
Anosmia: A Clinic Based Review

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Abstract

Anosmia and hyposmia, the inability or decreased ability to smell, is estimated to afflict 3–20% of the population. Risk of olfactory dysfunction increases with old age and may also result from chronic sinonasal diseases, severe head trauma, and upper respiratory infections, or neurodegenerative diseases. These disorders impair the ability to sense warning odors in foods and the environment, as well as hinder the quality of life related to social interactions, eating, and feelings of well-being. This article reports and extends on a clinical update commencing at the 2016 Association for Chemoreception Sciences annual meeting. Included were reports from: a patient perspective on losing the sense of smell with information on Fifth Sense, a nonprofit advocacy organization for patients with olfactory disorders; an otolaryngologist's review of clinical evaluation, diagnosis, and management/treatment of anosmia; and researchers' review of recent advances in potential anosmia treatments from fundamental science, in animal, cellular, or genetic models. As limited evidence-based treatments exist for anosmia, dissemination of information on anosmia-related health risks is needed. This could include feasible and useful screening measures for olfactory dysfunction, appropriate clinical evaluation, and patient counseling to avoid harm as well as manage health and quality of life with anosmia.

Keywords: genetics, neural reorganization, olfactory dysfunction, quality of life, stem cell regeneration, treatment

Introduction

Smell accounts for 95% to 99% of chemosensation; while, taste accounts for the rest of chemosensation. Anosmia is the inability to perceive smell/odor. It can be temporary or permanent and acquired or congenital. There are many causes. For example, any mechanical blockage preventing odors from reaching the olfactory nerves can cause a loss of sense of smell. This blockage can be due to inflammatory processes like simple infections causing mucus plugs or nasal polyps.

Neurological causes can include disturbances to the sensory nerves that make up the olfactory bulb or

anywhere along the path in which the signal of smell is transferred to the brain. To better understand this process, it is helpful to understand how people can perceive smell.

When a particle with odorant molecules in the air is present, it travels up through the nasal canals to the nasal cavity, where olfactory receptor neurons extend from the olfactory bulb that sits on the cribriform plate of the brain. Each nasal cavity contains about 5 million receptor cells or neurons. There are 500 to 1000 different odor-binding proteins on the surface of these olfactory receptor cells. Each olfactory receptor cell expresses only one type of binding protein.

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These afferent olfactory neurons (cranial nerve I) facilitates the transfer of a chemical signal (particles in the air) to an electrical signal (sensed by afferent receptor neurons) which is then transferred and ultimately perceived by the brain. From the olfactory bulb, the signal is further processed by several other structures of the brain, including the piriform cortex, entorhinal cortex, amygdala, and hippocampus. Any blockage or destruction of the pathway along which smell is transferred and processed may result in anosmia.¹

Etiology

As stated in the introduction, any problems that cause a disturbance in the pathway that leads to the perception of smell, whether mechanical or along the olfactory neural pathway can lead to anosmia.

Inflammatory and Obstructive Disorders (50% to 70% of cases of anosmia)²

These are the most common causes of anosmia, and these include nasal and paranasal sinus disease (rhino-sinusitis, rhinitis, and nasal polyps). These disorders cause anosmia through inflammation of the mucosa as well as through direct obstruction.

Head Trauma

Head trauma is another common cause of anosmia as trauma to the head can cause damage to the nose or sinuses leading to a mechanical blockage and obstruction. Other ways an injury can cause anosmia is by trauma or destruction to the olfactory axons that are present at the cribriform plate, damage to the olfactory bulb, or direct injury to the olfactory areas of the cerebral cortex. The central (CNS) nervous system trauma leading to anosmia can be temporary or permanent depending on the area and extent of the injury. Olfactory neurons have regenerative capabilities that other CNS nerves in the body do not. This unique ability is the center of much current stem cell-related research.

Aging and Neurodegenerative Processes³

These processes are associated with the loss of smell that can eventually result in anosmia. Normal aging is associated with decreased sensitivity to smell. As individuals age, they lose the number of

cells in the olfactory bulb as well as the olfactory epithelium surface area which is important in sensing smell. Interestingly, there have been studies that associate the impairment of the ability to smell with neurodegenerative disorders such as Alzheimer disease, Parkinson disease, and Lewy Body dementia. Studies linked low ability to perceive smell associated with increased risk of development of neurodegenerative diseases. The highest association is between anosmia and later development of alpha-synucleinopathy including Parkinson disease, diffuse Lewy body disease, and multisystem atrophy.

Congenital Conditions

Congenital conditions that are associated with anosmia include Kallmann syndrome and Turner syndrome.

Infective Conditions⁴

Anosmia is said to be one of the early symptoms of COVID-19 infection.

Other Traumatic or Obstructive Conditions

Other causes of anosmia include *toxic agents* such as tobacco, drugs, and vapors that can cause olfactory dysfunction, post-viral olfactory dysfunction, facial traumas involving nasal or sinus deformity, *neoplasms* in nasal cavity or brain that prohibits the olfactory signal pathway, and subarachnoid hemorrhages. Olfactory groove meningioma can present with slowly worsening impaired olfaction.

Common conditions that can uncommonly cause a decreased sense of smell or anosmia include *diabetes mellitus* and *hypothyroidism*.

Medications can sometimes lead to olfactory defects as an unwanted side effect. These medications include beta-blockers, anti-thyroid drugs, dihydropyridine, ACE inhibitors, and intranasal zinc.

Epidemiology⁵

Anosmia afflicts 3% of the adult population older than the age of 40. The prevalence of impaired olfaction increases with age. In 2016, the National Health and Nutrition Examination Survey (NHANES) measured olfactory dysfunction which involved 1818 participants. Data showed that olfactory dysfunction

was 4% at age 40 to 49 years of age, 10% at 50 to 59, 13% at 60 to 69, 25% at 70 to 79, and 39% for those over 80 years of age. Anosmia affected 14% to 22% of those over 60 years of age.

History and Physical

When taking a history of the possible causes of anosmia, it is important a clinician keep the possible etiologies (listed above) in mind when asking relevant questions.

Sudden smell loss is often associated with head injuries or viral infections, while a gradual loss is more associated with allergic rhinitis, nasal polyps, and neoplasms. An intermittent loss is often common in allergic rhinitis and with the use of topical drugs.

It is important to ask about preceding events and the patient's medical history, as the most common causes of anosmia are chronic rhinitis and head trauma.

The patient's age can be helpful because if the patient is very young and has other symptoms, the clinician might investigate congenital causes such as Kallmann syndrome. Under such circumstances, careful examination of the gonads and neurological exams are very important. If the patient is elderly, the clinician may investigate whether the sense of smell is due to normal aging or if there are other symptoms to suggest an early stage of a neurodegenerative disorder like Parkinson disease.

Social history is also important in assessing occupation-associated exposures to toxins or allergens that can lead to anosmia. Medication history is always important, and sometimes the causal relationship can only be established by stopping the suspected offending agent.

Clinicians should pay attention to associated symptoms as anosmia is a symptom and not a diagnosis. Headaches and behavior disturbances may indicate problems with the CNS.

During the physical examination, clinicians should closely examine the nasal cavity and paranasal sinuses. Findings may be important depending on information retrieved from the patient's history.

A neurological examination may be useful in

revealing other neurological deficits that can suggest a larger neurological problem causing the loss of smell. Fundoscopy for evidence of raised intracranial pressure will help to pave the way for neuroimaging testing.

Examination and skin testing by an allergist might play an important role to evaluate whether rhinitis (if the cause) is allergic or non-allergic.

Evaluation

Simple office testing of smell with chocolates or coffee is sometimes conducted informally by a primary care provider. This test is subjective. If the clinician is concerned about any findings, detailed smell testing can be conducted at the smell centers. Tests include chemosensory testing, butanol threshold test, among others. These formal tests can give a more accurate level of "loss of smell" in that a minimum concentration of a chemical at which the patient can detect can be given and compared to the average threshold for that patient's age group. UPSIT, the University of Pennsylvania Small Identification Test is the most widely used odor identification test which can be administered in about 10 minutes.⁶

Other evaluations can be performed depending on the clinician's suspicion of the underlying cause of the patient's anosmia. Based on the history and physical examination, if the clinician is suspicious of head trauma, sinus disease, or neoplasm, they may order a magnetic resonance imaging (MRI) or computed tomogram (CT).

If there is concern about allergic rhinitis, a referral to an allergist and subsequent allergen skin testing might be revealing. If the patient has other symptoms that are suggestive of diseases that are inflammatory, a sedimentation rate might be helpful. Other labs that can be considered depending on the suspected etiology include complete blood count (CBC), plasma creatinine, liver function, thyroid profile, ANA, measurements of heavy metal, lead, and other toxins.

It is important to note that imaging (MRI) in those with idiopathic olfactory loss is often unrevealing. In olfactory loss, MRI was used to evaluate idiopathic olfactory loss 55% of the time, but only successfully found an imaging abnormality that would explain the loss in 0.8% of the time.

Treatment / Management⁷

The treatment and management depend on the etiology as anosmia is not a diagnosis but a symptom.

As stated above, inflammatory and obstructive diseases are the most common cause of anosmia (para-nasal and nasal sinus diseases), intranasal glucocorticoids can often manage these causes. Other medications that can be given include antihistamines and systemic glucocorticoids. Antibiotics such as ampicillin can be prescribed for bacterial sinus infections. Surgery can be an option for those with chronic sinus problems and nasal polyps that fail conservative medical management.

For all causes of anosmia, treatment and management depend on the treatment and management of the underlying disease and whether that disease is refractory to medical intervention.

Differential Diagnosis⁸

- Hyposmia - Reduced ability to smell
- Parosmia - An altered perception of an odor after stimulus presentation
- Phantosmia - Perception of odors without a stimulus

Prognosis⁹

For olfactory impairment caused by damage to the olfactory neurons due to trauma, there is no specific treatment. However, olfactory neurons do have the ability to regenerate. But the time and degree of regeneration depend on the extent of damage, and there is a difference in regenerative abilities between individuals. Regeneration can span over the course of days to years, and complete recovery is not a guarantee.

Complications

Anosmia by itself is unlikely to cause any complications. The inability to identify harmful smells can be life-threatening. Also, the ability to enjoy the taste of food properly may also be affected if there is anosmia.

Deterrence and Patient Education

Anosmia amongst patients can have safety

implications as those without the ability to smell might miss important warning odors such as smoke from a fire or natural gas leaks.

Pearls and Other Issues

In the evaluation of anosmia without an initial clear cause (sinus disease/head trauma), it is important to assess for other neurological deficits as to not miss a central nervous system hemorrhage, aneurysm, or neoplasm.

Enhancing Healthcare Team Outcomes

Because of the diverse cause of anosmia, an interprofessional team should be involved that includes an internist, endocrinologist, neurologist, ENT surgeon, a rheumatologist, and an infectious disease specialist. Anosmia is a symptom of a disease process, which needs to be treated. Inflammatory and obstructive diseases are the most common cause of anosmia (para-nasal and nasal sinus diseases). Surgery can be an option for those with chronic sinus problems and nasal polyps that fail conservative medical management. For olfactory impairment caused by damage to the olfactory neurons due to trauma, there is no specific treatment. However, olfactory neurons do have the ability to regenerate. Regeneration can span over the course of days to years, and complete recovery is not a guarantee. The overall prognosis for patients with anosmia is good as long as the primary condition has a cure or can be treated.

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