

## Anosmia:

an evidence-based approach to diagnosis and management in primary care

### INTRODUCTION

Anosmia is a relatively common presentation. The number of patients with smell disturbance is expected to increase over the next few months to years given its association with COVID-19 infection.<sup>1</sup> Prior to the COVID-19 pandemic the point prevalence was 19.1%, including both complete and partial loss of smell.<sup>2</sup> With a wide-ranging differential diagnosis, disturbance in smell can affect patients of all ages. The condition is significantly more common in advancing age, with around half of the population reporting disturbance in olfaction between 65 and 80 years, and even larger numbers >80 years.<sup>3,4</sup>

As one of our five key senses, disturbances in smell have a profound effect on patients' quality of life, with strong associations with mental health disease.<sup>5</sup> Smell is essential for protecting against dangers of day-to-day life, including smelling gas leaks and identifying spoiled food. Despite this, the condition is poorly understood and often dismissed as a symptom in both primary and secondary care. This may be as it is often accompanied by other, more well-understood conditions such as nasal blockage, or if it presents in isolation is thought to be a non-sinister symptom. Box 1 includes a list of definitions for anosmia and related conditions.

### THE OLFATORY PATHWAY

A basic understanding of the olfactory pathway will be reviewed to aid the understanding of smell perception. Disturbances at any of the points along this pathway can lead to a loss or alteration in smell.

Smell is the detection of environmental organic molecules at the olfactory cleft.<sup>5</sup> These stimuli are detected on the olfactory neuroepithelium. This is a small area of the nasal mucosa (approximately 2 cm<sup>2</sup>) located superomedially in the nasal cavity around the cribriform plate.<sup>4,5</sup> In order for an odorant to be detected, it has to pass uninhibited into the nasal cavity. It must then reach this

area without being obstructed by changes in the intranasal anatomy, for example, inflamed mucosa, nasal polyps, and so on. Another important route for stimuli to reach the olfactory neuroepithelium is by retrograde airflow during swallowing. In this process the stimuli are passed via the nasopharynx on swallowing a food bolus and reach the olfactory epithelium in a retrograde path. This, combined with sensory input from taste and touch, provides flavour to food. In fact, the majority of patients who complain of a reduced sense of taste are actually reporting an unrecognised reduction or loss of smell.<sup>6</sup>

Once the stimulus is detected by the olfactory neuroepithelium, an impulse is passed to the olfactory bulb on the cribriform plate. Neurons pass from here, underneath the frontal lobe, and relay information to the thalamus, hypothalamus, and frontal cortex. This explains the complex associations of smell with memories and emotions.<sup>5</sup>

The majority of smell sensation is transmitted via cranial nerve I (olfactory) with a small proportion (somatosensory sensations such as burning, cooling, and irritation) being detected by cranial nerve V (trigeminal) and triggering a protective response such as causing increased secretions.<sup>5</sup> This explains how some people lose their sense of smell but can still be sensitive to irritant odorants (for example, sulphur, ammonia, alcohol).<sup>5</sup>

### Box 1. Definitions

Anosmia	No perceivable sense of smell
Hyposmia	Reduced sense of smell
Cacosmia/parosmia	Distorted or unpleasant sense of smell
Phantosmia	Smell perception in the absence of a stimulus

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## Box 2. Causes of olfactory disturbance

Conductive	Sensorineural
Chronic rhinosinusitis	Viral/post-viral (including COVID-19)
Nasal polyps	Head trauma
Allergic rhinitis	Medication related (for example, ACE inhibitors, diuretics, calcium channel blockers, statins, tobacco. Alcohol and illicit drug (especially cocaine) abuse
Gross septal deviation	Neurological (temporal lobe epilepsy, multiple sclerosis, cerebrovascular disease)
Intranasal tumours	Neurodegenerative disease (for example, Parkinson's and Alzheimer's)
Granulomatous disease of the nose	Space-occupying lesion (that is, anterior cranial fossa tumours)
Iatrogenic (for example, nasal surgery and laryngectomy)	Congenital (for example, Kallmann's)

### EVALUATION OF OLFACTORY DYSFUNCTION

#### History

In all patients presenting with olfactory dysfunction, a thorough history should include:

- duration of symptoms;
- taste disturbance;
- nasal discharge (mucous, purulent, cerebrospinal fluid);
- preceding events (head trauma, recent upper respiratory tract infection/viral symptoms);
- previous sinonasal surgery;
- use of recreational drugs (including alcohol and tobacco);
- current medication review;
- chronic medical conditions (especially diabetes, renal or hepatic dysfunction, Alzheimer's disease, and Parkinson's);
- rhinological symptoms (facial pain/pressure, epistaxis, nasal obstruction); and
- neurological symptoms (headaches, seizures, and so on).

#### Examination

Examination may reveal potential causes for the olfactory disturbance but in general practice this will be more limited because of the lack of endoscopes and the increased use of remote consultations. It is worth noting that examinations are frequently negative and therefore a good history is paramount. A general examination can be undertaken of the external nose for signs of trauma and gross nasal deformity as well as examination of the entry to the nasal cavity, which may reveal nasal discharge, deviated nasal septum, large nasal polyps or masses, foreign bodies, or signs of overt

rhinitis. A neurological examination should be guided by the history. In general, a cranial nerve examination focusing on the optic nerve, trigeminal nerve, and facial nerve is useful. The optic disc can be examined for signs of raised intracranial pressure. Memory assessment and examination for signs of Parkinson's disease may be required if suggested by the history.<sup>5</sup>

More detailed quantitative assessment of the sense of smell can be done with standardised smell identification tests. These are generally only carried out in dedicated smell clinics within secondary care because of the resources required to undertake them.<sup>7</sup>

### DIFFERENTIAL DIAGNOSES

In the same way that we are all familiar with categorising hearing loss, disturbance to smell can also be considered to be either conductive (there is a physical barrier preventing the stimulus reaching the olfactory neuroepithelium) or sensorineural (failure of the neurological pathway). The common causes, as well as causes that are less common but should not be missed, are listed in Box 2.<sup>4,5,8</sup> This is clearly not an exhaustive list, but covers the vast majority of causes for olfactory disturbance seen in primary care.

#### Conductive loss

Building on the knowledge of the olfactory pathway, any physical barrier to the odorant accessing the small area of olfactory neuroepithelium can cause a permanent, temporary, or fluctuating alteration in the sense of smell. Diseases causing congestion and inflammation of the nasal mucosa, such as chronic rhinosinusitis and allergic rhinitis, can obstruct this pathway. Nasal polyps obstructing the olfactory cleft can cause a physical barrier. On simple anterior rhinoscopy, small polyps blocking the olfactory epithelium may not be identified.<sup>9</sup> A loss of sense of smell from a deviated septum is uncommon but gross deviations could lead to a reduced sense of smell. Other physical barriers to the passage of stimuli through the nasal cavity include intranasal tumours and destructive lesions for granulomatous diseases, such as granulomatosis with polyangiitis.<sup>4</sup> These should usually be suspected by the presence of red flags for intranasal pathology (Box 3).<sup>1,4,5,10</sup> Endoscopic sinus surgery, especially extended skull base surgery, may cause an iatrogenic loss of sense of smell, due to damage of the olfactory mucosa intraoperatively.<sup>11</sup> Diversion of the upper respiratory tract following operations such

## Box 3. Red-flag symptoms

Unilateral nasal symptoms
Bleeding
Crusting/scabbing within the nasal cavity
Cacosmia (perceived malodorous smell)
Orbital symptoms (swelling, visual symptoms, or ophthalmoplegia)
Severe frontal headaches
Frontal swelling
New neurological/meningitic symptoms

as total laryngectomy will bypass the nasal cavity so will inevitably be associated with loss of smell.

### **Sensorineural loss**

Damage to the olfactory pathway at any point from the olfactory neurons to the cortex will cause a sensorineural loss. There are a vast array of pathologies that could affect this pathway. The most common cause of olfactory dysfunction (along with rhinosinusitis) is head injury.<sup>12</sup> Up to 30% of patients who sustain a significant head injury report olfactory dysfunction.<sup>13</sup> Shearing of the olfactory neurons as they pass through the cribriform plate into the nasal cavity, as well as haematomas and contusions, can all be responsible for olfactory loss.<sup>4,13</sup>

The next most common causes of changes to olfaction are post-viral losses. These usually present following a recent upper respiratory tract infection. This is of particular relevance currently as a presenting symptom of COVID-19 infection, where a recent meta-analysis suggests around 55% of patients may present with anosmia.<sup>1</sup> Preceding upper respiratory tract infections are reported in 20–30% of patients with olfactory dysfunction.<sup>4</sup>

Olfactory dysfunction associated with medication use is widely reported in the literature.<sup>5</sup> It is listed as a side effect in a wide array of medications but is particularly associated with antihypertensives and statins.<sup>4</sup> Cigarette smoking is also a well-recognised irritant to the olfactory system.

A large number of neurological conditions can cause disturbances in the sense of smell, including epilepsy (particularly temporal lobe epilepsy), multiple sclerosis, and previous strokes. Anosmia has also been reported as a presenting symptom in neurodegenerative disorders such as Parkinson's and Alzheimer's disease.<sup>14</sup> Finally, intracranial tumours can also disrupt the olfactory pathway. This is particularly true of anterior cranial fossa tumours, meningiomas, and frontal lobe lesions.<sup>5</sup> In the presence of neurological symptoms, or findings of raised intracranial pressure, these should be excluded as a priority.

### **MANAGEMENT**

A large proportion of patients with olfactory dysfunction can be managed in primary care. The indications for referral to secondary care include patients with any 'red flag' symptoms or >6 weeks of olfactory dysfunction.<sup>10</sup> This differs if the symptoms coincide with symptoms of COVID-19 infection. In this case, referral

should be made after 3 months to allow spontaneous resolution.<sup>10</sup> In addition, where a patient has an atypical presentation or has not responded to initial treatment, this would be an indication for referral to secondary care.

Treatment should be targeted at the primary pathology. In primary care the majority of this is related to a primary nasal pathology (chronic rhinosinusitis, allergic rhinitis, acute sinusitis, and so on). Added to disease-specific treatments, intranasal corticosteroids are the mainstay of treatment for these patients.<sup>4,5,14,15</sup> The latest recommendations state that, in cases of anosmia persisting for >2 weeks, a trial of intranasal corticosteroids should be instigated.<sup>10</sup> This can be augmented by a course of more potent steroid drops and nasal saline douching at the clinician's discretion. Oral corticosteroids have been shown to have a positive effect on smell in chronic rhinosinusitis, as well as to some degree in post-viral anosmia (although the evidence is less strong in this case).<sup>4,15</sup> The recommendations for management of COVID-19-associated anosmia is to consider a short course of high-dose oral steroids after 2 weeks for persistent symptoms, following resolution of other symptoms related to COVID-19.<sup>10</sup>

If no cause is identified and the anosmia is thought to be idiopathic or post-viral, there have been suggestions of various different dietary supplements. These include zinc, alpha lipoic acid, vitamin a, and omega 3.<sup>5,10</sup> The evidence for their efficacy is poor and does not support their use.<sup>5,10</sup> A consensus statement from ENT UK suggests the optional use of Omega 3.<sup>10</sup>

Imaging will generally be considered in secondary care and will be dictated by the suspected cause. For example, a CT scan may be undertaken for conductive causes such as nasal polyps. In cases where no cause can be identified, or a sensorineural cause is considered, Magnetic resonance imaging (MRI) may be undertaken to exclude intracranial pathologies such as anterior cranial fossa tumours or demyelinating conditions.<sup>5</sup>

If no surgical treatment is required and medical management has failed, referral to a dedicated smell clinic for olfactory retraining is possible. The results from these clinics are encouraging, especially in post-infective losses.<sup>5</sup> Half of patients with anosmia have concurrent mental health concerns, with feelings of isolation, depression, and difficulties in relationships.<sup>4</sup> It is therefore important to remember to take a holistic approach to these patients

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and address mood issues during the consultation and follow-up. Our sense of smell is also required as a warning system to protect against dangers such as gas leaks and spoilt food. It is therefore worth discussing these things with patients and stressing the importance of fire alarms, carbon monoxide monitors, and checking food expiry dates.

## PROGNOSIS

The prognosis from new-onset anosmia depends on the underlying cause. The outcomes are better for those with hyposmia rather than anosmia.<sup>5</sup> When there is a specific underlying medical trigger then cessation of that trigger often leads to good recovery (that is, smoking and medications).<sup>5</sup> Around 30% of patients with traumatic olfactory dysfunction can expect recovery, with the majority within 12 weeks.<sup>5</sup>

Post-viral anosmia has a wider range of recovery, estimated to be between 35% and 67%.<sup>4</sup> It is worth noting that COVID-19-related losses currently are reported to significantly improve within 4 weeks in 90% of patients.<sup>1</sup>

## CONCLUSION

Disturbances in smell have a wide variety of aetiologies. A thorough history is key to achieving a correct diagnosis. It is also key to address the holistic needs of the patient and discuss specific safety measures to be aware of.

There are dedicated websites, support groups, and charities that offer a wealth of information for patients with anosmia, and they should be signposted to the patient to help involve them in their own management (for example, Fifth Sense, AbScent, and ENT UK).

## Provenance

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