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STATE OF THE ART REVIEW

Olfaction and Its Alteration by Nasal Obstruction, Rhinitis, and Rhinosinusitis

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The sense of smell has been largely ignored by otorhinolaryngologists, even though 1) its medical stewardship falls within their specialty's purview, 2) olfactory dysfunction is not uncommon in the general population, and 3) disorders of olfaction have significant quality of life, nutritional, and safety consequences. This report provides a succinct overview of the major intranasal neural systems present in humans (namely, cranial nerves O, I, and V, and the nonfunctional accessory [vomeronasal] organ system), along with a summary of notable findings resulting from the application of modern olfactory tests to patient populations, emphasizing diseases of the nose. Such tests have led to the discovery of significant influences of age, gender, smoking, toxic exposure, and genetics on the ability to smell. Within the field of otorhinolaryngology, they have revealed that 1) surgical and medical interventions in patients with rhinosinusitis do not, on average, lead to complete recovery of olfactory function, despite common beliefs to the contrary, and 2) associations are generally lacking between measures of airway patency and olfactory function in such cases. These findings have thrown into question the dogma that olfactory loss in rhinosinusitis is attributable primarily to blockage of airflow to the receptors and have led to histopathological studies demonstrating significant olfactory epithelial compromise in sinonasal syndromes. ***Key Words:*** **Iatrogenesis, nasal disease, olfaction, polyposis, psychophysics, rhinosinusitis, smell.**
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INTRODUCTION

The sense of smell largely determines the flavor of foods and beverages and serves as an early warning system for the detection of environmental hazards, including spoiled foods, leaking natural gas, smoke, and various airborne pollutants. This primary sensory system contributes significantly to the quality of life, allowing for the full appreciation of flowers, perfumes, spices, and a vast array of foods and beverages, as well as the seashore, the mountains, and the seasons of the year. Thus, it is no wonder that losses or distortions of smell sensation are of considerable significance to patients, particularly those dependent on this sense for their livelihood or safety (e.g., cooks, homemakers, plumbers, firefighters, perfumers, fragrance sales persons, wine merchants, food and beverage distributors, and employees of numerous chemical, gas, and public works industries). Indeed, altered smell function can adversely influence food preferences, food intake, and appetite.

In this report, we review the influences of nasal obstruction, rhinitis, and rhinosinusitis (as well as well as their medical and surgical treatments) on the ability to smell. Because this neglected sensory system receives so little attention in most medical textbooks, including those of clinical allergy, otolaryngology, neurology, and immunology, an overview of olfactory anatomy, physiology, and measurement is also presented.

ANATOMY AND PHYSIOLOGY

Intranasal Neural Systems—Cranial Nerves O, I, and V

In humans, three specialized neural systems are present within the left and right nasal chambers: 1) the main olfactory system (cranial nerve I [CN I]), 2) the trigeminal somatosensory system (cranial nerve V [CN

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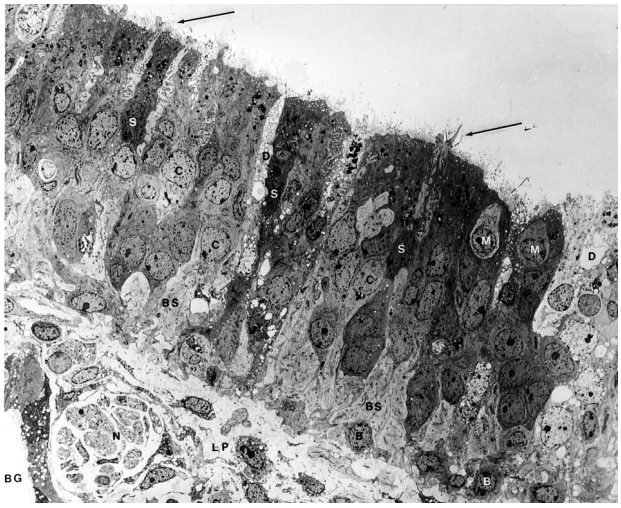

Fig. 1. Low-power electron photomicrograph of cross section of the human neuroepithelium depicting the four major types of cells: bipolar receptor cells (arrows point to cilia at dendritic knob; c = cell body), microvillar cells (M), sustentacular cells (S), and basal cells (B). BG = Bowman's gland; LP = lamina propria; N = collection of axons within an ensheathing glial cell; D = degenerating cells; BS = basal cell undergoing mitosis. From Moran et al.,[134] with permission.

V]), and 3) the nervus terminalis or terminal nerve (Cranial nerve O [CN O]). CN I mediates odor sensations (e.g., chocolate, strawberry and apple), whereas CN V mediates, through both chemical and nonchemical stimuli, somatosensory sensations, including those of burning, cooling, irritation, and tickling. The coolness of menthol and peppermint are mediated by CN V, as, for example, are the sharp sensations induced by ammonia vapors and various acids. The function of CN O, a ganglionated neural plexus that spans much of the nasal mucosa before traversing the cribriform plate to enter the forebrain medial to the olfactory tract, is unknown in humans. This nerve, whose disruption in some rodents alters reproductive behavior,[1] was discovered after the other cranial nerves had been named and is highly conserved among the vertebrates, including humans.[2,3]

Despite the fact that nearly all adult humans possess, in the lower recesses of each nasal chamber, a rudimentary vomeronasal (Jacobson's) organ (VNO) and a VNO duct approximately 15 to 20 mm from the posterior aspect of the external naris, they lack an accessory olfactory bulb, a structure necessary for its function. Thus, in adult humans this system is nonfunctional, and no neural connection from the VNO to the brain has been established.[4] Nonetheless, local electrophysiological responses have been recorded within the human VNO lumen.[5]

Olfactory Neuroepithelium

The olfactory neuroepithelium, which harbors the sensory receptors of the main olfactory system and some CN V free nerve endings, lines the upper recesses of the nasal chambers, including the cribriform plate, superior turbinate, superior septum, and sectors of the middle turbinate. This epithelium loses its general homogeneity postnatally, and as early as the first few weeks of life metaplastic islands of respiratory-like epithelia begin to appear, presumably as a result of insults from environmental viruses, bacteria, and toxins. Such islands increase in extent and number throughout life. Surprisingly, the exact size of the olfactory neuroepithelium in humans is still not well established, and there is recent suggestion that it may extend further onto the middle turbinate than previously believed.

On the basis of morphological and biochemical criteria, the mature olfactory epithelium comprises at least six distinct cell types (Fig. 1).[6] The first, the bipolar sensory receptor neuron, is estimated to number approximately 6,000,000 cells in the adult, exceeding the number of receptor cells in any other sensory system except vision. The olfactory receptors are located on the ciliated dendritic ends of these cells, whose surface area probably exceeds 22 cm^2 in the human. The receptor cell axons coalesce into ~40 bundles (termed the olfactory fila), which are ensheathed by Schwann-like cells. The fila traverse the cribriform plate of the ethmoid bone to enter the anterior cranial fossa and collectively constitute CN I. The second cell type, positioned near the surface of the epithelium, is the microvillar cell. These cells are said to number approximately 600,000 in the adult. Each microvillar cell, whose function is unknown, contains microvilli. The third cell type, the supporting or sustentacular cell, also projects microvilli into the mucus. These cells are believed to 1) insulate the receptor cells from one another, 2) regulate the local ionic composition of the mucus, 3) deactivate odorants, and 4) help protect the epithelium from damage from foreign agents. The supporting cells contain xenobiotic-metabolizing enzymes (e.g., cytochrome P-450), a feature shared with the fourth cell type, the cell that lines the Bowman glands and ducts. The Bowman glands are a major source of mucus within the region of the olfactory epithelium. The fifth and six cell types are the globose (light) basal cell and horizontal (dark) basal cell, cells that are located near the basement membrane from which the other cell types arise. The same type of basal cell, probably a globose cell, can give rise to both neurons and nonneural cells when the olfactory epithelium is damaged, expressing a multiple potency rarely observed in stem cells. It is noteworthy that the olfactory ensheathing cells, which form the bundles of axons that make up the olfactory fila, enhance remyelination and axonal conduction in demyelinated spinal tract nerves, as well as in severed rat sciatic nerves,[7] exhibiting both Schwann cell–like and astrocyte-like properties.

The cilia of the olfactory receptor cells lack dynein arms (hence, intrinsic motility). Odorant transport through the mucus to the cilia is aided by "odorant binding proteins." Approximately 1000 classes of odorant receptors are currently believed to exist, reflecting the expression of the largest known vertebrate gene family, a family accounting for approximately 1% of all expressed genes. In general, the olfactory receptors are linked to the stimulatory guanine nucleotide-binding protein G_{olf}. When stimulated, they activate the enzyme adenylate cyclase to produce the second messenger adenosine monophosphate

(cAMP) and subsequent events related to depolarization of the cell membrane and signal propagation.

Although a given receptor cell seems to express only one type of receptor derived from a single allel, each cell is electrophysiologically responsive to a wide but circumscribed range of stimuli. This implies that a single receptor accepts a range of molecular entities and that coding occurs via a complex cross-fiber patterning of responses.

The Olfactory Bulb and Cortex

The olfactory bulb is a complex processing center, receiving both afferent and efferent input. This ovoid structure has clear concentric layers discernible using light microscopy. The layers are, in succession, the outermost olfactory nerve layer, the glomerular layer, the external plexiform layer, the mitral cell layer, the internal plexiform layer, and the innermost granule cell layer. In the human, the receptor cell axons of the olfactory fila, after traversing the cribriform plate, form the olfactory nerve layer and synapse in the second bulbar layer within the spherical glomeruli. In general, receptor neurons expressing a given receptor type project to one or, at most, two glomeruli, making the glomeruli in effect functional units. Thus, a given odorant activates a spatially defined or restricted set of glomeruli. Hence, the olfactory code is reflected, at this early stage, not only as different patterns across the mucosa, but across the glomeruli as well.

The major second-order neurons of the olfactory bulb (the mitral and tufted cells) project their axons centrally to elements of the olfactory cortex. The olfactory cortex comprises 1) the anterior olfactory nucleus ([AON], which in the human has a large segment in the posterior olfactory bulb), 2) the olfactory tubercle (poorly developed in humans), 3) the prepiriform cortex, 4) the lateral entorhinal cortex, 5) the periamygdaloid cortex, and 6) the cortical nucleus of the amygdala. The afferent olfactory signal is modulated at all levels of the system, from the olfactory bulb to the olfactory cortex. Olfaction is unique in that information from the olfactory bulb goes directly to cortical structures without passing through the thalamus. However, thalamic connections are present for relays between various elements of the primary and secondary olfactory cortices.

PRACTICAL MEASUREMENT OF HUMAN OLFACTORY FUNCTION

The most widely used tests for assessing the ability to smell are those of odor threshold and odor identification. Because these are the only tests routinely used in clinical settings, and because such tests are available commercially, the current discussion focuses on these measures. The reader is referred elsewhere for discussions of the comparative reliability, sensitivity, and validity of various types of modern olfactory tests.[8,9]

Olfactory Threshold Tests

The lowest concentration of an odorant that can be reliably detected is termed the detection or absolute threshold. Usually, at lower perithreshold odorant concentrations, no odor quality can be discerned, only something different from air or the comparison diluent blank or blanks. In modern olfactory detection threshold testing, the subject is asked to report which of two or more stimuli (i.e., an odorant and one or more blanks) smells strongest, rather than to simply report whether or not an odor is perceived. Such "forced-choice" procedures are less susceptible to contamination by response biases (e.g., the conservatism or liberalism in reporting the presence of an odor under uncertain conditions) than non–forced-choice procedures. In addition, they are more reliable and produce lower threshold values.[8] The instructions provided to a subject are critical in measuring a detection threshold because, if the subject is instructed to report which stimulus produces an odor rather than which stimulus is stronger, a spuriously high threshold value may result because the subject's attention is diverted away from subtle differences in the presented stimuli (odor quality is present only at higher perithreshold concentrations).

The recognition threshold is the lowest concentration where odor quality is reliably discerned. However, it is nearly impossible to control criterion biases in recognition threshold measurement. Thus, in a forced-choice situation, guesses are not randomly distributed among alternatives, potentially leading to a spuriously low recognition threshold for the preferred alternative. A classic example of this problem comes from taste psychophysics, in which some subjects report "sour" much more frequently than the other primary qualities in the absence of a clearly discernible stimulus, resulting in a erroneously low sour taste recognition threshold measure.

Two types of threshold stimulus presentation procedures have received the most use in modern times: the ascending method of limits procedure (AMS) and the single staircase procedure (SS). In the AML procedure, an odorant (and comparison blanks) is sequentially presented from low to high concentrations and the point of transition between detection and no detection is estimated. In the SS method, the concentration of the stimulus is increased following trials on which a subject fails to detect the stimulus and decreased following trials in which correct detection occurs. An average of the up-down transitions ("reversals") is used to estimate the threshold value. In both the AML and SS procedures, the direction of initial stimulus presentation is made from weak to strong in an effort to reduce potential adaptation effects of prior stimulation. In general, the SS procedure is preferred to the AML procedure because it is more reliable, since most investigators who employ the AML technique present only a single ascending stimulus series. Unfortunately, widespread use of the single-series AML procedure has led to the erroneous conclusion that threshold measures exhibit a high degree of intrasubject variability, a conclusion not borne out when thresholds are determined using the SS procedure.[8]

A modern, commercially available threshold test kit that employs an SS procedure is shown in Figure 2. This kit uses squeeze bottles containing various half-log step concentrations of an odorant known to stimulate primarily CN I, namely, the rose-like smelling odorant phenyl ethyl alcohol (PEA). Norms based on hundreds of subjects spanning the entire age range allow for the practical

Fig. 2. The Smell Threshold Test™, a commercially available test for assessing odor detection thresholds. Concentrations of phenyl ethyl alcohol, ranging from 10^{-2} to 10^{-10} log vol/vol in half-log concentration steps, are provided, along with blanks for forced-choice testing. (Photograph courtesy of Sensonics, Inc., Haddon Heights, NJ. Copyright 2000, Sensonics, Inc.)

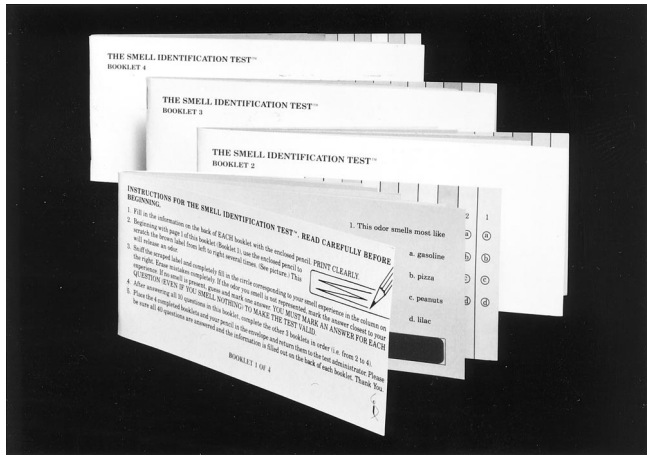

Fig. 3. The four booklets of the 40-odorant University of Pennsylvania Smell Identification Test (UPSIT). Each page contains a microencapsulated odorant that is released by means of a pencil tip. This test, which has been administered to approximately 200,000 patients since its development, is the most widely used olfactory test in the world (commercially known as the Smell Identification Test™). The UPSIT is considered to be the "eyechart for the nose." (Photograph courtesy of Sensonics, Inc., Haddon Heights, NJ. Copyright 2000, Sensonics, Inc.)

application of this test in medical and industrial applications.

Odor Identification Tests

The development and proliferation of easy-to-use, self-administered "scratch and sniff" tests of odor identification have significantly increased our understanding of smell function in humans, including the influences of such factors as age, gender, exposure to toxic agents, smoking behavior, and various disease states. Such quantitative tests, derived from test measurement theory, focus on the comparative ability of individuals to identify a number of odorants at the suprathreshold level. The most popular of these tests are the 40-odorant University of Pennsylvania Smell Identification Test ([UPSIT], known commercially as the Smell Identification Test™ [or SIT])[10,11]; the 12-odor Brief-Smell Identification Test ([B-SIT], also known as the Cross-Cultural Smell Identification Test™),[12] and the 3-odor Pocket Smell Test™ (PST) (Sensonics, Inc., Haddon Heights, NJ).[8] The UPSIT has been used most widely, having been administered to approximately 200,000 people in Europe and North America since 1985. This test, shown in Figure 3, employs norms based on nearly 4000 persons and is available in English, French, German, and Spanish language versions. For a given item, the patient simply scratches open a microencapsulated label with a pencil tip, smells the label, and signifies the odor quality from four alternatives provided. Even if no smell is perceived, a response is required (i.e., the test is forced-choice). In addition to indicating the level of absolute smell function (i.e., normosmia, mild hyposmia, moderate hyposmia, severe hyposmia, total anosmia), this test provides a percentile rank for each age and gender group. Malingering is detected on the basis of improbable responses.

In general, when equated for test length, tests of odor identification are more reliable than tests of odor detection threshold and require less administration time. Furthermore, most identification tests can be self-administered and tend to correlate better with a patient's complaint than measures of detection threshold. Nonetheless, tests of odor identification and detection are typically correlated with one another.[8]

MAJOR FINDINGS DERIVED FROM OLFACTORY TESTS

Among major nonclinical findings derived from modern sensory tests, primarily the UPSIT, are the following: first, the ability to identify odors has a strong genetic basis, as determined from twin studies[13,14]; second, women, on average, are better able than men to identify odors, and this superiority is noticeable as early as 4 years of age and is culture independent[15–18]; third, significant loss of olfactory function occurs after the age of 65 years, with more than half of persons between 65 and 80 years of age and more than three-quarters of those 80 years of age and older having such loss[16,18,19]; fourth, women, on average, retain the ability to smell longer than men[16]; fifth, the decreased smell ability associated with smoking is present in prior cigarette smokers, and recovery to pre-smoking levels, while possible, can take years, depending on the amount and duration of prior smoking[20]; and sixth, olfactory function is compromised in urban residents and in workers in some industries, including the paper and chemical manufacturing industries.[21–25]

Clinical studies employing such methodology during this period have found decreased smell function relative to matched controls in dozens of diseases and disorders (see

examples in Table I). The straightforward ability to quantify olfactory function, along with recent advances in in vivo medical imaging, has made it possible to better understand the physiological basis of a number of chemosensory deficits. For example, it is apparent today that congenital anosmia is nearly always associated with markedly deformed or absent olfactory bulbs and stalks. Furthermore, head trauma–related smell loss is typically accompanied by decreased bulb and tract size that presumably reflects mitigation of trophic factors from the olfactory receptor neurons, which are often sheared off or otherwise altered in head trauma. The smell loss associated with chronic alcoholism has been found to be correlated with magnetic resonance imaging (MRI)–determined 1) increased cortical and ventricular cerebral spinal fluid volumes and 2) reduced volumes of the thalamus and of cortical and subcortical gray matter.[26] The smell loss of multiple sclerosis is directly associated with the number of active plaques in central brain regions,[27,28] and that of schizophrenia with diminished olfactory bulbs and tracts.[29]

Olfaction Function and Adrenalectomy

The presence of hypertrophied adenoid tissue can significantly block the nasal airflow of children whose airways are otherwise patent. Crysdale et al.[30] noted a 43% reduction in nasal resistance following adenoidectomy in a group of 67 children ranging in age from 4 to 17 years before surgery, and Fielder[31] reported a 19% postoperative reduction in such resistance in a group of 19 children admitted for adenoidectomy and myringotomies (with or without tonsillectomy) who had at least 1 g of adenoid tissue removed.

In 1983, Ghorbanian et al.[32] evaluated the degree to which nasal obstruction influences the olfactory sensitivity of children. This work, which has been subsequently replicated by others,[33] determined phenyl ethyl alcohol detection thresholds in 65 children with varying degrees

TABLE I.
Examples of Medical Conditions or Disorders Associated With Olfactory Dysfunction, as Measured by Modern Quantitative Tests of Olfactory Function, Particularly the UPSIT.

Medical Condition	Example References
Alcoholism and drug abuse	26,83,84
Amyotrophic lateral sclerosis (ALS)	85,86
Attention deficit/hyperactivity disorders	87
Alzheimer's disease	88–90
Anorexia nervosa–severe stage	91
Breast cancer–estrogen receptor-positive	92
Chemical exposure	21–23,25,93
Chronic obstructive pulmonary disease	94
Cystic fibrosis	95
Down's syndrome	96–98
Epilepsy and temporal lobe resection	99–101
Guam ALS/PD/dementia	102,103
Head trauma	104,105
Human immunodeficiency virus (HIV)	106
Huntington's disease	107,108
Kallmann's syndrome	109
Korsakoff's psychosis	110
Multiple sclerosis (MS)	27,28,111,112
Multiple system atrophy	113
Nasopharyngeal carcinoma	114
Nasosinus disease/rhinitis	42,43,46–48,58,61,74
Parkinson's disease (PD)	89,115–120
Pseudohypoparathyroidism	121
Psychopathy	122
Restless leg syndrome	123
Schizophrenia	124,125,126–129
Schizophrenia-like affective disorders	126
Schizotypy	130
Seasonal affective disorder	131
Sjögren's syndrome	132,133
Surgical/radiological interventions	44,72,75,114

UPSIT = University of Pennsylvania Smell Identification Test.

of nasal obstruction and in 13 children without such obstruction. The threshold values were directly related to clinical ratings of the degree of nasal obstruction. These findings, shown in Figure 4, suggest that in this subject population the degree of nasal obstruction is associated with commensurate impairment in the ability to smell and that reduction in the degree of nasal obstruction results in commensurate recovery of smell function.

Olfactory Function and Acute Viral-Related Rhinitis and Rhinosinusitis

It is well documented that the common cold can result in *permanent* loss of smell function. However, such loss usually occurs in later life after the olfactory membrane has presumably undergone considerable cumulative damage. For this reason, temporary smell loss following an upper respiratory infection is much more common. In general, virus-related acute rhinitis or rhinosinusitis follows three predictable phases; namely, a predromal phase, a cathartic phase, and a viscous phase.[34] The predromal phase is characterized by sweating, shivering, headaches, loss of appetite, and other nonspecific feelings of being ill. During this phase, tickling, burning, or dryness within the nose is common and the mucosa typically appears pale. The cathartic phase follows a few hours after the predromal phase and is characterized by increased mucosal redness and swelling, nasal obstruction, and secretion of watery mucus. A few days later, during the viscous phase, the nasal secretions thicken and the intensity and frequency of the aforementioned decline, disappearing after about a week.

Two studies have quantitatively assessed olfaction following the onset of the common cold, with an attempt to establish whether changes in smell function are coincident with changes in nasal congestion and secretion. In the first of these studies, Akerland et al.[35] measured 1-butanol odor detection thresholds in a group of student volunteers before and 4 days after nasal inoculation with the coronavirus 229E. The nine individuals who developed a cold had impaired olfactory thresholds on the postinoculation test relative to the controls. Whereas the change in smell function correlated with the degree of nasal congestion, it did not correlate with the amount of nasal discharge.

The second study on this topic led to the conclusion that the common cold may, in fact, affect olfactory function independent of nasal congestion.[34,36] In this experiment, whose main purpose was to evaluate the potential dose-related effects of oxymetazoline (administered unilaterally) on olfactory function, both psychophysical (intensity ratings, odor discrimination, butanol detection threshold) and electrophysiological (event-related potentials to H_2S and CO_2) data were obtained. Nasal volume was assessed by acoustic rhinometry. Thirty-six subjects (18 women, 18 men) were evaluated soon after they experienced the natural onset of a cold. After rhinitis onset (day 0), sensory and airway measurements were obtained on days 2, 4, 6, and 35. The cold produced a decrease in the volume of the anterior nasal cavity and an increase in mucus secretion, an increase in olfactory thresholds, a decrease in intensity ratings, and a decrease in N1 evoked potential amplitudes to both olfactory and trigeminal stimuli. When mucus secretion of the contralateral nasal cavity was controlled with oxymetazoline, N1 amplitudes to olfactory stimuli were still affected by the cold, as indicated by the significant increase of amplitudes as subjects recovered; however, this phenomenon was not found for any of the other test measures or for the responses to the trigeminal stimuli. Overall, the olfactory test scores tended to improve during the viscous phase.

Olfactory Function in Rhinitis and Rhinosinusitis

A number of studies have sought to determine the influences of acute or chronic rhinitis on olfactory func-

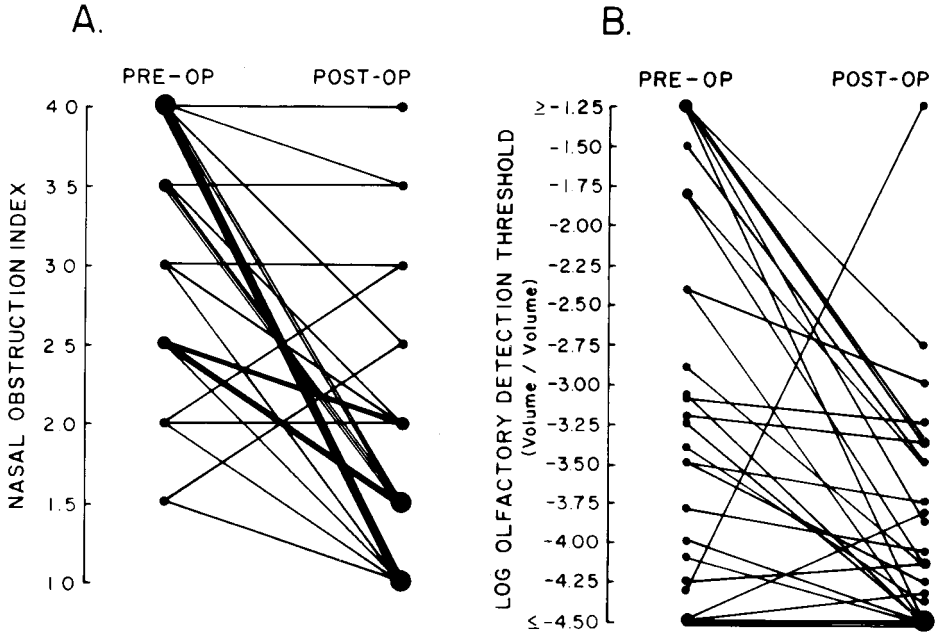

Fig. 4. (**A**) Nasal obstruction ratings, based on assessment of mouth breathing and hyponasality, in 28 children before and after adenoidectomy. (**B**) Phenyl ethyl alcohol odor detection thresholds before and after adenoidectomy in the same study population. Each line joins preoperative and postoperative values for an individual subject. (Reprinted with permission from Ghorbanian et al.[32] Copyright 1983, American Academy of Pediatrics.)

tion. Some such studies have differentiated between rhinitis and secondary nasal and sinus disease (i.e., sinusitis and/or polyposis), although this distinction is often difficult to maintain. Currently, the term rhinosinusitis is preferable to the term sinusitis because invariably inflammation of the sinuses coexists with inflammation of the nose. Rhinosinusitis can be further divided into acute, subacute, recurrent acute, and chronic types, during which acute exacerbation of chronic symptoms can occur. However, no studies have comparatively evaluated olfactory function in these various forms or stages of nasal disease. Nonetheless, as described below, there is strong suggestion from numerous quarters that the degree of olfactory loss is correlated with disease severity.

Among the first nonquantitative studies in the English literature on olfaction in rhinosinusitis and/or polyposis were those of Hotchkiss[37] in the mid 1950s and Fein et al.[38] in the mid 1960s. Hotchkiss evaluated self-reported olfactory function in 30 patients with nasal obstruction secondary to polyposis who reported smell loss. All were treated with a total dose of 70 mg of prednisone over a 6-day period. Restoration of smell was said to follow the systemic steroid therapy, with the magnitude of the restoration being proportional to the amount of polyp shrinkage. The restoration was reportedly unrelated to the duration of the loss of olfactory function. However, the self-rated improvement lasted only (on average) 10 days after the discontinuation of therapy. Fein et al. examined 18 patients who reported loss of smell associated with allergic rhinitis. Of these patients, 14 had other diseases, including sinusitis, polyposis, and bronchial asthma. Again, no objective sensory testing was performed. On the basis of self-report, the severity of the smell dysfunction was classified as mild, moderate, or severe. Of the four patients who had only allergic rhinitis, two were said to have had mild smell loss, and two, moderate smell loss. Of the 14 patients with other diseases, two reportedly had mild loss, six moderate loss, and six severe loss. In the latter group, severe loss was said to be associated with the presence of both polyposis and sinusitis. Although improvement in some of the subjects from hyposensitization, antibiotics, polypectomy, or various combinations of treatments was noted, a lack of a well-defined experimental protocol employing quantitative olfactory tests and the introduction of the treatments in various combinations without control for their order or time precludes a determination of the relative efficacy of the interventions.

More recently, Tos et al.[39] had 91 patients with polyposis rate their olfactory function on a 0–3 scale (0 = normal, 1 = slight impairment, 2 = moderate impairment, and 3 = anosmia) before and after 6 weeks of twice-daily nasal corticosteroid treatment. Before treatment, the mean rating of the 44 patients who were to receive the corticosteroid sprays was 2.09, whereas that of the 47 patients who were to receive the placebo was 2.19. Following treatment, the self-ratings were 1.86 for the corticosteroid-treated subjects and 2.19 for the placebo-treated subjects. Even though a statistically significant change occurred in the ratings after the administration of the corticosteroid, the degree of average self-rated improvement was not marked and, for all practical purposes, moderate loss of smell function was still reported.

In contrast to these largely subjective reports are a number of studies, most appearing since 1990, that have quantitatively assessed smell dysfunction in patients with rhinosinusitis. Among the first of these studies was that of Goodspeed et al.[40] In this work, systemic prednisone 50 mg was administered each day for 7 days to 20 anosmic or severely hyposmic patients of several types whose olfactory function was monitored using butanol thresholds and odor identification tests. Loss of smell function following the cessation of prednisone treatment was variable and was not quantitatively tested after the discontinuance of the therapy.

Another early empirical study[41] sought to determine the efficacy of flunisolide nasal spray in restoring olfactory function in a selected set of patients with perennial rhinitis and nasal polyposis. In this report, flunisolide and nasal decongestant sprays were introduced, with the decongestant being discontinued a week later. The olfactory testing was performed at home, and the self-administration of the nasal sprays was performed in the Moffett position to enhance delivery. Daily subjective ratings and a self-administered smell test revealed a return of smell function to the mid hyposmic range in five of the seven patients after approximately 2 weeks of the flunisolide treatment.

The first large-scale empirical study of olfaction in allergic rhinitis was that by Cowart et al.[42] in 1993. Quantitative detection threshold measures for the rose-like smelling odorant phenyl ethyl alcohol were obtained in this well-designed and carefully executed study from 91 patients with symptoms of allergic rhinitis and from 80 nonatopic control subjects. The allergy patients exhibited significantly higher detection thresholds than did the controls, with 23.1% of the patients demonstrating a clinically significant loss (i.e., a threshold at or above the 2.5 percentile of control values). Clinical or radiographic evidence of rhinosinusitis or nasal polyps or both in allergy patients was found to be associated with hyposmia: 14.3% of the allergy patients with no associated rhinosinusitis exhibited hyposmia, whereas 42.9% of the allergy patients with associated rhinosinusitis did so. No association between the smell test scores and nasal resistance was seen in either the patient or control groups, although nasal resistance was higher among patients than among control subjects.

Two years later, Apter et al.[43] reported that 28 patients with chronic rhinitis and no associated polyposis or rhinosinusitis had an average olfactory test score (based on a composite of odor identification and detection tests) indicative of moderate hyposmia. Thirty-four such patients with polyps and/or chronic sinusitis were found to be generally anosmic. These results were interpreted to mean that chronic rhinitis without associated sinusitis could result in some degree of olfactory loss, but that severe loss was usually associated with the presence of polyposis and/or rhinosinusitis.

In the first study on this topic to employ the UPSIT, Golding-Wood et al.[44] evaluated olfactory function once before and once after 6 weeks of betamethasone treatment

in 25 well-documented patients with perennial rhinitis. The patient group was initially divided into two groups: those who answered the question "Is your sense of smell impaired?" affirmatively (n = 15) and those who did not (n = 10). The UPSIT scores of each of the 15 members of the former group were higher after the betamethasone treatment (respective group means [SD], 18.93 (9.4) and 33.4 (4.01)]. This was not the case for those who initially thought that they had no problems smelling (respective pretreatment/post-treatment means [SD], 33.40 (4.01) and 32.8 (4.94)]. As in earlier studies, however, the average post-treatment UPSIT score was still indicative of a mild hyposmic condition. In general, the UPSIT scores of the patients retained a similar rank order before and after treatment (Spearman's correlation coefficient [r] = 0.75). Moderate correlations were found between the UPSIT scores and the self-ratings of olfactory function both before ($r = -0.52$) and after ($r = -0.58$) treatment.

A year after this study, Mott et al.[45] sought to determine the efficacy of topical corticosteroid nasal spray treatment after 8 weeks in severe olfactory loss associated with severe nasal and sinus disease. On average, the objective measures of olfaction improved significantly, and a decrease in the signs of nasal and sinus disease were noted on rhinoscopic evaluation. Two-thirds of the patients noted a subjective improvement in smell function. These data, along with those of Golding-Wood et al.,[44] imply that in many patients topical corticosteroid nasal spray, when administered in a head-down-forward position, mitigates, at least to some degree, the olfactory loss associated with severe nasal and sinus disease.

In perhaps the most extensive study of olfaction in rhinitis and rhinosinusitis to date, Simola and Malmberg[46] compared odor detection thresholds obtained from 105 rhinitis patients to those of 104 healthy control subjects. Age and rhinitis were found to be associated with smell dysfunction. Both the proportion of hyposmic persons and the degree of the impairment of the sense of smell were significantly higher in the rhinitis group than in the control group. The nonallergic rhinitis patients' sense of smell was found to be poorer than that of the patients with seasonal or perennial allergic rhinitis. A history of operations for nasal polyposis was associated with hyposmia, but operations for chronic maxillary sinusitis were not.

Two other studies appeared more or less contemporaneously with the study by Simila and Malberg. In the first, Kondo et al.[47] administered the UPSIT to 36 Japanese patients with a history of sinusitis/polyposis and to 131 control subjects. The mean UPSIT score of the patients was significantly ($P < .001$) lower (23.80, SD = 7.12) than that of the controls (32.08, SD = 3.57), despite some culture-related attenuation in the test scores of both groups. Detection and recognition thresholds showed a similar association. As in the case of the study by Golding-Wood et al.,[44] moderate correlations emerged between the odor test scores and the scores on a smell ability questionnaire (Spearman's r ranging from 0.58 to 0.69). In the second study, Apter et al.[48] assessed odor detection and identification in 1) 60 patients who presented to a smell and taste clinic with self-described olfactory loss and were found to have allergic rhinitis and 2) 30 patients with allergic rhinitis from an allergic clinic who had no chronic rhinosinusitis or polyposis. As might be expected, the patients presenting to the smell and taste clinic with olfactory dysfunction had significantly lower olfactory test scores than those who came from the allergy clinic and who were not specifically presenting with olfactory loss. In accord with the findings of several of the prior studies, olfactory function was inversely associated with the severity of the disease. However, no meaningful relationship was apparent between the visibility of the olfactory clefts (determined from endoscopic rhinoscopy) and smell function, regardless of the disease status. Self-reported fluctuations in function were less frequent in the groups without chronic rhinosinusitis than in those with chronic rhinosinusitis and/or polyposis. Interestingly, self-reported distortions in smell function were generally associated with a history of upper respiratory tract infections and were more apparent in individuals with less severe disease. Duration of nasal symptoms alone was not meaningfully correlated with the degree of olfactory loss.

Recently, Rydzewski et al.[49] assessed olfactory function using the Elsberg blast-injection procedure in 240 patients with perennial rhinitis, seasonal rhinitis, and bronchial asthma. Of their patients, 13.8% were hyposmic, and 7.6% anosmic. Surprisingly, using electrogustometry, these authors found taste disorders in even a larger percentage of these patients (30.7%). The olfactory component of this work, however, must be viewed with caution in light of the methodological problems with Elsberg olfactometry. This procedure has been criticized on numerous grounds, including 1) the lack of a forced-choice response, 2) the confounding of pressure with the number of molecules in the stimulus, 3) the introduction of a very unnatural stimulus pulse into the nose, and 4) the production of highly unreliable sensitivity measures.[50,51]

In aggregate, the studies reviewed above suggest that the degree of olfactory loss is usually associated with the severity of nasal sinus disease, with the greatest loss occurring in patients who have rhinosinusitis and polyposis. Employing quantitative tests, smell function has been shown to improve in some patients following systemic administration of corticosteroids, as well as topical administration of corticosteroid sprays when administered in a head-down-forward position. Nonetheless, no study has compared the latter mode of delivery to that of a standard mode, and no one has administered such drugs in a blind, placebo-controlled study. Importantly, the limited data available suggest that only rarely has corticosteroid treatment restored function to normal levels, implying that either 1) some chronic permanent loss of olfactory function is present or 2) such treatments are not 100% effective in reversing the disease processes responsible for the olfactory loss. Interestingly, no study has been able to document in rhinitis patients an association between olfactory test scores and intranasal airway access factors save total or near-total blockage, whether measured by rhinoscopy, rhinomanometry, or acoustic rhinometry.

There is currently considerable support for the hypothesis that factors other than, or in addition to, nasal airflow are responsible for many instances of smell loss in

patients with rhinosinusitis, in support of the notion that chronic inflammation may be toxic to olfactory neurons. For example, Kern[52] presented data, albeit preliminary, that the severity of histopathological changes within the olfactory mucosa of patients with chronic rhinosinusitis is positively related to the magnitude of olfactory loss, as measured by the UPSIT. In addition, authors have shown that olfactory secretions are probably regulated by both mineralcorticoids and glucocorticoids.[53,54] Feron et al.[55] reported, in a study group of 33 subjects, that nasal biopsy specimens from the posterior superior turbinate, posterior medial turbinate, and posterodorsal septum of patients with nasal disease were less likely to contain olfactory neuroepithelium than analogous biopsy specimens from patients with no such disease. Lee et al.[56] have demonstrated that biopsy specimens from the region of the olfactory epithelium of anosmic patients with rhinosinusitis were less likely to contain olfactory epithelial tissue than those from rhinosinusitis patients who were not anosmic (27% vs. 61% positive biopsy results, respectively). Although detailed examination by Lee et al. of the epithelium from rhinosinusitis patients with normal smell function did reveal islands of respiratory-like epithelium interspersed throughout the biopsy samples, such islands were much less prevalent than in the anosmic patients for whom olfactory epithelium could be found. Abnormalities in the arrangement of the epithelial cell types was common in the anosmic biopsy specimens, and in cases where olfactory epithelium was identified, it was typically atrophic and thin, often comprising mainly sustentacular and basal cells.

Olfactory Function in Natural or Experimental Allergic Rhinitis Nasal Challenge Studies

Hilberg[57] evaluated the effect of the oral antihistamine terfenadine (a histamine type 1 [H_1] blocker) on an allergen challenge in subjects with nasal allergy uncomplicated by polyposis and compared these results with those obtained using the topical steroid budesonide. Although both drugs had an effect on the hay fever symptoms during the nasal pollen challenge, only the budesonide improved the challenge-related decrement in olfactory sensitivity. This steroid also was more effective in increasing nasal volume. However, the improvement in olfactory function occurred in less than half of the patients (7/17 [41%]).

Lane et al.[58] employed an abbreviated 20-item version of the UPSIT and acoustic rhinometry to assess olfactory and nasal function, respectively, in the immediate response to a nasal allergen challenge in eight pollen-sensitive subjects. A significantly greater decrease in the cross-sectional nasal airway measure occurred following allergen challenge relative to a control challenge (70% vs. 22%). As in the case of other allergic rhinitis and rhinosinusitis studies, no association was found between the olfactory and acoustic rhinometric test measures. Despite the small sample size and the use of an abbreviated UPSIT, a modest decrease in odor identification performance was seen following the allergen challenge (16%, $P = .08$).

In 1997, Hinriksdottir et al.[59] evaluated odor detection thresholds in 20 patients with known allergic rhinitis to birch pollen before and after a topically applied birch pollen challenge during a nonsymptomatic period. Following the provocation, olfactory function decreased. The change in threshold was related to the measured amount of nasal secretion but not to the patients' report of nasal obstruction or measures of nasal resistance. Analogous findings were subsequently noted in a study by Klimek and Eggers[60] in which measures of odor identification, discrimination, and detection threshold were obtained in 17 patients with allergic rhinitis to grass pollen. In this work, testing was performed preseasonally and 3, 7, 14, and 21 days into the grass pollen season. After 2 weeks of pollen exposure, most subjects were hyposmic; by 3 weeks, all patients, without exception, had mild to severe hyposmia.

In another study examining patients with grass-related allergic rhinitis, Moll et al.[61] examined the same olfactory measures as those used by Klimek and Eggers[60] in 28 patients with allergic rhinitis to grass pollen preseasonally and 3 weeks into the grass pollen season. In addition, 47 patients with allergic rhinitis to mites and 66 healthy control subjects were evaluated on a single test occasion. The mite-sensitive patients performed more poorly than the controls on all three olfactory tests. However, they outperformed the grass-sensitive patients (tested preseasonally) on the odor detection threshold test, but not on the other two measures. The intraseasonal test results of the grass-sensitive patients were decreased for all measures relative to the preseasonal tests. Nevertheless, the grass-sensitive patients in the preseason period performed more poorly than the controls only on the odor detection threshold test. The intraseasonal grass-sensitive patients outperformed the mite-sensitive patients on the identification and detection threshold tests, but underperformed the mite-sensitive patients on the odor discrimination test. This finding is paradoxical, however, because these three types of olfactory measures are typically positively correlated in a wide range of test situations. The authors of the study concluded, "Therefore, the different kind of allergen exposure seems to result in a different pattern of allergic olfactory dysfunction."

Influences of Septoplasty on Olfaction

To our knowledge, only two studies have sought to determine empirically whether septoplasty improves olfactory function,[62,63] despite the widespread use of this procedure by otolaryngologists attempting to correct smell deficits. In the first of these studies, Stevens and Stevens[62] measured the olfactory thresholds of 100 patients before and after surgery. Of the 100 patients examined, the primary surgical procedure of 63 patients was nasal septoplasty; of 24, septorhinoplasty; of 3, turbinate resection; and of 10, polypectomy. Although the authors concluded that the surgical procedures, including septoplasty, improved olfactory function, the data for each type of operation was not provided separately, and their general conclusion is weakened by methodological considerations. In addition to not having a control group to examine the influences of repeated testing on the dependent

measure, the questionable Elsberg blast injection procedure[64] was used to determine olfactory sensitivity.

In the second study to provide data on this topic, Kimmelman[63] administered the UPSIT before and after septoplasty to 34 patients, 31 of whom had septal deformity and 3, nasal septal perforations. Again, no control group for repeated testing effects was provided, although it is known that UPSIT scores on average change little on repeated testing. The mean (SEM) UPSIT scores of these largely normally functioning patients were essentially equivalent before and after the operation (36.0 [0.4] versus 35.8 [0.4]).

Influence of Rhinoplasty on Olfaction

In perhaps the first published study to specifically address the effects of rhinoplasty on olfactory function, Champion[65] questioned 200 patients who had undergone rhinoplasty about their ability to smell. Ten percent of patients reported temporary anosmia lasting from 6 to 18 months after the operation, and all apparently reported regaining normal smell function. Because no empirical olfactory testing was performed, the accuracy of these observations is unknown.

Two years later, using ground coffee, oil of peppermint, and oil of clove as test stimuli, Goldwyn and Shore[66] performed both preoperative and postoperative olfactory tests on 64 patients who had undergone rhinoplasty alone, 22 who had undergone rhinoplasty in combination with submucous resection, and 11 who had undergone submucous resection alone. In addition, 57 control subjects were tested. The subjects were simply asked to identify the odors that were presented. Apparently, no clear benefits of the operations on smell function were found, as the findings of this study were interpreted as supporting Champion's conclusion that none of these types of operations have any long-term deleterious influences on smell function. However, this work is severely limited by not differentiating between patient types and by the use of a brief non–forced-choice identification test.

In 1994, Kimmelman[63] administered the UPSIT before and 2 to 4 weeks after surgery to 15 rhinoplasty patients. A small but statistically significant increase in performance was noted postoperatively (respective preoperative and postoperative means [SEM] = 33.9 [0.5] and 35.7 [0.6]). However, again no control group was tested to what degree repeated testing, per se, may have accounted for this improvement.

Influences of Other Forms of Nasal Surgery on Olfaction

In 1989 Gross-Isseroff et al.[67] obtained threshold and UPSIT measures in children with choanal atresia before and after surgical repair at relatively advanced ages (8–31 y). The three patients who had bilateral atresia had permanent olfactory deficits, whereas the one patient who had unilateral atresia appeared to have normal function. These findings suggest that early sensory exposure may be needed for the normal development of olfactory function, although, as the authors pointed out, the small number of cases involved necessitates additional research on this point.

The most common operative procedures impacting on the ability to smell are performed in patients with chronic rhinosinusitis and/or polyposis after more conservative treatments (e.g., allergen avoidance, nasal corticosteroids) have failed. Most recent studies have administered corticosteroids both preoperatively and postoperatively, although some have used such medication only after surgery, confounding the interpretation of the findings. Given the variation in olfactory measurement techniques used in such studies, this section is divided into 1) studies that have employed the standardized UPSIT (and in some cases additional tests); 2) studies that have employed a standardized combination of identification, discrimination, and detection threshold procedures[68]; and 3) studies that have used other types of olfactory tests.

Studies using the University of Pennsylvania Smell Identification Test. In perhaps the first report of the influences of nasal surgery on smell function of the modern era, Jafek et al.[69] in 1987 noted dramatic improvement in UPSIT and butanol detection threshold scores in one patient 4 months after an intranasal sphenoethmoidectomy (and intranasal antrostomies) and a continued 5-mg-daily regimen of prednisone (UPSIT scores increased from 10 to 31, the latter still indicative of mild microsmia; threshold values decreased by 4%). In another patient, even greater improvement was evidenced on the apparently sole post-treatment test performed a year after bilateral intranasal sphenoethmoidectomy and a regimen of triamcinolone acetonide (UPSIT scores increased from 9 to 38, the latter being normal; threshold values decreased by 45%). The authors concluded that these patients had received no benefit from either prior surgery or corticosteroid treatment alone, noting that "the results of this report raise an interesting question: why was the combined treatment with corticosteroids and surgery effective in long-term reversal of anosmia, whereas individual treatment with either modality had proved ineffective?" Quantitative testing had not been performed after the earlier surgeries, which were not as extensive as those subsequently performed by Jafek et al., and the duration and dosage of prior steroid treatment were not noted.

In 1988, Seiden and Smith[70] examined olfactory function in five patients before and after endoscopic intranasal surgery within the osteomeatal complex. Specifically, endoscopic intranasal ethmoidectomy and antrostomy were performed. On average, the degree of smell loss before surgery was indicative of total anosmia (mean UPSIT score = 15.8, SD = 8.73), although apparently some individuals had moderate hyposmia. Four weeks to 8 weeks after surgery, all five patients exhibited marked improvement in their olfactory function, which fell, on average, within the microsmic range (mean UPSIT score = 33.4, SD = 4.02).

In 1994, Eichel[71] administered the UPSIT before and after intranasal surgery to 10 patients complaining of anosmia who had advanced obstructive bilateral nasal polyposis and pansinusitis. The surgery included bilateral nasal polypectomies, bilateral sphenoethmoidectomies, and bilateral nasal antral windows. All patients received testing 6 and 12 months postoperatively; four received an

additional test at 18 months. Postoperatively, all were treated with a topical corticosteroid nasal spray. The surgery was associated with improved UPSIT scores in 7 of the 10 patients (respective median preoperative and 6- and 12-mo postoperative UPSIT scores: 10.5, 28, and 25.5), although average postoperative function was in the severe microsmic range.

Kimmelman[63] administered the UPSIT to nine patients undergoing ethmoidectomy and nine patients undergoing polypectomy before and 2 to 4 weeks after their surgeries. A small nonsignificant increase in UPSIT scores was noted postoperatively in the ethmoidectomy group, although, as in the study of Eichel, average postoperative performance was in the moderate (nearly severe) microsmic range (respective mean [SEM] scores = 25.56 [3.47] and 27.89 [3.13]; $P = .07$). Although a statistically significant improvement in UPSIT scores occurred in the polypectomy group ($P = .025$), the postoperative scores were indicative of severe microsmia (preoperative and postoperative scores [SEM] = 17.0 [2.54] and 22.1 [3.02], respectively).

el Nagger et al.[72] assessed olfactory function in 29 patients with bilateral nasal polyps before and after a polypectomy. Following the operation, the patients received a 6-week course of beclomethasone nasal spray (Beconase) to one nostril only, with the other acting as a control. Although the UPSIT scores were higher for most individuals on the postoperative than on the preoperative tests, the changes in the observed UPSIT scores were modest and essentially of the same order of postoperative severity as seen in the study of Kimmelman. One arrives at the following preoperative and postoperative mean UPSIT scores, respectively, from the data presented by these authors in the first two of their figures: 17.08 and 19.84 for the Beconase nostrils and 16.44 and 21.42 for the control nostrils. From this perspective, neither the operative procedure nor the beclomethasone spray had much of an effect on overall smell function which, on average, fell within the anosmic or severe microsmic range.

Lund and Scadding[73] evaluated the olfactory function of 50 hyposmic (UPSIT scores <31) patients with chronic rhinosinusitis for 3 months before and after endoscopic nasal surgery. The postsurgical evaluations were performed at 1 year. The endoscopic procedure included uncinectomy, anterior ethmoidectomy, and perforation of the ground lamella of the middle turbinate in all cases, with posterior ethmoidectomy, sphenoidectomy, clearance of the frontal recess, and enlargement of the maxillary ostium in some cases. Intranasal steroids were used up to the time of the surgery and for at least 3 months afterward. Significant preoperative/postoperative improvement in UPSIT scores and in threshold values were observed in this group of patients (respective mean UPSIT scores = 19.5 and 25.0), although, again, on average, the postoperative UPSIT scores were indicative of marked microsmia.

In 1996, Downey et al.[74] administered the UPSIT before and after endoscopic sinus surgery to 50 patients with subjective anosmia and symptoms of progressive sinusitis. After surgery, 52% of patients self-reported significant improvement in smell and had higher UPSIT scores. Of the remaining patients, some had intermittent improvement, but most remained hyposmic or anosmic despite clinically well-healed ethmoid surgical beds. A relationship was observed between UPSIT scores and the severity of the disease, as defined using the Kennedy staging system. Thus, the mean UPSIT scores were 35, 31, 26, and 23 for stages I to IV of the disease, respectively. Disease extending beyond the ethmoids, as determined by preoperative computed tomography, was typically associated with persistent anosmia.

Recently, Friedman et al.[75] administered the UPSIT to 50 patients before and 5 weeks after endoscopic sinus surgery with middle turbinate medialization and preservation. Iatrogenic synechia formation was produced by initially abrading the caudal end of the middle turbinate and the opposing septal mucosa using a microdebrider. No statistically significant differences in preoperative/postoperative UPSIT scores were found (respective mean UPSIT scores = 35.18 and 35.57), leading the authors to conclude that middle turbinate medialization has no discernible adverse effect on olfaction.

Studies using quantitative measures other than the University of Pennsylvania Smell Identification Test. In 1988, Leonard et al.[76] administered odor detection and threshold tests to 25 patients known to have olfactory dysfunction. The tests were administered before and after unilateral or bilateral transantral ethmoidectomy. Smell function reportedly returned to normal in nine of the patients in one or both nasal chambers after surgery (36%), whereas four evidenced mild hyposmia (16%), five moderate to severe hyposmia (20%), and the remainder no improvement (28%). Surgery on one side of the nose appeared in some cases to improve smell function on the contralateral side.

Five years later, Hoseman et al.[77] administered a "qualitative and a semiquantitative olfactory function test" to each side of the nose of 111 patients before and after intranasal surgery for chronic polypoid ethmoiditis. Eighty-seven of these patients received a complete sphenoethmoidectomy, and 24 a partial resection of the ethmoidal cell system. The olfactory test comprised a non–forced-choice odor identification component, in which the subject was required to report the quality of vanillin (or cinnamon oil), peppermint oil, menthol, and acetic acid with "corrective feedback, when needed" and an odor detection threshold component. In the threshold component, non–forced-choice detection thresholds to three stimuli (phenylethanol, benzylacetate, and formic acid) were established. Before surgery, 65% of the patients were reportedly hyposmic or anosmic, whereas after surgery only 8% were similarly smell deficient. No association was noted postoperatively between the size of the middle turbinate and smell ability. However, the authors concluded that their results largely reflected improvement of airflow to the receptors and that "an inflammatory affection of the sense organ itself could not be responsible [for the loss]."

A year after the study of Hoseman et al.,[77] Delank and Stoll[78] evaluated odor detection thresholds to 2-phenylethanol and dimethyldisulfide before and after nasal endoscopic sinus surgery in 78 patients with chronic sinusitis with nasal polyposis. Employing an ascending

threshold procedure, they noted preoperative hyposmia or odor discrimination problems in 40% of their sample, and anosmia in another 36%. However, only 22% of their patients complained spontaneously of smell dysfunction. Following endoscopic surgery, 71% of the smell-deficient patients reportedly improved. Postoperative thresholds for 2-phenylethanol and dimethyldisulfide worsened in 9% of the patients. Postoperative olfactory discrimination deteriorated in 11%. Preoperative and postoperative olfactory function was not predictable in individual cases when nasal polyposis was limited.

In a similar subsequent study, these authors extended the patient group to 115 patients with chronic sinusitis.[79] Preoperatively, only about half of the patients (58%) were aware of or complained of an olfactory deficit. However, the threshold testing found 83% to be either hyposmic (52%) or anosmic (31%). After surgery, 70% of the patients reportedly exhibited some improvement in olfactory function; normosmia, however, was relatively rare, being achieved in only 25% of the hyposmic patients and 5% of the anosmic patients. The olfactory function of 8% of the patients was worse after surgery than before surgery. Therefore, the authors concluded that "the prevalence of olfactory dysfunction in chronic sinusitis is preoperatively higher, and the rate of [postoperative] improvement is lower, than generally assumed." The authors also noted that "resections of the middle turbinate may have a negative effect on olfaction, due to damage to the olfactory fila or alteration of the normal aerodynamic pattern within the olfactory cleft." As noted by earlier investigators, the degree of olfactory dysfunction was associated with the degree of intranasal polyposis.

Min et al.[80] determined, in 1995, butanol thresholds before and after functional endoscopic nasal surgery in 80 patients with chronic sinusitis. Patients with prior surgery, asthma, aspirin intolerance, nasal allergy, or cystic fibrosis were screened from the study group. In accord with other studies (e.g., Downey et al.,[74]) preoperative dysfunction was associated, in general, with the severity of sinusitis (determined in this case from computed tomography scans of the ostiomeatal-unit complex). The percentages of persons with normosmia, hyposmia and anosmia before surgery were reported as 22%, 45%, and 33%, respectively. After surgery, these percentages were 36%, 48%, and 16%. Although a postoperative average reduction in threshold values was noted, the postoperative mean threshold value remained within the range considered indicative of hyposmia. No association was present between the degree of postoperative olfactory improvement and either the severity or duration of the sinusitis.

More recently, Klimek et al.[81] tested the odor identification, discrimination, and identification ability of 31 patients with nasal polyps 1 to 3 days before endonasal polyposis surgery and six postoperative times thereafter (approximately 1 wk and approximately 1, 2, 3, and 6 months). On average, the olfactory function, as measured by all three tests, fluctuated postoperatively, with best recovery (i.e., mild hyposmia) occurring approximately 3 months after surgery. Six months after surgery moderate hyposmia was noted to about the same degree as was observed before the surgery. The authors concluded: "This study demonstrates that olfactory function is impaired in patients with nasal polyps. Endonasal sinus surgery might improve olfactory function with best results within 3 months after surgery."

Studies using ratings of self-perceived olfactory function. In 1997, Jankowski et al.[82] asked patients to remember what their sense of smell was like before and after either 1) a radical ethmoidectomy in which all the bony lamellae and mucosa within the labyrinth were removed, including a large antrostomy, sphenoidotomy, frontal sinusotomy, and middle turbinectomy (n = 39) or 2) a less systematic ethmoidectomy adapted to the extent of the disease (n = 37). They were also asked to remember what their sense of smell seemed like at 6-month intervals after the operation up to the time of filling out the questionnaire. The patients were required to mark their remembrances on a 10-point scale ranging from no functional improvement to complete recovery. In general, the ratings suggested similar improvement in olfactory function in both groups 6 months after surgery, and a maintenance of the same level 36 months after nasalization. Some decrement was noted in reported smell function 24 months after the less extensive ethmoidectomy. However, this study suffers from many problems, not the least of which was the lack of an actual sensory measure, the requirement of a patient remembering function retrospectively over long periods, and demand characteristics attendant on being asked to report the effectiveness of an operative procedure to which they had subjected themselves.

CONCLUSIONS

Remarkable progress has been made in the last decade in understanding the function of the olfactory system. At the transduction level, the discovery of the gene family that controls the expression of olfactory receptors has been a monumental event. At the measurement level the development and proliferation of practical and reliable olfactory tests has spawned hundreds of studies that otherwise would not have been made, demonstrating olfactory dysfunction in a wide range of clinical disorders and leading to the discovery that olfactory loss is a very early clinical sign of several major neurodegenerative diseases. The comparatively few studies that have employed modern psychophysical tests to patients with rhinitis or rhinosinusitis have generally found an association between the degree of smell loss and the severity of nasal disease, although, except in cases of marked obstruction, no relationship is apparent between airway patency and olfactory dysfunction. This observation, along with recent histopathological studies of the olfactory mucosa in these disorders and the fact that even after nasal surgery and corticosteroid treatments, smell function rarely returns, on average, to normal levels, suggests that airflow access is not the only factor determining smell loss in such patients. Although the weight of the evidence suggests that nasal steroid sprays, when appropriately administered, can improve olfactory function in some patients, not a single double-blind study employing placebos has evaluated the efficacy of such procedures in restoring smell function. It is hoped that the widespread availability of

easy-to-use tests of olfactory function will lead to such controlled studies in the not-too-distant future.

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