions between adjacent taste buds. Successively lower perceptual thresholds in humans may be reached by stimulating multiple adjacent papillae with gustatory stimuli (discussed in Miller and Reedy, 1990b).

Gustatory physiology

A common observation in neurophysiologic studies of the gustatory system is that individual neural elements are usually sensitive to a variety of chemical stimuli. Receptor cells, afferent nerve fibers, and central neurons are often responsive to diverse chemical stimuli that elicit qualitatively different sensations in humans. The central issue in gustatory coding has been to determine how broadly responsive neurons code for such distinct sensations as sweet, salty, sour, and bitter. Recent work has focused on organizing gustatory neurons at different levels of the sensory pathway into neuron types (reviewed by Travers et al, 1987b). Although many neurons are multiply sensitive to different-tasting stimuli, these sensitivities are not random. Neurons are no specifically tuned to a single stimulus but typically respond best to one of the stimuli representing the four basic taste qualities. The representation (coding) of quality is thought to be mediated by these classes of neurons.

Sensory transduction

Gustatory receptor cells respond with graded depolarizing (occasionally hyuperpolarizing) potentials in response to chemical stimuli. The size of the receptor potential predicts the magnitude of spike discharge in the afferent nerve and may represent the generator potential necessary for the release of a neurotransmitter at the receptor cell/afferent nerve synapse. The neurotransmitter or neurotransmitters released have not been identified.

Several different types of transduction mechanisms have been proposed for the gustatory system (reviewed in Teeter and Brand, 1987; Teeter and Cagan, 1989). Proposed receptor mechanisms include the binding of a stimulus molecule to a receptor macromolecule in the cell membrane that alters membrane permeability and allows ionic flow. Other transduction mechanisms involve the direct movement of stimulus ions across specific membrane channels. Because different receptor mechanisms are associated with different chemical stimuli and individual receptor cells are broadly sensitive, it appears that different receptor mechanisms may coexist for the same cell.

One of the transduction mechanisms for sodium salts (for example, sodium chloride) involves the direct movement of sodium cations across the cell membrane, which results in depolarization (DeSimone et al, 1984). The passive sodium channel blocker amiloride blocks the depolarization of receptor cells from stimulation with sodium chloride but leaves responses to other chemical stimuli (for example, sucrose, potassium chloride) largely intact. Further, amiloride selectively blocks responses of afferent fibers optimally responsive to sodium chloride (Hettinger and Frank, 1990). Psychophysical studies in both humans and rats indicate that the application of amiloride to the tongue is associated with a decrement in perception of Na+ and Li+ salts but not K+ salts (Schiffman et al, 1983). The electrophysiologic and psychophysical response to other salts, for example, potassium chloride, is not blocked by amiloride, nor is the sodium chloride response completely abolished, suggesting multiple receptor mechanisms for salt.

Although monovalent salts do not bind to cell membranes at physiologic concentrations, the binding of a ligand to a receptor on the cell membrane is probably the initial step in the transduction of compounds such as sugars and amino acids, many of which taste either sweet or bitter to humans. The specific binding of L-alanine and L-arginine to a fraction containing catfish taste epithelia suggests distinct amino acid receptors (Teeter and Cagan, 1989). The binding of amino acids to a membrane receptor either depolarizes the receptor cell directly by opening specific ion channels or alters membrane conductance through second-messenger system. Although the hydrogen ion concentration of a stimulus correlates with sourness, specific receptor mechanisms are as yet unknown. Recent intracellular studies in mud puppy taste cells, however, indicate that sour stimuli decrease the resting conductance of the membrane to K+, thereby depolarizing the cell (Kinnamon and Roper, 1988).

Peripheral sensitivity

The broad sensitivity to chemical stimuli observed in single receptor cells of experimental animals is evident following stimulation of single human papillae. Initial observation that single fungiform papillae were sensitive to a single taste quality resulted from stimulus concentrations that were too low (Bealer and Smith, 1975). In taste, as in other sensory systems, there is a trade-off between the area stimulated and the threshold concentration. The lingual threshold for a given gustatory stimulus requires progressively higher concentrations for progressively smaller areas. When single papillae are stimulated with sufficiently high concentrations, the majority of fungiform papillae mediate multiple taste sensations. Sixty-six percent of the fungiform papillae tested elicited recognition of at least three of the four standard taste qualities (Bealer and Smith, 1975).

Gustatory receptors sample food or fluid as it is ingested, masticated, and transported to the back of the mouth for swallowing. Receptor densities appear greatest at critical junctures of the ingestive sequence outlined in Fig. 65-3. Gustatory receptors at the tip of the tongue are contacted immediately as food enters the mouth and are optimally situated to determine whether to continue or abort the ingestive sequence. A second population on the back and sides of the tongue and on the opposing palate is probably stimulated during mastication when food is crushed between the molars. Because subpopulation of gustatory receptors vary in their overall sensitivity to chemical stimuli, subpopulations of gustatory receptors may differentially contribute to oral function.

The chorda tympani nerve in many animal species is highly sensitive to a variety of salts (for example, sodium chloride). This sensitivity is consistent with human psychophysical studies that show a low threshold to sodium chloride on the anterior aspect of the tongue (Collings, 1974). Studies in rats indicate that many individual chorda tympani fibers are sensitive to both sodium chloride and hydrochloric acid (which tastes sour to humans) but that only a subset of peripheral nerve fibers are responsive exclusively to sodium salts (Hettinger and Frank, 1990). When the sodium channel blocker amiloride was applied to the surface of the tongue, only the sodium-specific fibers lost their responsiveness to sodium chloride. Those chorda tympani fibers sensitive to both salts and hydrochloric acid maintained their sensitivity to sodium chloride stimuli in the presence of amiloride, implying that the sodium-specific neurons are particularly important for coding the salty quality of sodium chloride. Moreover, the recognition of sodium chloride decreases following chorda tympani nerve section in rats, further indicating a specialized role for this nerve in sodium recognition (Spector et al, 1990).

The high sensitivity of the anterior aspect of the tongue to sweet stimuli in humans is more variable in experimental animals. The chorda tympani of rats, in particular, is not very sensitive to sweet-tasing stimuli; however, a sweet sensitivity is found in the anterior oral cavity in the nasoincisor ducts on the hard palate that lie in apposition to the anterior tongue (Travers et al, 1986). The nasoincisor ducts are innervated by the greater superficial petrosal nerve, a branch of the facial nerve. Regardless of the precise location of the "sweet" receptors, many animals have a sensitivity to sugars and other sweet-tasting compounds in the anterior oral cavity. Gustatory receptors in the posterior oral cavity are highly sensitive to aversive stimuli and can initiate powerful rejection responses to unpalatable chemical stimuli. Sectioning the glossopharyngeal nerves in rats attenuates the rejection response to quinine monohydrochloride to a greater degree than sectioning the chorda tympani nerves

(Travers et al, 1987a).

A specific oral function is particularly apparent for the superior laryngeal nerve. Chemoresponsive fibers in the superior laryngeal branch of the vagus nerve differ greatly from both facial and glossopharyngeal nerve sensitivities (reviewed in Travers et al, 1987a). In general, superior laryngeal nerve fibers are insensitive to sodium chloride and sucrose but respond well to stimulation with potassium chloride, ammonium chloride, and many acid stimuli (Bradley et al, 1983; Dickman and Smith, 1988). Moreover, many superior laryngeal nerve fibers are responsive to mechanical and water stimulation (Storey and Johnson, 1975). The location of superior laryngeal nerve-innervated taste buds in the larynx and on the epiglottis indicates a protective-reflex role for these receptors, rather than contributing to gustatory quality perception. The superior laryngeal nerve is a particularly low-threshold nerve for eliciting swallows that could protect the airway (Miller, 1982).

Human psychophysical studies show clear regional variation in the recognition thresholds to different gustatory stimuli (Collings, 1974). The front of the tongue had the lowest threshold for both salty and sweet stimuli; sour stimuli had the lowest threshold when applied to the foliate papillae. Although the front of the tongue also had the lowest threshold for bitter stimuli, such as quinine monohydrochloride, circumvallate papillae stimulation produced a steeper intensity function than obtained by stimulating the front of the tongue. The psychophysical scaling results for quinine monohydrochloride are consistent with the often reported observation that bitter sensations are more intense in the back of the mouth. With the exception of the high sensitivity to sour stimuli on the sides of the tongue, the gradient for the threshold to chemical stimuli on the tongue follows the gradient for thresholds to mechanical stimuli, with the anterior region the most sensitive.

Despite these regional variations in threshold and concentration response functions, sensations of sweet, sour, salty, and bitter can be elicited from loci widely distributed within the oral cavity. Moreover, loss of a single gustatory nerve may not be apparent to the individual and can often be ascertained only by specific psychophysical procedures (Bartoshuk, 1989). In general, the high degree of specialization among the different gustatory nerves of experimental animals is not as obvious in humans. Destruction of the chorda tympani from middle ear surgery destroys taste sensitivity from the front of the tongue (Bull, 1965; Jeppson and Hallen, 1971), but there have been no reports of a disruption of salt intake. It is interesting to note, however, that humans with laryngectomies reported thirst less often and were less able to localize thirst as compared with a control group, suggestive of a role for the superior laryngeal nerve in mediating thirst (Miyaoka et al, 1987). The regional intraoral variation of taste sensitivity of humans may represent only a vestigial form of reflex organization, superseded by a wider distribution of gustatory sensitivities within the oral cavity and by an increase in the voluntary neural control of ingestion.

In general, there is a great deal of individual variation in the absolute thresholds to gustatory stimuli. Several studies have demonstrated as much as a hundredfold variation in detection thresholds or both sucrose and sodium chloride over a wide range of ages (presented in Bartoshuk et al, 1986). Recent studies indicate that some of the variation in the perception of gustatory intensity may relate to individual differences in the number of taste buds (Miller and Reedy, 1990a, 1990b). When the tongues of (live) human subjects were stained with 0.5% methylene blue, taste pores could be counted videomicroscopically and subsequently

correlated with individual suprathreshold intensity ratings. Subjects with more taste buds gave significantly higher intensity ratings to standard concentrations of both salt and sucrose solutions applied to the tongue. It is unclear, however, whether the correlation between taste bud number and intensity ratings explains the human loss of gustatory sensitivity with age (Miller, 1989). The loss of taste sensitivity with age is well established for both detection and recognition thresholds (Murphy, 1986; Schiffman, 1986), but initial studies showing fewer taste buds with age have not been substantiated in recent human or animal studies (Bradley et al, 1985; Miller, 1989).

Central gustatory pathways and function

Afferent gustatory fibers in the facial, glossopharyngeal, and vagus nerves synapse in the nucleus of the solitary tract of the medulla with a rostral to caudal organization (Fig. 65-5). An ascending gustatory pathway reaches the cortex via a thalamic projection or via an additional synapse in the parabrachial nuclei of the pons, depending on the species (reviewed in Finger, 1987). A second gustatory pathway projects to the ventral forebrain, including the hypothalamus, amygdala, and other limbic structures. The thalamo-cortical pathway may be specialized for perceptual/discriminative gustatory functions; the limbic projections may be more involved in the hedonic/motivational attributes of taste (Pfaffmann et al, 1979). Local brainstem gustatory pathways, however, have the capacity to mediate basic gustatory discriminative functions. Both decerebrate animals and anencephalic human infants discriminate palatable from unpalatable gustatory stimuli (Pfaffmann et al, 1979).

Gustatory pathways are in close anatomic proximity with central pathways controlling autonomic nervous system function. This proximity provides a substrate for interactions between gustatory and autonomic afferent information (Norgren, 1985). Changes in the firing pattern of gustatory-responsive neurons in the nucleus of the solitary tract in response to distension of the gut is indicative of interaction between the autonomic nervous system and the gustatory system (Glenn and Erickson, 1976). Similarly, hypertonic saline infused into the hepatic portal vein of the rat influences taste responses in the parabrachial nucleus (Rogers et al, 1979). Both phenomena suggest that visceral signals generated during feeding may influence orosensory perception. Human studies have documented the postingestion effects of feeding on gustatory preference. The preference of specific tastes, such as glucose, for example, diminishes as a function of the amount consumed (Cabanac, 1971).

Chronic metabolic conditions also influence the hedonic perceptions of taste stimuli. Obese and slightly overweight individuals rate glucose solutions as more pleasant than do normal-weight individuals, although the perceived intensity of the glucose solutions does not vary between the two groups (Rodin et al, 1976). Hypoglycemic individuals prefer higher concentrations of sucrose as compared with individuals with high blood glucose (Mayer-Gross and Walker, 1946), and studies of diabetic patients reported elevated psychophysical thresholds to glucose (reviewed in Settle, 1986). Loss of gustatory sensitivity in diabetics may result both from a systemic lack of glucose receptors and from general neuropathy. Even short-term increases in blood glucose, however, appear to differentially affect neural responses in the nucleus of the solitary tract in response to sugar solutions presented to the tongue of experimental animals (Giza and Scott, 1983).

Systemic electrolyte levels also affect the gustatory system. Sodium chloride thresholds are lower both for individuals on low-sodium diets and in hypertensive patients (discussed in Schiffman, 1983a, 1983b). Physiologically, decreases in the chorda tympani nerve response to sodium chloride flowing over the tongue have been observed in sodium-deprived experimental animals (Contreras and Frank, 1979). The convergence between gustatory afferent fibers and visceral interoceptors on central neurons is one explanation for systemic metabolic and electrolyte influences on the gustatory system (Norgren, 1985).

Gustatory-salivatory reflexes are another example of an interaction between the gustatory and autonomic nervous systems (Spielman, 1990). Direct gustatory influences over salivation are mediated by short axon pathways between second-order gustatory neurons in the lateral division of the nucleus of the solitary tract and preganglionic parasympathetic salivatory neurons located in more medial portions of the solitary nucleus and the adjacent reticular formation (Norgren, 1985). In addition, the oral cavity provides a peripheral site for interactions between the autonomic and gustatory systems and for general metabolic influences on the gustatory system via the vasculature.

Interaction between saliva and taste

The presence of saliva in the mouth continually stimulates gustatory receptors with low levels of salt ions. Correspondingly, recognition thresholds for sodium cloride are somewhat raised when the tongue is adapted with a solution containing salivary levels of sodium (3. mM) as compared with recognition thresholds using distilled water rinses (0.054 mM) (McBurney and Pfaffmann, 1963). By implication, the presence of other salivary constituents as a result of either disease or medication may affect gustatory sensitivity (reviewed in Christensen, 1986). Salivary concentrations of pirmenol in patients being treated for ventricular arrhythmias, for example, may produce the bitter taste reported by these patients (Johnson et al, 1986). Increased salivary levels of glucose in diabetics provide one mechanism for the increased detection thresholds for glucose in this patient population (Settle, 1986).

Saliva may also exert a trophic influence on gustatory receptors. Patients suffering long-term salivary loss as a result of Sjögren's syndrome had increased detection and recognition thresholds to many gustatory stimuli (Henkin et al, 1972). Biopsies of the circumvallate papillae from a subset of these patients indicated a profound loss of taste buds. The effects of desalivaton on both taste bud morphology and gustatory sensitivity has also been explored in experimental animals (Cano and Rodrigues-Echandia, 1980; Nanda and Catalanotto, 1981). Surgically removing the salivary glands was associated with increased keratosis of the lingual epithelium and shrinking of the circumvallate papillae. Correlated with these morphologic changes was the increased consumption of nonpreferred gustatory stimuli, indicative of a loss of gustatory sensitivity. Electron microscopic observation of the circumvallate papillae showed the infiltration of bacteria, suggesting that the loss of antibacterial agents in saliva permitted degenerative microbial action. Lack of salivation by acute pharmacologic manipulations in experimental human studies, however, had relatively little effect on gustatory sensitivity (Christensen et al, 1984).

The loss of taste acuity in humans after radiotherapy to the head and neck could result both directly from the destruction of taste buds and indirectly from reduced salivary flow (Conger, 1973; Mossman, 1986). Direct irradiation of gustatory structures in experimental animals produced a loss of taste buds (Conger and Wells, 1969). Radiotherapy can also influence the gustatory system through the formation of conditioned taste aversions (Bartoshuk, 1990; Bernstein and Webster, 1980). Clinical observations of hedonic changes in taste may result, in part, from the pairing of a conditioned stimulus (food) with an unconditioned stimulus, the gastrointestinal distress resulting from either chemotherapy or abdominal radiation (Bernstein and Webster, 1980). An extensive experimental animal literature indicates that such pairings can have a profound impact on gustatory preferences (reviewed in Chamber, 1990). Experimental animal studies indicate that the formation of a conditioned taste aversion is a central phenomenon that requires an intact forebrain.

Vascular taste

Although the taste pores and microvilli are oriented toward the oral cavity, chemical stimuli gain access to gustatory transduction mechanisms (and ultimately perception) via the vasculature (Bradley, 1973). The extent to which vascular taste mechanisms contribute to the rather extensive number of drugs that have unpleasant gustatory side effects remains to be determined (Rollin, 1978).