Olfaction and Olfactory Dysfunction

An intact sense of smell enables important environmental and social functions:
Provides information regarding:

- Safety of a substance for example spoiled foodstuff.
- Safety of environment such as leaking liquified petroleum gas (LPG itself has no smell, but mercaptan, an odourant is added to it for safety) or smoke of a fire.
- Aethetic properties of objects such as a rose or dirty laundry.
- Essential communication cues for example a mother and infant.

It aids digestion of food by triggering normal gastrointestinal secretions.
Loss or dysfunction leads to reduced quality of life, impacting livelihood (e.g. food critic, firefighter, wine merchant), psychological wellbeing and longevity. Mortality risk in non-demented older persons is 2.5 times higher in those with low odour identification test scores vs high odour test scores.

Anatomy & Physiology

- Human nose has 2 independent nasal passages – serve respiratory and olfactory functions.
- Warm / humidify / filter pathogens / pollutants.
- Olfactory neuroepithelium covers the upper septum, middle and superior turbinates.
- Only 10-15% of the nasal airstream reaches this olfactory mucosa.
- Retronasal airflow from the nasopharynx occurs during swallowing → this stimulates olfactory receptors adding 'smell' to taste.
- Odourants enter the nose in a gas phase and must pass through the olfactory cleft.
- Odourants then dissolve in the mucous of the olfactory epithelium.
- Mucous provides:
    - Moist/protective environment for olfactory neuroepithelium
    - Aids spread (diffusion) of odourants to olfactory receptors

Olfactory neuroepithelium:

- Pseudostratified columnar epithelium with highly vascularised lamina propria
- 6 classes of cells
    - Bipolar sensory receptor neuron – extends odourant receptor-containing cilia into the mucous
    - Supporting cell – regulates mucous production, degrades odourants
    - Duct cell of Bowman's glands – secretes most mucous in the olfactory region
    - Microvillar cell – sends tufts of microvilli into nasal mucous
    - Dark basal cells – stem cell
    - Light (globose) basal cells – multipotent basal cell that can give rise to neurons and non-neuronal tissue
- Olfactory receptors reflect the expression of about 1000 genes (1% of all expressed genes, giving an idea of its importance)
- 6 million receptors coalesce into 30-50 fascicles forming olfactory fila
- Olfactory fila cross the cribriform plate and pia mater and synapse with 2nd order neurons in the glomeruli of the olfactory bulb
- Neurotransmitters – Glutamate is excitatory, and dopamine is a modulator

- For the chemical energy of odourant-receptor binding to be transduced into a neural signal (electrical energy) the activation of G-proteins and several 2nd messenger enzymes is required

Olfactory Dysfunction

Definitions:

- Hyposmia – reduced sense of smell
- Anosmia – no sense of smell
- Hyperosmia – heightened response to an odour (not increased ability to smell)
- (e.g. pregnancy, Addison's disease, head trauma, migraine)
- Dysosmia – altered perception of smell
    - intact olfactory system, at least in part, compared to anosmia
    - E.g Cacosmia – perception of a normal smell as foul or malodourous, consider cancer or granulomatous nasal disease although most causes of smell disturbance may result in cacosmia

History:

- Onset
    - Acute (viral upper respiratory tract infection is the most common cause for permanent olfactory loss)
    - Sudden (head trauma / prior surgery) – injury to olfactory tract or cortex
    - Chronic (nasal / sinus disease e.g. allergic rhinitis / chronic rhinosinusitis)
    - Progressive (Sinonasal tumours / neurodegenerative diseases – e.g. Alzheimer's / Parkinson's disease / Multiple Sclerosis)

Olfactory dysfunction may be the first sign of Alzheimer's disease (AD) and idiopathic Parkinson's disease (PD) and can be used in diagnosis and prognostication. The University of Pennsylvania Smell Identification Test (UPSIT) score has a better predictive value than any cognitive testing for predicting PD and AD development.

- Sinonasal cause – Look for other symptoms:
    - Nasal obstruction / congestion
    - Rhinorrhoea (watery = cerebrospinal fluid leak [CSF]; mucoid = chronic rhinosinusitis)

- Red flags
    - Cacosmia
    - Pain
    - Cranial nerve fallout / other focal neurology
    - Clear rhinorrhoea (CSF leak)
    - Epistaxis

Examination:

- Features of skull base fracture – raccoon eyes / battle sign / reduced GCS / CSF leak / Cranial nerve deficit / Long tract signs
- Eyes / Nasal framework / skin / V2 changes – ?Cancer
- Anterior rhinoscopy – mucopus / crusting / inflamed mucosa / large inferior turbinates / polyps / masses

Investigation:

- Sniffen sticks (pen-like device used to assess odor threshold, discrimination and identification)
- ENT referral for nasal endoscopy (exclude sinonasal disease / mass)
- Imaging if:
    - Suspect skull base injury – CT
    - No cause found for anosmia – MRI (to exclude intracranial lesion)
    - Any other neurological fallout / concern for IC lesion

Prognosis:

It is not clear what predisposes someone to viral-induced smell dysfunction or the mechanism behind it. COVID -19 seems to affect the olfactory supporting cells and not directly infect the neurons so is more often temporary.

Chronic rhinosinusitis (CRS) may cause a conductive and sensorineural (SN) smell loss, thus is not always reversible with surgery. A trial of oral prednisone with restoration of smell in a patient with CRS pre-operatively is a favourable prognostic feature and surgery is likely to be beneficial (mostly a conductive smell loss reversed by surgery).

Management:

Management depends on the cause

- Conductive loss is more amenable to treatment than SN dysfunction

- If a structural / anatomical problem, then referral needed
    - e.g. CRSwNP or anterior cranial fossa lesion → ENT / Neurosurgery
    - Options: Medication / Surgery / Chemo- Radio- therapy
    - Medical – Inhaled nasal corticosteroids +/- systemic steroids
    - Surgery – Endoscopic sinus surgery / Polypectomy
- Acute bacterial rhinosinusitis – systemic antibiotics / decongestant / analgesia / anti-pyretic

- SN Olfactory loss has a worse prognosis
    - Most patients that recover after trauma do so in <12 weeks (may take years)
    - If for other reasons for example post – infection/trauma/toxins/idiopathic then:

Olfactory retraining therapy

- Use 4 scents – rose / lemon / clove / eucalyptus (vanilla / coffee) (1ml onto cotton in 50ml jar)*
- 2x daily, each scent for 20-30 sec for 24 weeks
- Higher concentration and more scents may be better
- Longer duration is better (1 yr vs 16 wks)[#]
- Post-infectious dysfunction does best e.g. post-COVID – consider steroid with retraining therapy

References:

- *Hummel T, Rissom K, Reden J, Hähner A, Weidenbecher M, Hüttenbrink KB. Effects of olfactory training in patients with olfactory loss. Laryngoscope. 2009 Mar;119(3):496-9.
- [#]Konstantinidis I, Tsakiropoulou E, Constantinidis J. Long term effects of olfactory training in patients with post-infectious olfactory loss. Rhinology. 2016 Jun;54(2):170-5. [PubMed]