Smell and Taste Disorders, A Study of 750 Patients From the University of Pennsylvania Smell and Taste Center

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- Smell and taste disorders are common in the general population, yet little is known about their nature or cause. This article describes a study of 750 patients with complaints of abnormal smell or taste perception from the University of Pennsylvania Smell and Taste Center, Philadelphia. Major findings suggest that: chemosensory dysfunction influences quality of life; complaints of taste loss usually reflect loss of smell function; upper respiratory infection, head trauma, and chronic nasal and paranasal sinus disease are the most common causes of the diminution of the sense of smell, with head trauma having the greatest loss; depression frequently accompanies chemosensory distortion; low body weight accompanies burning mouth syndrome; estrogens protect against loss of the sense of smell in postmenopausal women; zinc therapy may provide no benefit to patients with chemosensory dysfunction; and thyroid hormone function is associated with oral sensory distortion. The findings are discussed in relation to management of patients with chemosensory disturbances.


T he chemical senses play an important role in determining the flavor and palatability of foods and beverages, as well as in the warning of fire, toxic vapors, and spoiled foodstuffs. In addition, their dysfunction has been associated with aging and with a broad range of diseases and anomalies, including Alzheimer’s disease and Parkinsonism. Hundreds of thousands of patients present to medical practitioners each year with complaints of smell and taste dysfunction. Such dysfunction can be of considerable practical consequence, particularly to individuals whose livelihood or immediate safety depends on the normal functioning of their senses of smell and taste (eg, cooks, firemen, plumbers, professional food and beverage tasters, employees of natural gas works, chemists, and numerous industrial workers).

In the present study, demographic, medical, and chemosensory data are presented from 750 patients who completed an extensive medical and sensory protocol at the University of Pennsylvania Smell and Taste Center, Philadelphia, during the period extending from 1980 through 1986. This interdisciplinary center utilizes expertise from many specialties to better understand the chemical senses in health and disease and is the first of several such centers in the United States supported by the National Institutes of Health, Bethesda, Md.

PATIENTS AND METHODS

The Study Population

Three hundred thirty-six men (mean age, 49.1 years; SD = 16.7 years) and 414 women (mean age, 51.5 years; SD = 17.4 years) were examined. These patients represent a consecutive series and were not selected on the basis of any particular cause of chemosensory dysfunction. The group was 87% white and relatively well educated, with 54% having had at least some post-high school education. Most were self-referred or referred by otorhinolaryngologists within the tristate area of Pennsylvania, Delaware, and New Jersey.

Intake Questionnaire and Physical Examination

Detailed information regarding each patient’s current health, medical history, and chemosensory complaint was obtained during patient interviews and medical examinations, as well as from a 270-item intake questionnaire completed by the patient prior to sensory evaluation. Medical information included a history and head and neck examination and, when required, imaging and other specialized tests.

The questionnaire, given to every patient, comprised seven sections: 1, General Information (questions regarding demographics, referral source, and drinking and eating habits); 2, Medical History (listing of major illnesses and injuries, hospital admissions, and medications taken in the year prior to and since symptom onset); 3, History of Present Illness (report of the problem, in the patient’s own words, including date of onset, duration, antecedent conditions, and treatments received); 4, Smell Symptoms (questions concerning problems with the sense of smell, general nasal health and abnormal nasal sensations, including nasal obstruction, rhinorrhea, and postnasal drip); 5, Taste Symptoms (questions related to problems with the sense of taste, general oral health, and abnormal oral sensations); 6, Endocrine Information (questions regarding endocrine status, including endocrine operations [eg, oophorectomy and thyroidectomy], and, in women, menstrual cycle length, oral contraceptive usage, and somatic or psychological...
changes during the menstrual cycle, as measured by Form T of the Moos Menstrual Distress Questionnaire; and 7, Depression (the Beck Depression Inventory [BDI]).

Sections 1 through 5 were designed to characterize, as completely as possible, the nature of the problem and possible factors associated with its occurrence. Sections 6 and 7 were included because of possible relations between chemosensory function and endocrine state and depression. Sections 1 through 3, 6, and 7 were completed by all patients (with the exception of the Moos questionnaire, which was completed only by premenopausal women), whereas completion of sections 4 and 5 depended on specific symptoms of the patient.

Chemosensory Test Battery

Seven psychophysical tests were used to assess chemosensory function: (1) the University of Pennsylvania Smell Identification Test (UPSIT), a standardized 40-stimulus microencapsulated “scratch-and-sniff” odor identification test; (2) a forced-choice single-staircase odor detection threshold test using phenyl ethyl alcohol (PEA), a rose-like smelling compound with comparatively little intranasal trigeminal stimulative properties; (3) a whole-mouth test of taste-quality identification utilizing suprathreshold concentrations of sucrose, citric acid, caffeine, and sodium chloride; (4) a taste-intensity rating test in which average suprathreshold intensity ratings were derived for low and high concentrations of the aforementioned tastants (termed throughout the text as the low-intensity taste [LIT] and high-intensity taste [HIT] tests, respectively); (5) a whole-mouth taste-detection threshold test for sucrose, citric acid, and sodium chloride; (6) a test of regional tongue-taste quality identification designed to detect the presence of a gross unilateral deficit on either the anterior two thirds of the tongue (innervated by the chorda tympani branch of cranial nerve [CN] VII) or the posterior third of the tongue (innervated by CN IX); and (7) an electrogustometric threshold test of the difference in sensitivity of the two sides of the anterior portion of the tongue to microamperes levels of current.

Tests 1 to 4 required from 1.25 to 2 hours per patient to administer. Because of the additional 2.5 hours required for the administration of the other tests and the infrequency of taste deficits found in earlier patients evaluated by our group, they were given less frequently and only when a patient's history or medical examination suggested a need for additional taste testing or a significant gustatory problem was suspected on the basis of the suprathreshold taste testing.

Olfactory Retesting

The olfactory function of 306 patients was retested using the UPSIT at intervals ranging from 5 months to 6.4 years following their initial testing. This testing provided information on longitudinal changes in olfaction.

Patient Classification

Based on data from the medical histories and examinations, each patient was assigned to one of 28 probable causal categories (eg, head trauma, upper respiratory infection, nasal and paranasal sinus disease, and exposure to toxic chemicals). Using the taste and smell psychophysical test data (or self-report in the case of chemosensory or oral somatosensory distortions), each patient was also classified as having, alone or in combination (1) normal smell function, (2) normal taste function, (3) absent or diminished smell function (ie, anosmia or hyposmia), (4) absent or diminished taste function (ie, ageusia or hypogeusia), (5) current dysosmia (or parosmia, ie, smell distortion), (6) previous dysosmia, (7) current dysgeusia (or parageusia, ie, taste distortion), (8) previous dysgeusia, (9) no current or previous dysosmia, (10) burning tongue or mouth, or (11) subjective complaints of halitosis or body malodor. In addition, subclassifications were made when appropriate. For example, cases of dysgeusia were classified as (1) transient or nontransient, (2) stimulated or nonstimulated (ie, whether or not an oral stimulus was required to induce the sensation), and (3) identifiable or not identifiable (eg, having or not having a sweet, sour, salty, bitter, or metallic “taste” or “taste combination”).

Statistical Analysis

A variety of standard statistical procedures were employed, depending on the statistical requirements of a given assessment (eg, categorical or continuous variables). The principal methods were t tests, χ² tests, regression analysis, and analysis of variance and covariance. For development of an appropriate linear model, a model including all of the independent variables (ie, age, gender, smoking, level of education, and time since onset of the problem) and selected interactions was first constructed, and the significance of each variable was tested. Variables and interactions for which the P value exceeded .10 were then removed. In many instances where statistical significance is cited parenthetically, the mean ± 1 SD is given. The P values are adjusted for covariates.

Age was included in many fitted models, since studies have shown that age influences chemosensory measures. Similarly, gender was included in almost all final-fitted models, since women scored significantly better than men on most measures, as has been noted in normal subjects in the general population. Smoking also was included in the models when taste-quality identification and caffeine HIT measures were analyzed, since smokers were found to perform more poorly on these measures (see references 24 through 26).

RESULTS

Following a general overview of the types of presenting chemosensory complaints and a description of the major causes, our major findings are presented under subheadings that reflect the observations.

General Overview of Chemosensory Complaints

The majority of the complaints from patients presenting to the center reflected concerns about loss of olfactory function, either alone (20.4%) or in combination with loss of gustatory function (57.7%), while 8.7% of patients complained of taste loss only (Fig 1, left diagram). Of these patients, 10.4% presented solely with complaints of dysosmia, dysgeusia, or burning mouth. A small percentage presented with other primary complaints.

Of the patients reporting loss of smell function, the most common complaint was that of total nontransient loss of the sense of smell (49.6%). In total, 241 patients (32.1%) reported experiencing dysosmia in addition to, or independent of, losses of the senses of smell or taste. Most of these patients (70.2%) reported the sensation as being unpleasant, 23.4% reported the sensation as being neither pleasant nor unpleasant, and 6.4% reported the sensation as being pleasant. Two hundred eighty dysosmics (90.5%) reported that the distortion was still present, either continuously or intermittently, at the time of their evaluation, whereas the remaining 23 dysosmics indicated that dysosmic episodes no longer occurred. Eighteen patients with dysosmia noted this as their only chemosensory complaint. The complaint of dysosmia was more frequent in women than in men (64.8% vs 28.9%).

Two hundred fifty-seven patients complained of dysgeusia either alone
Complaints of Taste Loss Typically Reflect Losses of Smell, Not Taste, Function.

Most patients reporting olfactory loss believed that they had at least partial gustatory loss (433 of 586 patients). However, the results revealed that fewer than 4% of the patients had a demonstrable gustatory deficit (Fig 1, right diagram). Notably, patients who complained only of loss of the sense of taste and who had demonstrable olfactory or gustatory loss were nearly three times more likely to show an olfactory deficit than a gustatory deficit.

Concurrent Experience of Dysgeusia and Dysosmia Depends on the Nature of the Dysgeusia

One hundred thirty-one patients reported experiencing both dysgeusia and dysosmia. Individuals who reported their dysgeusia as being identifiable (eg, bitter) were less likely to report a concurrent dysosmia than individuals whose dysgeusia had no identifiable quality (Fig 2). Also, individuals who reported their dysgeusia condition to be stimulated by eating were more likely to report a concurrent dysosmia than individuals reporting a dysgeusia not associated with eating.

Cause of Chemosensory Dysfunction: Upper Respiratory Infection, Head Trauma, and Nasal and Paranasal Sinus Disease Account for the Majority of Cases

A variety of probable causes were associated with chemosensory disorders, with no single cause accounting for more than 26% of the cases (Table 1). However, the three categories of...
upper respiratory infection/cold (URI), head trauma (HT), and nasal and paranasal sinus disease (NSD) accounted for approximately 60% of patients. Of the few cases with documented hypogeusia or ageusia, 30.4% were of iatrogenic origin.

Since the URI, HT, and NSD groups each comprised a sufficient number of patients to allow detailed subgrouping and statistical assessment, they became the focus of many of the analyses described in this article and are referred to throughout as the “three major causes.” Examination of age and gender distributions revealed that a larger proportion of women than men in the patient population evidenced URI-related chemosensory deficits (29.5% vs 20.8%, P < .01), and that patient age at onset of the disorder was higher in the women than in the men of this group (54.6 vs 49.4 years; P < .025). A greater proportion of male than female patients evidenced head trauma-related deficits (21.4% vs 14.5%; P < .02), and the age of onset did not differ significantly between genders (men, 37.4 years; women, 36.0 years; P > .40). The proportion of men and women with NSD-related chemosensory deficits did not differ significantly (16.4% vs 13.0%; P > .50), and the age of onset did not differ significantly between genders (men, 40.2 years; women, 39.9 years; P > .90).

**Chemosensory Deficits Secondary to Head Trauma Are More Severe Than Deficits Secondary to Upper Respiratory Infections or Nasal and Paranasal Sinus Disease**

On average, patients with head trauma performed more poorly than did patients with URI or NSD on a number of the olfactory and gustatory measures (Table 2). This difference occurred on odor identification and taste-identification tests, as well as with the LIT ratings for sucrose, citric acid, and caffeine, and with the HIT ratings for all taste qualities (comparison Ps < .05). The prevalence of dysosmias and dysgeusias also differed among the three major causes, with HT having the highest prevalence and NSD having the lowest prevalence (Table 2).

Taste-threshold scores did not differ significantly between the patients with HT and the patients with URI or NSD (comparison Ps > .05). This finding may be due to the relatively small number of patients to whom taste-threshold tests were administered in these three groups (n values ranging from 17 to 47).
Nasal and paranasal sinus disease patients with nasal polyps and identified olfactory deficits had lower UPSIT scores than did NSD patients without nasal polyps (11.9 ± 3.6, n = 19; 17.2 ± 8.1; n = 61, respectively; P < .01).

**A Small Percentage of Patients Demonstrated Recovery of Olfactory Function**

Preliminary analysis indicated that only a small percentage of patients demonstrated recovery of olfactory function, as defined by a significant increase on the UPSIT score at retest. For instance, there was no evidence of improvement of smell function across the two administrations of the UPSIT in those patients whose olfactory loss was secondary to HT or to URI (respective test 1 and test 2 UPSIT scores ± SD): 14.6 ± 6.2 vs 16.3 ± 9.3; 19.6 ± 7.5 vs 22.2 ± 9.4 (P values > .30). Furthermore, no association between the duration of time between the two tests and change in UPSIT score was established (P > .20). However, on retesting, patients with olfactory deficits secondary to nasal or paranasal sinus disease demonstrated slight improvement in olfactory function across this period (respective test 1 and test 2 scores ± SD): 16.1 ± 7.7 vs 22.7 ± 10.1; P < .01).

**Gradual Onset of Olfactory Symptoms More Commonly Associated With Nasal and Paranasal Sinus Disease Than With Upper Respiratory Infection or Head Trauma**

The incidence of sudden or gradual onset of the symptom in patients with loss of smell function differed among the three major causes. Of the patients with hyposmia or anosmia, 66.3% reported gradual onset, while 17.3% of the patients with HT and 30% of the patients with URI did so (P < .001). In patients who provided more detailed accounts of the gradual onset, the onset occurred within a 6-month period in 14 of 19 patients with HT, in 13 of 44 patients with URI, and in 22 of 58 patients with NSD. Two patients with HT, 10 patients with URI, and 17 patients with NSD reported that the interval to symptom onset was greater than 6 months.

**Symptoms of Psychological Depression Are Greatest in Patients Experiencing Dysosmia and Dysgeusia**

In the patient group, 28.5% had scores on the BDI indicative of mild-to-severe depression. However, some subgroups of the study population scored higher on the BDI than did others. As seen in Table 3, patients reporting the presence of dysosmia or dysgeusia had higher BDI scores (8.1 ± 7.9, n = 374) than did patients without such complaints (5.9 ± 6.4, n = 362) (P < .001). In fact, over a third of the patients reporting chemosensory distortions had BDI scores indicative of mild-to-severe depression. In contrast, less than a quarter of the patients who reported only

### Table 2.—Chemosensory Test Scores for the Three Major Causes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Head Trauma</th>
<th>Upper Respiratory Infection</th>
<th>Nasal Sinus Disease</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olfaction UPSIT</td>
<td>17.8 ± 9.7†</td>
<td>23.2 ± 9.4</td>
<td>21.4 ± 11.4</td>
<td>.001</td>
</tr>
<tr>
<td>Log PEA threshold values</td>
<td>-2.3 ± 2.2</td>
<td>-3.0 ± 2.2</td>
<td>-2.6 ± 2.4</td>
<td>NS</td>
</tr>
<tr>
<td>% Reporting parosmia</td>
<td>41.4</td>
<td>35.1</td>
<td>27.5</td>
<td>.10</td>
</tr>
<tr>
<td>Taste</td>
<td>80.3 ± 17.7†</td>
<td>85.1 ± 13.2</td>
<td>83.6 ± 17.7</td>
<td>.05</td>
</tr>
<tr>
<td>High-intensity taste ratings</td>
<td>5.4 ± 1.8†</td>
<td>5.7 ± 1.5</td>
<td>6.1 ± 1.3</td>
<td>.02</td>
</tr>
<tr>
<td>Sucrose high</td>
<td>5.1 ± 1.7†</td>
<td>5.5 ± 1.6</td>
<td>5.9 ± 1.3</td>
<td>.01</td>
</tr>
<tr>
<td>Sodium chloride high</td>
<td>6.4 ± 2.0†</td>
<td>6.8 ± 1.6</td>
<td>7.1 ± 1.4</td>
<td>.05</td>
</tr>
<tr>
<td>Citric acid high</td>
<td>5.7 ± 2.0†</td>
<td>6.3 ± 1.9</td>
<td>6.4 ± 1.4</td>
<td>.05</td>
</tr>
<tr>
<td>Low-intensity taste ratings</td>
<td>3.2 ± 1.2†</td>
<td>3.4 ± 1.2</td>
<td>3.5 ± 1.0</td>
<td>.10</td>
</tr>
<tr>
<td>Sucrose low</td>
<td>3.1 ± 1.3</td>
<td>3.4 ± 1.4</td>
<td>3.5 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>Sodium chloride low</td>
<td>4.7 ± 1.6†</td>
<td>5.1 ± 1.6</td>
<td>5.3 ± 1.4</td>
<td>.05</td>
</tr>
<tr>
<td>Citric acid low</td>
<td>3.5 ± 2.0†</td>
<td>4.1 ± 1.8</td>
<td>4.1 ± 1.7</td>
<td>.05</td>
</tr>
<tr>
<td>% Reporting dysgeusia</td>
<td>84.8</td>
<td>30.7</td>
<td>19.3</td>
<td>.05</td>
</tr>
</tbody>
</table>

*Values are means ± SDs unless otherwise noted. Refers to significance of the categorical grouping factor in the analysis of variance, except in the case of percent reporting dysosmia or dysgeusia, where a x^2 value was computed.

†Indicates a significant planned comparison between head trauma (HT) and upper respiratory infection (URI) groups. UPSIT indicates the University of Pennsylvania Smell Identification Test*; PEA, phenyl ethyl alcohol; NS, not significant.

§Indicates a significant planned comparison between URI and NSD.

### Table 3.—Prevalence of Depression*

<table>
<thead>
<tr>
<th>Severity of Depression</th>
<th>Patients Reporting Dysosmia or Dysgeusia (n = 374), %</th>
<th>Patients Not Reporting Dysosmia or Dysgeusia (n = 362), %†</th>
</tr>
</thead>
<tbody>
<tr>
<td>No depression (scores, 0-9)</td>
<td>66.1</td>
<td>76.2</td>
</tr>
<tr>
<td>Mild depression (scores, 10-15)</td>
<td>19.2</td>
<td>14.1</td>
</tr>
<tr>
<td>Mild-to-moderate depression (scores, 16-19)</td>
<td>7.6</td>
<td>5.0</td>
</tr>
<tr>
<td>Moderate-to-severe depression (scores, 20-29)</td>
<td>5.6</td>
<td>4.4</td>
</tr>
<tr>
<td>Severe depression (scores, 30-63)</td>
<td>2.5</td>
<td>0.3</td>
</tr>
</tbody>
</table>

*Measured by the Beck Depression Inventory in patients experiencing chemosensory distortions (dysosmia or dysgeusia).

†Difference in prevalence of depression between individuals with or without chemosensory distortions (F[1733] = 17.91, P < .001).
losses of smell or taste had BDI scores indicative of this degree of depression. This latter prevalence of depression is analogous to that reported in other medical outpatient populations.38

**Low Body Weight Is Associated With BMS**

Although 44% of the population reported that their body weight had changed as a result of their chemosensory problem, patients with BMS (2.4% of the population) were the only group with oral or chemosensory dysfunction to have lower than expected body weight. On the average, the body weight of these patients was 12% lower than the average body weight expected in the general population of persons of equivalent height, age, and gender.39

**Regional Gustatory Deficits Associated With Iatrogenic Factors**

Nine patients were identified as having a regional gustatory deficit. In four patients, the disorder resulted from damage to the chorda tympani branch of the facial nerve (CN VII) in middle ear surgery or oral surgery. In oral surgery, nerve conduction block anesthesia may have damaged the chorda tympani nerve fibers. These injuries likely represent disruption of the chorda tympani in its course in the middle ear, between the medial and lateral pterygoid muscles, or with the lingual nerve. Of the remaining five patients, two had regional gustatory deficits following URI and three had regional deficits of unknown cause. Importantly, five of nine patients reported an identifiable, nonstimulated dysgeusia.

**Exogenous Estrogens May Protect Against Olfactory Dysfunction in Postmenopausal Women**

Many of the women presenting to our center with complaints of chemosensory dysfunction were postmenopausal. The possibility that postmenopausal women who use conjugated estrogen preparations may be protected, to some degree, from loss of smell function was examined (given reports of positive influences of estrogens on epithelial tissue37). The frequency of estrogen usage in postmenopausal women who had loss of smell function was compared with that of women in the general population. This comparison was followed by a determination of whether scores on the olfactory or gustatory tests differed between patients taking and patients not taking conjugated estrogens.

Only four (4.0%) of 99 postmenopausal women who had loss of the sense of smell were taking Premarin or other conjugated estrogens prior to the onset of the olfactory deficit. This percentage stands in contrast with the reported frequency of estrogen usage in women of comparable age in the general population. In five major studies, the median percentage of postmenopausal women taking conjugated estrogens was 16%, with a range of 10% to 51%.43 The frequency of estrogen usage in our patients was lower than that reported in each of these studies (Ps<.001).

Postmenopausal women who were taking estrogens performed better on the UPSIT than those not taking estrogens (respective mean ± SD values, 32.7 ± 10.5 and 22.4 ± 11.2; P<.005). There was no statistically significant difference in mean olfactory detection thresholds of postmenopausal women taking estrogens and postmenopausal women not taking estrogens (P>.15).

Only four postmenopausal women had deficits in taste function, and no estrogen-associated effects on taste could be determined from such a small sample.

**Antihypertensive, Anxiolytic, and Antidepressant Drugs May Be Associated With Chemosensory Distortion**

In light of anecdotal evidence that certain classes of drugs are associated with alterations in chemosensation,3 we sought to establish whether such associations were present in our study population. Because it was not possible in this study to distinguish between the effects of medication, per se, and those of the underlying medical problem for which the medication was prescribed, the effects noted below may be due to either the drug or the underlying disease.

Patients with dysosmia as their only chemosensory complaint (n=20) were more likely to be using antihypertensive (eg, metoprolol) or anxiolytic drugs (diazepam) than patients with no complaints of chemosensory distortion (respective antihypertensive usage, 44.4% vs 8.4%, and anxiolytic usage, 27.8% vs 6.6%; P<.01). Additionally, patients suffering from identifiable, nonstimulated dysgeusias reported using antidepressants (eg, imipramine) (11.1%) and anxiolytics (13.0%) more frequently than patients with no complaints of chemosensory distortion (respective usage, 2.4% and 6.6%; P<.05). Patients reporting dysgeusia as their only chemosensory complaint were more likely to be taking antidepressants (16.7%) than were patients with no complaints of chemosensory distortion (2.4%) (P<.001). In patients reporting identifiable, nonstimulated dysgeusias, antidepressant therapy was reported to be less frequent after onset of the disorder than prior to the disorder.

**Chemosensory Function Did Not Differ Between Those Taking Zinc and Those Not Taking Zinc**

A large number (n=254) of the patients who had previously taken, or were currently taking, an oral zinc supplement for their chemosensory problem. The majority (94.1%) reported that they noticed no influence of the zinc treatment on their dysfunction. Of the 15 patients who reported that zinc therapy may have improved their condition, six were found to be anosmic and seven had UPSIT scores less than the 10th percentile for their age and gender. Of the remaining two patients, one had a partial loss of the sense of taste and the other complained of dysosmia and dysgeusia.

For olfactory deficits, neither average UPSIT score nor average PEA score differed significantly between patients who had taken zinc and patients who had not taken zinc (UPSIT, P>.10; PEA, P>.15). In individuals with olfactory loss, the incidence of dysosmia was not significantly different in those taking zinc compared with those not taking zinc (P>.15). Taste-quality identification scores, results of LIT and HIT tests, and taste-detec-
tion thresholds did not differ significantly between those taking zinc and those not taking zinc ($P > .80$; $P > .10$; $P > .20$, respectively). In patients reporting identifiable, nonstimulated dysgeusias, various measures of gustation including taste-identification scores, LIT and HIT scores, and taste-detection threshold scores did not differ significantly between those taking zinc and those not taking zinc ($P > .70$; $P > .20$; $P > .10$, respectively).

**Thyroid Function Associated With Burning Mouth and Dysgeusia**

Thirty-nine patients reported taking levothyroxine at the time of their visit to the center. Twenty-five of these patients had identifiable causes of their sensory disorders (e.g., URI), and, in 14 patients, the causes could not be determined. Five patients had BMS. These 39 patients were more likely to experience burning mouth (23.1% vs 8.4%; $P < .01$) and identifiable, nonstimulated dysgeusias (20.5% vs 9.4%, $P < .05$) than were the remainder of the study population. Although patients taking levothyroxine complained of loss of the sense of taste more frequently than did the other study patients (82.1% vs 65.6%; $P < .05$), they scored higher on the taste-identification test (89.7% vs 82.6%; $P < .05$) and reported the low concentration of caffeine as having greater intensity as rated on a nine-point scale than did the other patients (5.0 vs 4.1; $P < .05$). The ratings of the other three taste stimuli at either the high or low concentrations did not differ significantly between those taking levothyroxine and the rest of the study population ($P > .50$). Taste thresholds did not differ significantly between those taking levothyroxine and the rest of the study population ($P > .15$). The incidence of olfactory distortion or olfactory loss did not differ significantly between those taking levothyroxine and the rest of the study population ($P > .50$).

**Dysonmia Can Be Induced by Inhalation of Steam or Warm Air**

Thirteen patients who reported dysosmia noted that steam or warm air (such as that from a boiling pot or from a heater vent) could induce the dyso-

**Current Dysosmia Associated With Less Severe Olfactory Dysfunction**

It has been hypothesized that strange smell sensations, which often occur in conjunction with losses of olfactory function, reflect either degenerative or regenerative changes in the olfactory neuroepithelium. To shed light on this issue, UPSIT and PEA threshold scores of dysosmic patients with quantified loss of smell function were compared with similar patients who had never experienced dysonmia.

The olfactory function of the former group was greater than that of the latter group, as indicated by average UPSIT and PEA threshold scores (respectively mean UPSIT scores, 19.1 ± 7.5 and 15.9 ± 7.3; $P < .001$; respective mean log PEA values, $-2.9 ± 2.4$ and $-1.8 ± 1.8$; $P < .001$). When the olfac-
tory function of these two groups was retested after 6 months or more using the UPSIT, the intertest difference did not differ significantly ($P > .05$).

**COMMENT**

A major finding of the present study is that chemosensory dysfunction impacts on the quality of life of patients with these afflictions. Most of the study population reported that their chemosensory problem influenced their appetite, body weight, and psychological well-being. Although decreases in body weight were demonstrated only in patients with BMS, it is conceivable that body weight changes also occurred in other patient groups, since body weight measures were based solely on patient report, and moderate changes could go undetected by our comparison procedure.

Our observation that most complaints of the loss of taste sensation reflect olfactory rather than gustatory dysfunction is in general agreement with observations of other studies. For example, in a report of 171 patients, Goodspeed et al observed only loss of olfactory function in the patients who reported loss of the senses of smell or taste. Such observations emphasize the critical role of olfaction in determining the appreciation of flavor in foods and beverages. Many patients fail to distinguish between taste and flavor. Since easy-to-use olfactory tests are commercially available, medical practitioners can easily establish the presence and degree of olfactory dysfunction. In many cases, an abnormality in gustatory function, per se, can be surmised quickly by asking the patient whether he or she can detect the sweetness of sugar, the sourness of grapefruit juice, the bitterness of coffee, and the saltiness of potato chips. If the answer is affirmative to these questions, it is unlikely that general gustatory dysfunction is present. Chemosensory disorders can stem from a large number of causes. However, the majority of such disorders result from a few causes, namely, URI, HT, and NSD. Of these three major causes, HT and NSD produce, on the average, the greater degree of olfactory decrement. It is generally assumed that the primary cause of olfactory dysfunction in head trauma is a shearing of the fila olfactoria at the cribriform plate, which eliminates olfactory input to the olfactory bulb. Blockage of airflow to the olfactory receptors presumably underlies most cases of allergic or polyposis-related olfactory alterations, although edema within the olfactory neuroepithelium or changes in the mucus overlying the olfactory neuroepithelium may also play a role. Some patients with allergic rhinitis or polyposis experience an improvement in their sense of smell with topical or systemic corticosteroid therapy and operative procedures, including antrostomy, nasal polypectomy, maxillary sinusotomy, and transantral or endoscopic transnasal ethmoidectomy. It is generally believed that the causative agent in anosmia associated with URI is a virus. It is likely that the virus destroys the olfactory neuroepithelium. Viral invasion of the central nervous system through the olfactory nerves is well established, and widespread destruction.
damage. The average patient in our study had been aware of their chemosensory disorder for approximately 5 years before evaluation, although considerable variation in the time from onset to our evaluation was present among causes, with patients with HT being seen, on the average, within 1 year of the problem onset and patients with NSD often having the problem for many years. Previous studies of patients with head trauma have suggested that if recovery were to occur, it usually does so within 6 months of the injury.56

It is well known that in the general population women have greater olfactory and gustatory sensitivity than do men.21,22 Such differences were also observed in our patient population. This observation is perhaps not surprising for the sense of taste, since few patients evidenced a gustatory deficit, allowing the expected gender difference to be expressed. However, this finding was unexpected for olfactory function, since a majority of the patients evidenced at least some loss of the sense of smell. One explanation is that those factors that damage the olfactory system do so to the same degree in men and women, indicating that gender differences in perception are maintained. Another possibility is that this difference results from a prophylactic effect of estrogens on the integrity of the olfactory neuroepithelium in women (eg, from viral or toxic insults). In support of this hypothesis, postmenopausal women taking conjugated estrogens were disproportionately underrepresented in our patient population, and those with olfactory deficits performed significantly better on olfactory tests than did their counterparts who were not taking estrogens.

The relative rarity of gustatory dysfunction, compared with olfactory dysfunction, likely reflects multiple innervation of the receptive elements (CNs VII, IX, and X), which, unlike the olfactory fila, appear to be less susceptible to damage from virus, environmental pollutants, and accelerative or decelerative impact. Although major losses of taste function were rare, reports of taste distortions were not. Approximately a third of the patient population complained of dysgeusia, and, of these, 43% reported the dysgeusia to reflect quality alterations likely mediated by the gustatory nerves (eg, salty, metallic, bitter, and sour). A number of the patients with unilateral taste deficits also had dysgeusia, a phenomenon noted by others.2,66 The high prevalence of dysgeusia, along with its association with depressive illness, suggests that both clinical and research efforts should be focused on understanding its basis.

A number of our patients were taking medications that conceivably were related to the experience of dysgeusia. For instance, antidepressant and anxiolytic drug usage was associated with dysgeusia, particularly when dysgeusia was the only chemosensory complaint. Whether this relationship reflects medication usage or the actual disease process cannot be determined from the present data. Notably, a greater number of dysgeusic patients were taking antidepressants prior to onset of the condition than after the onset of the condition. Several investigators have reported that some patients experiencing distortions of chemosensory function initially present as depressed, leading to misidentification of the primary disorder.2,66 This emphasizes the close relationship between the experiences of depression and chemosensory distortions.

The use of zinc as a treatment for chemosensory dysfunction has been controversial.67 Because an initial, large-scale clinical trial of zinc sulfate was conducted single-blind and had no time-matched control subjects,24 a double-blind crossover study of zinc was performed.25 The results indicated no significant influences of zinc on either gustatory or olfactory dysfunction. The fact that patients taking zinc did not have better taste or smell function than did the rest of the study population in the present study is consistent with the conclusion that treating patients who do not have frank zinc deficiency (eg, dialysis patients)2,25 with zinc does not improve their chemosensory function. It should be noted, however, that individuals who may have benefited from zinc therapy would not be in our sample of patients.

The lack of change in UPSIT scores observed on retest of patients with olfactory dysfunction appears to be in conflict with animal studies that indicate that the olfactory neuroepithelium has a propensity for regeneration.40,45 Several hypotheses for this apparent discrepancy can be postulated. First, it is possible that such regenerative processes are influenced by age-related factors and are minimal or nonexistent in the age range in which most olfactory dysfunction occurs.47 This could explain why relatively young persons rarely present to our center with chemosensory dysfunction (eg, in this study, only 8% of the patients were 25 years of age or younger). Second, it is conceivable that human beings do not enjoy the degree of recovery that occurs in some other animals when marked destruction of the olfactory neuroepithelium or fila occurs. Cadaver studies suggest that intercalation of respiratory epithelium in the olfactory receptor region occurs soon after birth and that cumulative destruction of the olfactory neuroepithelium develops over time.47 Third, our patient population may disproportionately represent persons with irreversible olfactory dysfunction. Thus, it is likely that most cases of olfactory loss stem from damage to the olfactory neuroepithelium. Progressive changes occur in this tissue soon after birth, and metaplasia to respiratory epithelium in the olfactory region is well documented.48-50 Exposure to airborne toxic chemicals, including cigarette smoke, causes widespread alterations in the olfactory neuroepithelium of animals.51-53 Alterations in the neuroepithelium following environmental insult likely explain the finding of dose-related alterations in olfactory sensitivity in current and previous cigarette smokers43 as well as the effects of exposure to low levels of a number of airborne chemicals on olfactory function.54-56 Notably, rats raised in a pathogen-free environment appear to have receptor cells that are relatively long lived, suggesting that some of the metabolic and regenerative activity in the olfactory neuroepithelium may be induced by environmental agents.40

Approximately a third of the patient ports of taste distortions were not. Losses of taste function were rare, reflecting possible differences in the metabolic and regenerative activity of the taste buds in the lingual epithelium. Men may be more resistant to the effects of environmental insults. Since patients with HT and NSD were not taking estrogen supplements, these factors were probably not responsible for the differences in UPSIT performance of men and women. The gender differences in UPSIT performance persisted when the patients were grouped by age. In support of this hypothesis, postmenopausal women taking conjugated estrogens were disproportionately underrepresented in our patient population, and those with olfactory deficits evidenced at least some loss of the sense of smell. One explanation is that those factors that damage the olfactory system do so to the same degree in men and women, indicating that gender differences in perception are maintained. Another possibility is that this difference results from a prophylactic effect of estrogens on the integrity of the olfactory neuroepithelium in women (eg, from viral or toxic insults). In support of this hypothesis, postmenopausal women taking conjugated estrogens were disproportionately underrepresented in our patient population, and those with olfactory deficits performed significantly better on olfactory tests than did their counterparts who were not taking estrogens.

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In the present study, a number of patients who were taking levothyroxine reported dysgeusia and burning mouth. The results indicated that these individuals perform better on tests of gustatory function than do the remainder of the patient population. Numerous reports have been published showing that antithyroid drug therapy can produce subjective loss of taste sensitivity. In addition, untreated hypothyroidism of prolonged duration and early asymptomatic hypothyroidism also have been associated with taste deficits (specifically, bitter and salty qualities) and with dysgeusia. In the present study, patients taking levothyroxine reported the bitter quality as having greater dysgeusia. This is consistent with the reported enhanced taste-identification ability, suggesting that these individuals may be experiencing gustatory hypersensitivity. This is consistent with the reported conversion from gustatory hyposensitivity to gustatory hypersensitivity when hypothyroid patients were treated with thyroxin hormones.

Additional research is needed to establish more definitively a number of the observations of this study. Indeed, the present research is limited in three major ways. First, this work relies on historical information that depends on patient recollection and accuracy in perception as well as on patient willingness to provide details of such events as visits to physicians and use of medications. This limitation is particularly important since, on the average, patients visited the center several years after the onset of the disorder. Second, the multiple interacting factors in this largely retrospective study preclude strong, cause-and-effect inferences between or among variables. Third, largely because of patient management and time constraints, not all tests were administered to all patients, which limited more definitive generalizations about some of these relationships. Despite these limitations, the present study elucidates a number of important associations relating to chemosensory dysfunction.

Data from the National Ambulatory Medical Care Survey published in the late 1970s suggest that, on an annual basis, hundreds of thousands of people in the United States complain to their physicians about a loss of the sense of smell or taste. Rarely, however, are such complaints objectively assessed. This situation is unfortunate for several reasons. First, without appropriate psychophysical testing, the validity of a patient's complaint cannot be determined. For example, many complaints of olfactory loss are misinterpreted as gustatory loss. Second, many persons (particularly in the elderly population) who report loss of the sense of smell perform as well or better than peers of the same age and gender. Informing them of this fact is often psychologically therapeutic. Third, quantitative measures are needed for accurate assessment of the effectiveness of therapeutic interventions. The efficacy for inducing recovery of chemosensory function can be determined for such procedures as allergy management; antibiotic therapy; corticosteroid therapy; and intranasal surgery for polyps, structural abnormalities, and nasal tumors. Fourth, accurate measurement of the senses of smell and taste is required for the determination of permanent impairment.

The aforementioned data indicate that chemosensory disorders are secondary to a variety of disease processes. Therefore, olfactory or gustatory complaints may serve as important presenting symptoms of a disease and may assist the physician in developing the differential diagnosis. In addition, the data imply that treatment of patients with these disease processes may reduce or alleviate the chemosensory complaint. Although treatments for many chemosensory disorders are presently unavailable, the present data, in combination with data from other study centers, provide insight and directions for the medical management of patients with these disorders.

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