
Olfactory Dysfunction:

What's that smell?

By Steven Sobol, MD, MSc; Saul Frenkiel, MD, FRCSC; and Debbie Mouadeb

The sense of smell plays an important role in protecting man from environmental dangers, such as fire, natural gas leaks and spoiled food. Physiologically, the chemical senses aid in normal digestion by triggering gastrointestinal secretions.¹ Smell influences the palatability of food. Defects in the sense of smell are associated with alterations in perceptions of flavor, leading to anorexia and weight loss. Psychologically, smell is powerful in establishing strong positive and negative memories, and affects socialization and interpersonal relationships. Smell dysfunctions often mean considerable disability and a lower quality of life.

Loss or decreased olfactory function affects approximately one per cent of Americans under the age of 60 and more than half the population over that age.² Aside from having a substantial impact on an individual's quality of life, olfactory dysfunction may signal an underlying disease. Smell disorders have been largely overlooked by the medical community because of a lack of knowledge and understanding of the sense of smell and its disease states, as well its diagnosis and management. Patients with olfactory disorders need to be clinically assessed, and the etiology and anatomical location of their disorder should be sought out.

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Summary

What are the causes of olfactory dysfunction?

1. **Conductive olfactory loss** is any process that causes sufficient obstruction in the nose preventing odorant molecules from reaching the olfactory epithelium.
2. **Sensorineural olfactory loss** is any process that directly affects and impairs either the olfactory epithelium or the central olfactory pathways.

How is olfactory dysfunction treated?

Therapy is dictated by pathologic conditions. Possible treatments include allergic management, antibiotics, and topical and systemic corticosteroid therapies.

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What causes Olfactory Dysfunction?

The two main causes of olfactory dysfunction are conductive and sensorineural. Conductive olfactory loss is any process that causes sufficient obstruction in the nose preventing odorant molecules from reaching the olfactory epithelium. Sensorineural olfactory loss is any process that directly affects and impairs either the olfactory epithelium or the central olfactory pathways.³ While this classification system is extremely useful to categorize the disease, based on its anatomical source, combined conductive and sensorineural disorders do exist.

Within these two broad categories, the particular causes of olfactory dysfunction can be classified further by the nature of its etiology: inflammatory, trauma, congenital-developmental, degenerative-toxic, endocrine-metabolic and neoplasia (see Table 1).

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The three most common causes of anosmia or hyposmia are nasal and sinus disease, postviral upper respiratory tract infections and head trauma. These three causes make up over two thirds of all patients with olfactory dysfunction.⁴

Definitions

Anosmia	A complete loss of the sense of smell.
Hyposmia	A general decreased sense of smell.
Specific anosmia	The inability to smell one of a few odorants in the presence of an otherwise normal sense of smell.
Heterosmia	The inability to distinguish between certain odors.
Agnosia	The inability to contrast or classify odors, although able to detect them.
Dysosmia	A distortion of the sense of smell, and may be in the presence (parosmia) or absence (phantosmia) of a stimulant odor.
Cacosmia	When a normal pleasant odor is inappropriately detected as foul or unpleasant (form of parosmia).
Hyperosmia	A rare condition that is defined as an increased sensitivity to all odors, and is often idiopathic in origin.

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ACTONEL provided
sustained results

- Provided sustained fracture reduction over a period of 3 years^{2,3†‡}

* Based on a data analysis from 4 large 3-year osteoporosis treatment trials involving 2,725 patients (Relative risk [RR] = 5.1, presence of ≥ 1 fracture, $p < 0.001$)

† Randomized, double-blind, placebo-controlled study of 2,458 postmenopausal women with at least one vertebral fracture. All patients received 1 g/d calcium and, if baseline levels were low, 500 IU/d vitamin D.

‡ Three-year clinical study (VERT-MN) in 1,226 postmenopausal women (18.1% vs 29%; $p < 0.001$). All patients received 1 g/d calcium and, if baseline levels were low, 500 IU/d vitamin D.

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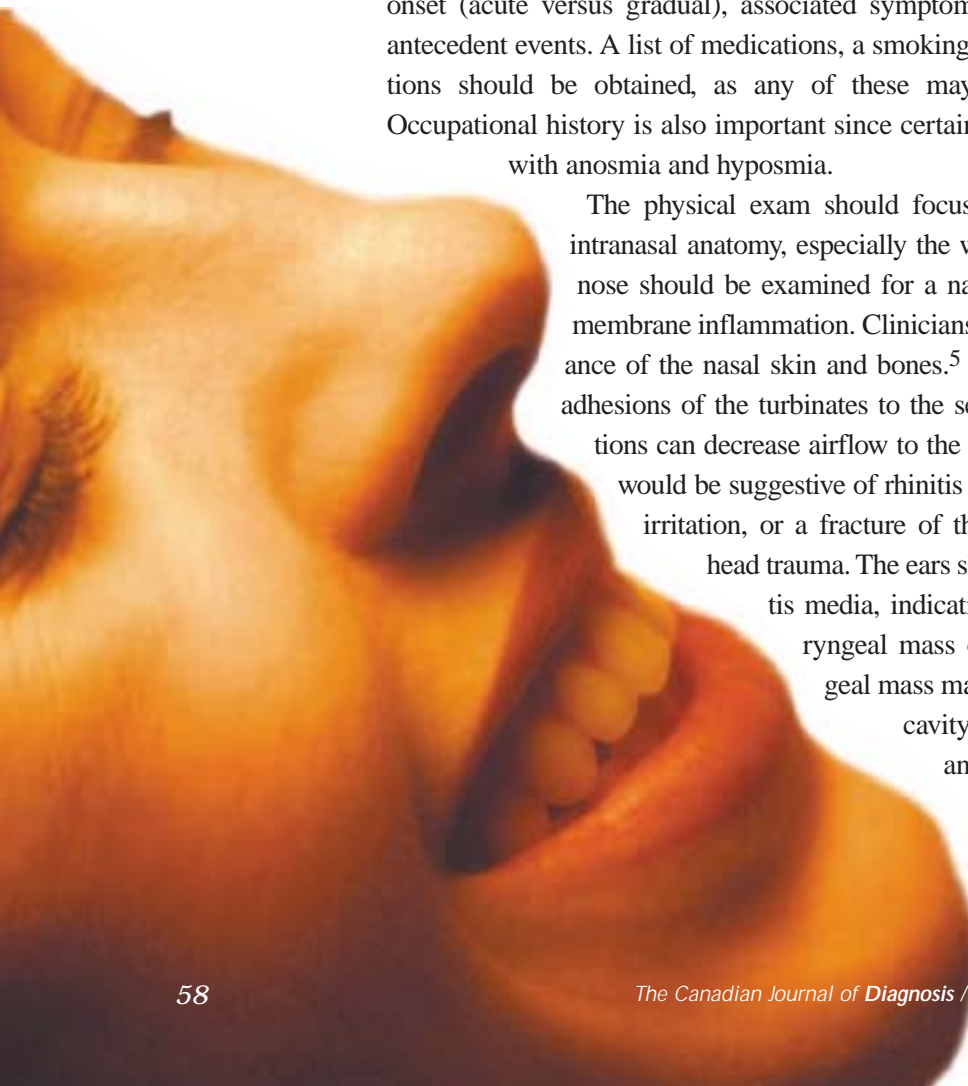
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How is it diagnosed?

A detailed history and physical exam help the clinician arrive at an accurate diagnosis. What most people perceive as a loss of taste is, in fact, a primary defect in olfaction. Gustatory dysfunction consists of an inability to distinguish between the four taste qualities: salty, sweet, sour and bitter. Olfaction allows one to appreciate the complete gamut of flavors depending on retronasal stimulation of the smell receptors. A patient with anosmia, with normal gustatory function, can distinguish the sour taste of lemon from the sweetness of sugar. This same patient, however, would not be able to appreciate the different tastes of chocolate, maple syrup, watermelon or a strawberry.

Clinical Evaluation: There are many possible causes of loss of or decreased olfactory function. Asking key questions about the patient's history can help narrow the differential. Points to cover include the nature and degree of olfactory loss, mode of onset (acute versus gradual), associated symptoms, previous operations and any antecedent events. A list of medications, a smoking history and concomitant conditions should be obtained, as any of these may cause the smell dysfunction. Occupational history is also important since certain industrial agents are associated with anosmia and hyposmia.

The physical exam should focus on the neurologic system and intranasal anatomy, especially the whole head and neck region. The nose should be examined for a nasal mass, clot, polyps and nasal membrane inflammation. Clinicians should also examine the appearance of the nasal skin and bones.⁵ The presence of polyps, masses, adhesions of the turbinates to the septum, and marked septal deviations can decrease airflow to the olfactory epithelium. Rhinorrhea would be suggestive of rhinitis secondary to allergy, infection or irritation, or a fracture of the cribriform plate secondary to head trauma. The ears should be examined for serous otitis media, indicating the possibility of a nasopharyngeal mass or inflammation. A nasopharyngeal mass may also be protruding into the oral cavity. Palpation for masses in the neck and thyromegaly is also important. The neurologic examination should include cerebral func-



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tion, cranial nerves and cerebellar function. When forming a differential diagnosis, clinicians should consider memory impairment, motor findings and cranial nerve dysfunctions.

Laboratory workup: Laboratory workup may include evaluation for allergies, nutritional deficiencies, malignancy or systemic disease, such as diabetes or hypothyroidism. Lab tests should be guided by the history and physical exam and not be conducted randomly.

Medical Imaging: Medical imaging can be useful, but should be reserved for specific indications. Computed tomography (CT) is ideal for investigations of sinus and nasal disease. It provides imaging of the nasal and sinus cavities, skull base and olfactory cleft. CT scans can provide detailed information on mucosal disease, structural abnormalities and the presence of sinusitis or a neoplastic process. Magnetic resonance imaging (MRI) is superior to CT to discriminate soft tissue, but an MRI is less sensitive to bone abnormalities or landmarks.⁶ MRI is the radiologic study of choice to evaluate olfactory bulbs and tracts, as well as intracranial causes of olfactory dysfunction.

The UPSIT Test: While several different tests of olfactory dysfunction are commercially available, the most widely used quantitative clinical test is the University of Pennsylvania Smell Identification Test (UPSIT). Quantitative testing of olfactory function is essential to establish the validity of a patient's complaint, characterize the specific nature and severity of the problem, and monitor any changes over time.⁶ The UPSIT test consists of four booklets containing 10 microencapsulated odors in a "scratch-and-sniff" format. There are four response alternatives accompanying each odor. The patient is asked to identify (or guess) each smell. The test can be self-administered in the waiting room or in the patient's home, and can be scored in less than a minute by non-medical personnel. Scores are compared to varying patient groups and compared against sex- and age-related norms. The patient's score is then classified into one of these categories: normosmia, hyposmia, anosmia and probable malingering-

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- ACTONEL was effective regardless of underlying disease, age, gender, glucocorticoid dose, or baseline BMD⁵

* Patients who had recently initiated or been on longer-term glucocorticoid therapy

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Table 1: Olfactory Dysfunction: selected etiologies

Class	Conductive disorder	Sensorineural disorder
Inflammatory	Bacterial rhinosinusitis Allergic rhinitis Vasomotor rhinitis Fungal rhinosinusitis Chronic inflammatory rhinitis (syphilis, tuberculosis, sarcoidosis, leprosy, Wegener's granulomatosis) Nasal polyposis Rhinitis medicamentosa Sjogren's syndrome/itis	Bacterial rhinosinusitis Allergic rhinitis Vasomotor rhinitis Fungal rhinosinusitis Chronic inflammatory rhinitis (syphilis, tuberculosis, sarcoidosis, leprosy, Wegener's granulomatosis) Nasal polyposis Postviral upper respiratory tract infection Cerebral abscess
Trauma	Mucosal edema Foreign body Nasal surgery Nasal septal deformity Laryngectomy	Closed head trauma, postsurgical (nasal surgery, skull base)
Congenital-developmental	Choanal atresia Vestibular stenosis Adenoid hypertrophy Cyst	Absence of neuroepithelium (agenesis, intrauterine or postnatal infection) Kallman's syndrome Turner's syndrome
Degenerative-Toxic	Atrophic rhinitis	Atherosclerotic cerebral vascular disease Alzheimer's Disease Parkinson's Disease Huntington's chorea Multiple Sclerosis Age Chemical toxins Drugs Ionizing radiation
Endocrine-metabolic	Pregnancy (rhinitis)	Diabetes Adrenal cortical insufficiency Cushing's syndrome Pseudohypoparathyroidism Hypothyroidism Vitamin deficiency (Vitamin A, B complex) Renal failure Cirrhosis of the liver
Neoplasia	Benign (papilloma, angiofibroma, osteoma, schwannoma) Malignant (squamous cell carcinoma, adenocarcinoma, metastasis) Tumors of the nasopharynx with extension	Benign (papilloma, meningioma, craniopharyngioma, glioma) Malignant (leukemia, ethesioneuroblastoma, metastasis) Temporal lobe tumors

Adapted from: Feldman JL, Wright HN, Leopold DA: The initial evaluation of dysosmia. *Am J Otolaryngol* 1986; 4:431-44.
Doty RL, Bartoshuk LM, Snow, JB Jr: Causes of Olfactory and Gustatory Disorders, In: *Smell and Taste in Health and Disease*. TV Getchell, et al. (eds.): Raven Press, New York, 1991.

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ing. Probable malingering is suspected in patients who score much lower on the test than expected by chance. The UPSIT test is very popular because of the high test/retest reliability, ease of administration and simplicity of taking the test.

How is it treated?

Unfortunately, treatment of olfactory disorders remains disappointing. Management of olfactory disorders depends entirely on the accurate diagnosis of the cause because therapy is dictated by the pathologic condition. Conductive disorders are most amenable to treatment, while sensorineural disorders remain challenging. The most common cause of anosmia or hyposmia is nasal or sinus disease. Aggressive treatment in these cases provides a good chance of improvement. Examples of treatment include allergic management, antibiotics, and topical and systemic corticosteroid therapies. Patients with polyps or sinus disease who are resistant to medical therapy can benefit from surgery to improve conductive defects. In cases where intranasal tumors are the cause of the problem, delicate surgical removal can sometimes restore olfactory function. Surgery is an option if the integrity of the olfactory epithelium remains intact.

Sensorineural olfactory defects have specific treatments as well, but the cases of these defects are fewer and treatment is less successful. If the cause of olfactory impairment is related to a particular toxin, the toxin should be eliminated. The degree of olfactory damage depends on the actual toxicity of the agent, and the length and frequency of exposure. No treatment exists once the damage has taken place. Some medications have olfactory dysfunction as a side effect. These medications should be discontinued and, in most cases, the olfactory ability returns to normal. Endocrine disturbances should be addressed, and nutritional deficiencies should be corrected. Some cases of olfactory disturbance caused by intracranial tumors may be reversible, if they are the result of simple compression of the olfactory pathway or cortex.⁷ For the most part, viral processes that damage the olfactory neuroepithelium have no specific remedies. Some patients will regain function, while others will be permanently impaired.

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The most common gastrointestinal adverse events for ACTONEL versus placebo were abdominal pain (11.8%/9.5%), dyspepsia (10.4%/10.5%), and gastritis (2.6%/2.4%).

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In patients where effective therapy is limited, counselling plays an important part in treatment. Patients need adapting strategies for dealing with fire detection, natural gas leaks and food spoilage. They also need tools to help them maximize the taste of food and improve their quality of life.

Conclusion

Smell disorders are common in the general population. Aside from having a substantial impact on quality of life, olfactory dysfunction may signal other medical conditions. Patients need to be properly assessed and the etiology and anatomical location of their disorder should be determined, when possible. A solid knowledge of anatomy, physiology and pathology of an organ system, coupled with the appropriate clinical evaluation and workup, should guide the clinician to reach an accurate diagnosis and proceed with appropriate management. **Dx**



References

1. Mattes RD: Physiologic responses to sensory stimulation by food: nutritional implications. *J Am Diet Assoc* 1997; 97:406-13.
2. Doty RL, Kobal G: Current trends in the measurement of olfactory function. In: Doty RL (ed.): *Handbook of Olfaction and Gustation*. Marcel Dekker, New York, 1995, pp. 191-225.
3. Doty RL, Snow JB Jr: Olfaction. In: Goldman J (ed.): *The Principles and Practice of Rhinology*. John Wiley, New York, 1997, p. 761.
4. Deems DA, Doty RL, Settle RG, et al: Smell and taste disorders: A study of 750 patients from the University of Pennsylvania Smell and Taste Center. *Arch Otolaryngol Head Neck Surg* 1991; 117:519-528.
5. Bromley SM: Smell and Taste disorders: A primary care approach. *Am Fam Physician* 2000; 61:427-36,438.
6. Goetz: *Textbook of Clinical Neurology*, First Edition. W. B. Saunders Company, 1999.
7. Ishimaru T: Reversible hyposmia caused by intracranial tumour. *J Laryngol Otol* 1999; 113(8):750-3.
8. Jafek BW, Hartman D, Eller PM, et al: Postviral olfactory dysfunction. *Am J Rhinology*. 1990; 4:91-100.
9. Duncan HJ, Seiden AM: Long-term follow-up of olfactory loss secondary to head trauma and upper respiratory tract infection. *Arch Otolaryngol Head Neck Surg* 1995; 121:1183-1187.
10. Hummel T: Perspectives in olfactory loss following viral infections of the upper respiratory tract. *Arch Otolaryngol Head Neck Surg* 2000; 126:802-803.
11. Costanzo RM, Zasler ND: Head Trauma. In: Getchell TV, Doty RL, Bartoshuk LM, Snow JB Jr (eds.): *Smell and Taste in Health and Disease*. Raven Press, New York, 1991, pp. 711-730.
12. Costanzo RM, Becker DP: Smell and Taste disorders in head injury and neurosurgery patients. In: Meiselman HL, Rivlin RS (eds.): *Clinical measurement of Taste and Smell*. Macmillan Publishing Co Inc., New York, 1986, pp. 565-78.

Suggested Readings

1. Miwa T, Furukawa M: Impact of olfactory impairment on quality of life and disability. *Arch Otolaryngol Head Neck Surg* 2001; 127:497-503.
2. Leopold D: Physiology of Olfaction. In: Cummings CW: *Otolaryngology Head and Neck Surgery*. 1998, pp. 770-798.
3. Shipley M, Reyes P: Anatomy of the human olfactory bulb and central olfactory pathways. In Laing DG, Doty RL, Breipohl W (eds): *The Human Sense of Smell*. Berlin, Springer-Verlag, 1991, pp 29-60.
4. Kern RC: Chronic sinusitis and anosmia: Pathologic changes in olfactory mucosa. *Laryngoscope* 2000; July:110.
5. Kern RC, Foster JD, Pitovski DZ. Glucocorticoid (type II) receptors in the olfactory mucosa of the guinea pig: RU 28362. *Chem sens* 1997;22:313-319.
6. Apter AJ, Gent JF, Frank ME: Fluctuating Olfactory sensitivity and distorted odor perception in allergic rhinitis. *Arch Otolaryngol Head and Neck Surg* 1999; 125:1005-1010.
7. Seiden AM, Duncan HJ, Smith DV: Office management of taste and smell disorders. *Otolaryngol Clin North Am*. 1992; 25:817-835.



13. Kern RC, Quinn B, Rosseau G, Farbman AI: Post-traumatic olfactory dysfunction. *Laryngoscope* 2000; 110: 2106-09.
14. Doty RL, Shaman P, Applebaum SL, et al: Smell identification ability: Changes with age. *Science* 1984; 226:1441-43.