Proposed classification scheme for quantitative olfactory function alterations

LUIS MARIA GIL-CARCEDO, MD, PhD, ELISA GIL-CARCEDO, MD, LUIS ANGEL VALLEJO, MD, PhD, and **PRIMITIVO ORTEGA, MD,**
Valladolid and Madrid, Spain

Given the need for a clinical classification for daily patient examinations to refer to each type of quantitative alteration in the sense of smell, we have created a topographic classification of such alterations, establishing groups to distinguish among patients with decreased or total loss of olfaction. Because the classification is based on the diagnosis of the different causes of anosmia, it implicitly includes etiologic and topographic considerations. We have established 3 main groups on the basis of the site of the causal lesion: conduction, sensorineural, and mixed anosmias. In addition, within the sensorineural anosmias, we distinguish between the epithelial, retroepithelial, and central anosmias. (Otolaryngol Head Neck Surg 1999;121:820-5.)

Often, little attention is paid to alterations of olfaction, both by the patient and by the medical staff. Greater refinement and social sophistication are increasingly changing this situation. Olfactory sensations have become a valued factor in enjoyment of life; the bouquet of wine, the aroma of a roast, and the fragrance of a perfume represent pleasures that are more and more appreciated. Olfactory problems are finding an increasingly relevant place in human pathology.

The saddest symptom for the anosmic patient is the inability to distinguish the flavors of food and drink and therefore to enjoy eating. In fact, the pleasure from food flavors is an intimate mixture of taste and smell sensations, but smell predominates. Patients with anosmia can detect only basic flavors (sweet, salty, acid, and bitter); from this poor differentiation plus tactile sensations from food consistency, temperature, and texture, they obtain scant satisfaction from the products they ingest.

In addition, olfaction plays a fundamental role in very different processes: in defense mechanisms to warn of toxic gases or spoiled food, to create digestive reflexes essential for salivation and gastric juice secretion, and to maintain interesting social, sexual, and hedonistic factors from the sensations it produces. Furthermore, when the sense of smell is altered, its failure leads to fundamental symptoms in the diagnosis of nasoparanasal and central nervous system diseases.

Quantitatively the problem is not banal. In the 1970s the National Advisory Neurological and Communicative Disorders and Stroke Council estimated that 2 million North American adults have disorders of taste and smell. In a more recent revision using sweep methods by "scratch and nasal inspiration," investigators at the National Geographic Society and the Monell Chemical Senses Center found a permanent loss of 1.23% and a temporary loss of 62.4% in the olfactory perception of 1.5 million volunteers.[1]

Individuals who are in optimal health generally possess an ideal olfactory situation (normosmia), perceiving smells at thresholds considered normal and distinguishing perfectly the wide range of smells offered by the different volatile substances that can act as odorivectors.[2]

OBJECTIVE

In our opinion, final classification of olfactory function disorders exists. Two large groups are accepted by everyone: quantitative alterations, which are pathological situations producing decrease or loss of the sense of smell; and qualitative alterations, which cause distortion of the olfactory sensation or ghost olfactory perception.

Normally, alterations (dysosmias) of olfaction manifest as threshold modifications, giving rise to quantitative olfactory alterations, generally hyposmias or anosmias but sometimes hyperosmias. These decreases, losses, or increases in olfactory perception usually apply to all smells; rarely is the threshold altered for only 1 specific odor.

From the Department of Otolaryngology–Head and Neck Surgery, Hospital Universitario "Del Rio Hortega" (Drs L. M. Gil-Carcedo and Vallejo); the Departments of Otolaryngology–Head and Neck Surgery (Drs. L. M. Gil-Carcedo and Vallejo) and Surgery (Dr E. Gil-Carcedo), Valladolid University; and the Department of Otolaryngology–Head and Neck Surgery, Hospital de Móstoles (Dr Ortega).

Presented at the Annual Meeting of the American Academy of Otolaryngology–Head and Neck Surgery, San Francisco, CA, September 7-10, 1997.

Reprint requests: L. M. Gil-Carcedo García, MD, PhD, Head of Ear, Nose and Throat Department, Cátedra de ORL, Facultad de Medicina, C/Ramón y Cajal s.n., 47005-Valladolid, Spain.

0194-5998/99/$8.00 + 0 **23/77/94215**

Fig 1. Basic system of subjective olfactometry was used to establish the threshold level. Air was added by syringe to a 500-mL glass vessel containing 50 mL of an odorous solution; the positive pressure then moved the air with odorous molecules toward an exit. The circuit ended in a rubber tube with a final bulb adapted to the patient's nostrils. In this way, when the exit was opened, a known quantity of air with odorous molecules was introduced into the nasal fossa.

In clinical practice, most patients with olfactory alterations have severe hyposmia or anosmia. Our goal is to create a classification of these quantitative olfactory alterations that will allow medical staff to easily place into different sections the varied diseases and lesions producing the symptoms.

METHODS

To draw up the classification of quantitative alterations of the olfactory function, we have used topographic criteria based on the analysis of the following 3 sources of information.

Animal Studies

In the Department of Otorhinolaryngology of the University of Valladolid, the structure of the principal olfactory tract has been studied in different animals. Between 1983 and 1995 a total of 155 animals were used: 29 hamsters *(Cricetus auratus)*, 96 Wistar-Lewis rats, 22 giant albino rabbits, and 8 cats.[3] The shape of the epithelium and the lamina propria of the olfactory mucus, the olfactory bulb structure, the connections between receptor neurons and bulb mitral cells, and the general composition of the principal olfactory tract have been studied. The results of these investigations were published partially in different media between 1985 and 1996.[4-6] All the animals used were treated according to the international care and use principles of laboratory animals.

Patient Analysis

From 1988 to 1995, 163 patients with different diseases or lesions, all manifesting olfactory alterations, were examined functionally. There were 89 women and 74 men (age range 7 to 72 years). All individuals were given a complete otorhinolaryngologic evaluation. Necessary image data and pertinent reports were obtained from other hospital services, principally neurosurgery, psychiatry, and neurology. In addition, olfactometry was performed in 35 patients who had received total laryngectomy; these patients made up a separate group.[7]

A basic system of subjective olfactometry was used to establish the threshold level (Fig 1). Although simple, it was enough to collect the elementary data needed. Air was added by syringe to a 500-mL glass vessel containing 50 mL of an odorous solution; the positive pressure then moved the air with odorous molecules toward an exit. The circuit ended in a rubber tube with a final bulb adapted to the patient's nostrils. In this way, when the exit was opened, a known quantity of air with odorous molecules was introduced into the nasal fossa. The patients had previously been instructed to take 3 or 4 short, rapid sniffs when the blast of air arrived because this directed the stimulus more easily to the olfactory region. Increasing concentrations were used, and the first perceived by the subject marked the smell threshold for the substance used.

The solutions are stable and conserve their concentration for months, but even so it is a good idea to replace them monthly. In addition, it is necessary to check the reliability of the system and the odorous solution frequently; to do so, a small group of normosmic individuals should be used as control subjects.

Basis on a Previously Accepted Classification System

Just as olfactometry has been related to functional auditory examination to create a system that expresses the intensity of quantitative olfactory alterations graphically,[8] we based our

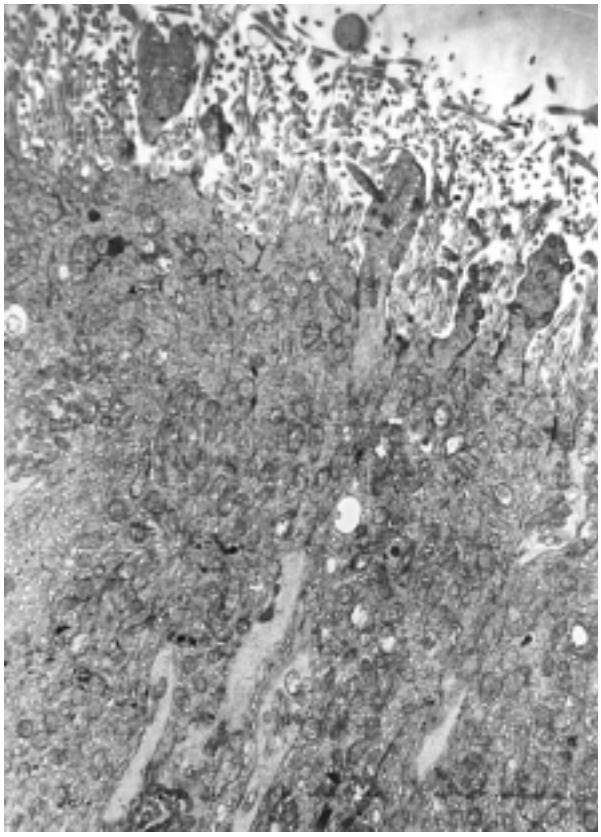

Fig 2. We subdivide the sensorineural anosmias into 3 groups: epithelial (epitheliopathy), retroepithelial (neuronopathy), and central anosmias. If the olfactory epithelium is normal (as in this image), we can exclude the possibility of epithelial anosmia.

system on the universally accepted topographic classification of the hypoacusis to classify the anosmias.

RESULTS

From a quantitative point of view, alterations of olfactory function are classified into hyposmias and anosmias, according to whether there is a decrease (more or less intense) or total loss of the sense of smell. Our topographic classification creates groups to distinguish between patients with decreased and those with total loss of smell. Because it is based on the diagnosis of the different causes of anosmia, it implicitly contains causes and topographies.

First, we created 3 large groups based on the site of the lesion originating the anosmia: conduction, sensorineural, and mixed. We consider conduction anosmias to be losses of olfactory capacity caused by obstruction of nasal aeration that prevent the odorous molecule from reaching the olfactory epithelial surface. The olfactory neurosensory epithelium is healthy and

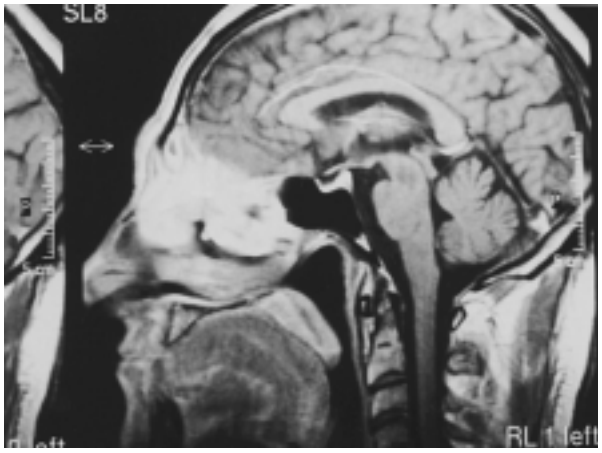

Fig 3. Surgery in this adenoid cystic carcinoma gave origin to retroepithelial anosmia.

normofunctional, but specific perturbations of the nasal cavity block the passage of air to the upper reaches, where the olfactory epithelium is located.

Of the 163 patients studied, 59 (36%) had conduction anosmia. Of the 59, 31 had nasal polyps, 23 chronic rhinitis and rhinosinusitis of differing causes, and 5 different neoplasias that caused nasal obstruction without directly lesioning the olfactory region.

We call sensorineural anosmias olfaction loss caused by olfactory tract lesions, wherever they are located (Fig 2). Of the 163 patients, 42 (26%) had sensorineural anosmias. We subdivide these into 3 groups: epithelial (epitheliopathy), retroepithelial (neuronopathy), and central anosmias.

Of the 42 patients with sensorineural anosmias, 6 (4% of all patients studied) had undergone olfactory epithelium alterations; we included these individuals in the epithelial anosmia group.[9,10] The dysfunction is caused by lesions at the level of the peripheral organ, with permanent disappearance of the receptor neurons of the olfactory epithelium. The cases were as follows: 19 patients who had sudden postinfluenzal anosmia, 7 who were chronic (massive) users of topical vasoconstrictors, 3 who had diabetes, and 2 who were drug addicts who sniffed cocaine.

In 6 (4% of total patients studied) of 42 patients with sensorineural anosmias, loss of the sense of smell was caused by lesions affecting cranial nerve I. These individuals were included in the retroepithelial anosmia group.[11,12] Three cases were from iatrogenic causes (combined approaches of the ethmoid and anterior cranial fossa surgery) (Fig 3), 2 from trauma (automobile accident and sports trauma),[13] and 1 from ethmoid fibrose dysplasia.[14]

The remaining 5 (3%) patients with sensorineural

anosmia had central anosmia. Three had Parkinson's disease, 1 had Alzheimer's disease, and 1 had severe frontal trauma with loss of encephalic mass, which evolved with behavior problems and psychosocial alterations.

We consider mixed anosmias to be those in which the deficit is caused by a disturbance affecting various olfactory structures simultaneously. We examined a group of 28 individuals (17% of the total patients studied), which we included in this subgroup. The cause was trauma in 9 cases, tumor in 8, anterior cranial fossa surgery in 5, various intoxications in 3, and congenital malformation in 3 (1 glioma and 2 meningoencephaloceles)[15] (Fig 4).

With the classification system we propose, we were able to classify 129 (79%) patients of the total 163 examined. The cause of anosmia and the site of the lesion producing it were unknown in 34 (21%) patients. Under these circumstances our topographic classification cannot be used, so we included these patients in a group that we call idiopathic anosmias.

Fig 4. Patient with a meningoencephalocele and mixed anosmia.

DISCUSSION

The need for a clinical classification to refer to each type of quantitative olfactory alteration in daily examinations is clear. We therefore consider it unnecessary to discuss the idea. What is open to debate is whether such a system should be based on topographic criteria referring to the site of the olfactory tract lesion (similar to that of auditory loss classifications) or whether a better possibility exists. We cannot think of a better, simpler form than the topographic criteria.

To be able to classify a patient within a specific group, it is necessary to know above all if the patient is truly anosmic. A basic system of subjective olfactometry to establish the threshold level is sufficient. Test reliability ranges, with respect to precise thresholds or fine qualitative olfaction, are much lower than ranges from other neurosensorial examinations.[16] For our needs, it is enough to know whether the patient has a sense of smell, and this is easily possible with simple tests.

A more sophisticated examination method could be considered, but in principle we do not think it is necessary. The T&T olfactometer, revised and used systematically by Japanese specialists, is based on thresholds for 5 different odors. The results are displayed on a graph on the basis of liminal tonal audiometry[8]: odor types are plotted on the abscissa, and the concentration at which each is perceived is shown on the ordinate.

To apply our classification, it is only necessary to evaluate 1 odor because, when there is loss or decrease in olfaction for 1 odor, it is generally the same for all odors. Threshold alteration for a single specific odor is very rare.[1] On the other hand, objective olfactometry methods—evoked potential register[17] and other electroencephalographic methods[18]—are not yet sufficiently standardized for systematic clinical use.

In practice, once individuals have identified themselves as anosmic and this has been checked with basic threshold olfactometry, we know whether they have an important deficit in olfaction.

It is usually more difficult to establish the cause of anosmia. This is sometimes evident, such as when the patient relates that the sense of smell disappeared during a case of influenza, after surgery of the anterior fossa, as a consequence of cranioencephalic trauma, or after the onset of Parkinson's disease. It is also easy to recognize the cause when polyposis, inverted papilloma that obstructs the nasal fossae bilaterally, or any other pathology related to olfactory disturbances appears during conventional clinical examination.

With respect to the usefulness of CT and, above all, MRI, it is unquestionable that the images obtained with these methods are of great help when the cause of anosmia is a tumor, a congenital anomaly,[19] a trauma, or any disease in which the images help delimit and follow tissue damage. However, when patients with such lesions have anosmia, the cause-and-effect relationship can be established with certainty, and the images serve only to confirm the clinical criteria.

Some doubts may arise as to whether anosmia is of

conduction or mixed with additional epithelial affectation, or whether a sensorineural anosmia is from epitheliopathy or central. In these cases the decision to include the case in one group or another is based on the most logical possibility. The doubt can be resolved by olfactory epithelium biopsy, but biopsy to study the anatomicopathologic substrate of olfactory alterations is not a routine procedure.

Yamagishi et al[20] have performed immunohistochemical studies in patients with anosmia produced by different causes: choanal atresia, chronic sinusitis, chronic and acute rhinitis, and cranial trauma. These constitute patterns that allow specialists to establish the degree of degeneration of the pathologic olfactory mucus. Furthermore, these data are not only of diagnostic value but also of prognostic value as to the functional future of the epithelium. With current endoscopies, the technique is not difficult, the risk is slight, and if these data are used, the possibility of classification error is less.

One point of discussion is the statistical reliability of the percentage distribution of cases between different types of anosmia. Because olfactometry is not routine in otorhinolaryngologic services, it is applied specifically to patients who we think may be of interest. Olfactometry is frankly exceptional in internal medicine, neurology, and neurosurgery. For these reasons the statistical results may be exposed to a distorting factor from the nonrandom case selection.

In otorhinolaryngologic diseases anosmia, when present, is detected from the case history. The data are therefore easily incorporated into the retrospective or prospective study in process. Anosmia produced by nonotorhinolaryngologic causes (cranial trauma, intoxication, degenerative central nervous system disease) is not generally of great importance to the specialists who treat the patient; the other specialists do not normally ask for the collaboration of the otorhinolaryngologist. Thus, if the corresponding hospital services are not visited to look for cases, patients with this disorder are not included; however, if cases at risk of having anosmia are sought, the final percentage results are distorted.

Congenital anosmia has been studied thoroughly by Jafek et al,[21] whereas we have only 3 cases well characterized by olfactometry. Two were 7- and 9-year-old children with a clear cause for their congenital anosmia because they had meningoencephaloceles.[15] Our other case was a patient who had never had olfactory sensation but still maintained normal taste perception to basic stimuli. In this individual's case history, there was no pathology related to the anosmia and the otorhinolaryngologic examination was normal. We therefore consider this to be a congenital, idiopathic anosmia.

CONCLUSIONS

- We consider a consensus for clinical classification of anosmias essential.
- We propose an original system we have created.
- We classify the anosmias as conduction, sensorineural, and mixed.
- We classify the sensorineural anosmias into the following subgroups: epithelial, retroepithelial, and central.
- We found that 21% of idiopathic anosmias could not be classified.
- We believe that the otorhinolaryngologist must have basic knowledge of the olfactory tract to understand disorders of the sense of smell and their classification.

REFERENCES

1. Leopold DA. Physiology of olfaction. In: Cummings CW, Fredrickson JM, Harker LA, et al, editors. Otolaryngology–head and neck surgery. St Louis: Mosby; 1992. p. 640-64.
2. Gil-Carcedo LM. La olfación. In: Abelló P, Traserra J, editors. Otorrinolaringología. Barcelona: Doyma SA; 1992. p. 286-93.
3. Vallejo Valdezate LA, Gayoso Rodriguez M, Garrosa M. Modificaciones ultraestructurales en el bulbo olfatorio del jerbo tras deprivación olfatoria funcional temprana [doctoral thesis]. Valladolid, Spain: Universidad de Valladolid; 1996.
4. Gil-Carcedo LM, Gonzalez M. Estudio morfológico, histológico y ultrastructural de la mucosa olfatoria. I. El epitelio olfatorio. An Otorrinolaringol Ibero Am 1985;12:291-304.
5. Gil-Carcedo LM, Gonzalez M. Estudio morfologico, histológico y ultrastructural de la mucosa olfatoria. II. La célula neurosensorial. El corion. An Otorrinolaringol Ibero Am 1985;12:385-402.
6. Gil-Carcedo LM, Gayoso M, Al Majdalawi A. Marcado de los glomérulos del bulbo olfatorio por transporte axónico de peroxidasa (HRP) depositada selectivamente en el epitelio olfatorio. An Otorrinolaringol Ibero Am 1988;3:79-85.
7. Alonso JL, Gil-Carcedo LM. Estudio morfológico y funcional de las fosas nasales en el laringuectomizado [doctoral thesis]. Valladolid, Spain: Universidad de Valladolid; 1989. p. 77-103.
8. Tagagi SF. A standardized olfactometer in Japan. Ann NY Acad Sci 1987;510:113-9.
9. Gil-Carcedo LM, Marcos M, Roman LA. Ciliary anomalies. In: Sacristan T, Alvarez-Vicent JJ, Antolí-Candela F, et al, editors. Otorhinolaryngology–head and neck surgery. Amsterdam: Kugler & Ghedini; 1990. p. 1-4.
10. Gil-Carcedo LM. Sustrato morfológico de la patología olfatoria. In: Capella G, editor. Pares craneales (nervi cranialis praeter octavum). XXVII Conventus Societas Oto-Rhino-Laryngologica Latina. Barcelona: J Uriach Cia SA; 1988. p. 61-5.
11. Gil-Carcedo LM, Alonso MV, Gayoso M. Study on connections between olfactory receptor site and olfactory bulb by using anterograde and retrograde axonic transport of horse-radish peroxidase (HRP). Rhinology 1988;(Suppl 1):57-8.
12. Gil-Carcedo LM, Alonso MV, Gayoso M. Estudio de las relaciones entre el órgano periférico de la olfacción y el bulbo olfatorio, utilizando el transporte axónico anterógrado y retrógrado de peroxidasa de rábano (HRP). Acta Otorrinolaringol Esp 1991; 42:465-73.
13. Gil-Carcedo LM. Fracturas del macizo facial. In: Urgencias de ORL. Madrid: GARSI; 1991. p. 140-160.
14. Gil-Carcedo, LM, Gonzalez M. Monostotic fibrous dysplasia of the ethmoid. Surgical treatment using a combined endocranial and transfacial approach. J Laryngol Otol 1986;100:429-34.

15. Izquierdo JM, Gil-Carcedo LM. Recurrent meningitis and transethmoidal intranasal meningoencephalocele. Dev Med Child Neurol 1988;30:245-51.
16. Doty RL, McKeown DA, Lee WW, et al. A study of the test-retest reliability of ten olfactory tests. Chem Senses 1995;6:645-56.
17. Westhofen M, Herberhold C. Trigeminal and olfactory synergism in the perception of smell. Acta Otorhinolaryngol Belg 1987;41: 66-78.
18. Harada H, Shiraishi K, Kato T, et al. Coherence analysis of EEG changes during odour stimulation in humans. J Laryngol Otol 1996;7:652-6.
19. Castillo M, Mukherji SK. Magnetic resonance imaging of the olfactory apparatus. Top Magn Reson Imaging 1996;2:80-6.
20. Yamagishi M, Nakamura H, Suzuki S, et al. Immunohistochemical examination of olfactory mucosa in patients with olfactory disturbance. Ann Otol Rhinol Laryngol 1990;99:205-10.
21. Jafek BW, Gordon AS, Moran DT, et al. Congenital anosmia. Ear Nose Throat J 1990;5:331-7.