

Can You Smell That?

Anatomy and Physiology of Smell

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Grand Rounds Presentation

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Olfaction

- The most ancient of distal senses
 - In nearly all air-, water-, and land-dwelling creatures
- Determines flavor of foods and beverages
- Significant role in nutrition, safety, and in the maintenance of quality of life
- 2.7 million (1.4%) adults in the U.S. alone with olfactory dysfunction

I'm an
Olfaction
sort of
guy!



“I sense a hint of oak and butterscotch”

- Many depend upon smell for livelihood or safety:
 - Cooks
 - Homemakers
 - Firefighters
 - Plumbers
 - Wine merchants
 - Perfumers
 - Cosmetic retailers
 - Chemical Plant Workers



The Sense of Smell

- Often downplayed
- Vital to our everyday existence
 - Stop and smell the roses
 - Has the milk expired?
- Essential in our ability to taste
- Occasionally the first sign of other disorders
- Rarely tested



Our Road Map



- Anatomy of the Nose
- Physiology of Smell
- Diagnostic Workup
- Common causes of Olfactory Disturbance
- Treatment Options

Definitions

- Total Anosmia: inability to smell all odorants on both sides of the nose
- Partial Anosmia: inability to smell certain odorants
- Specific Anosmia: lack of ability to smell one or a few odorants
- Hyperosmia: abnormally acute smell function and often interpreted as hypersensitivity to odors
- Dysosmia: distorted or perverted smell perception

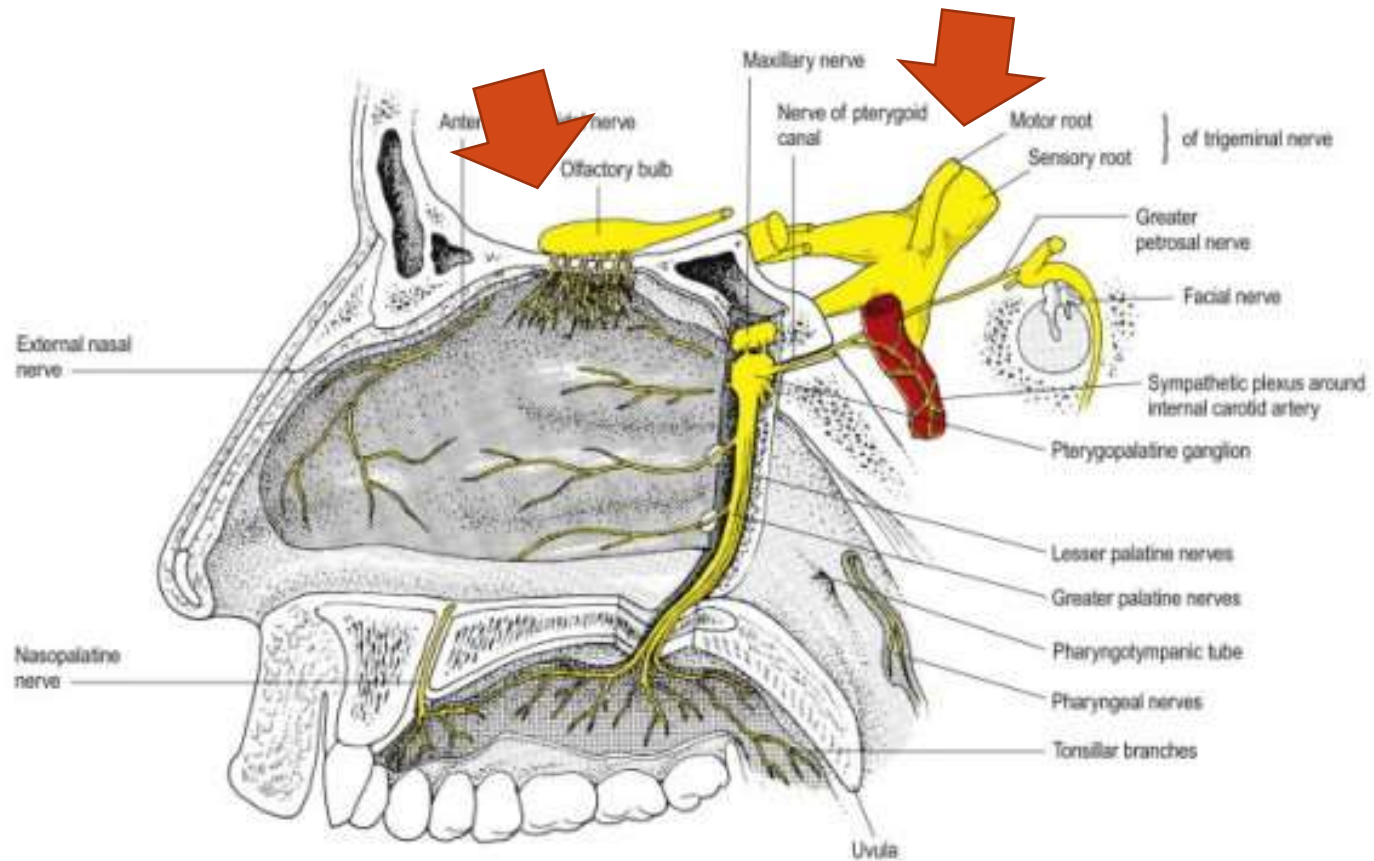
Definitions

- Parosmia/Cacosmia: change in quality of an olfactory cue
- Phantosmia: odor sensations in absence of an olfactory stimulus
- Olfactory agnosia: inability to recognize odor sensations despite olfactory processing, language, and intellectual function intact
 - Seen in certain stroke and postencephalitic patients
- Presbyosmia: smell loss due to aging

Nasal Anatomy and Olfaction

- Odor reception is a result of input from:
 - Olfactory Nerve (CN I)
 - Trigeminal Nerve (CN V)
 - Glossopharyngeal Nerve (CN IX)
 - Vagus Nerve (CN X)

Nasal Anatomy

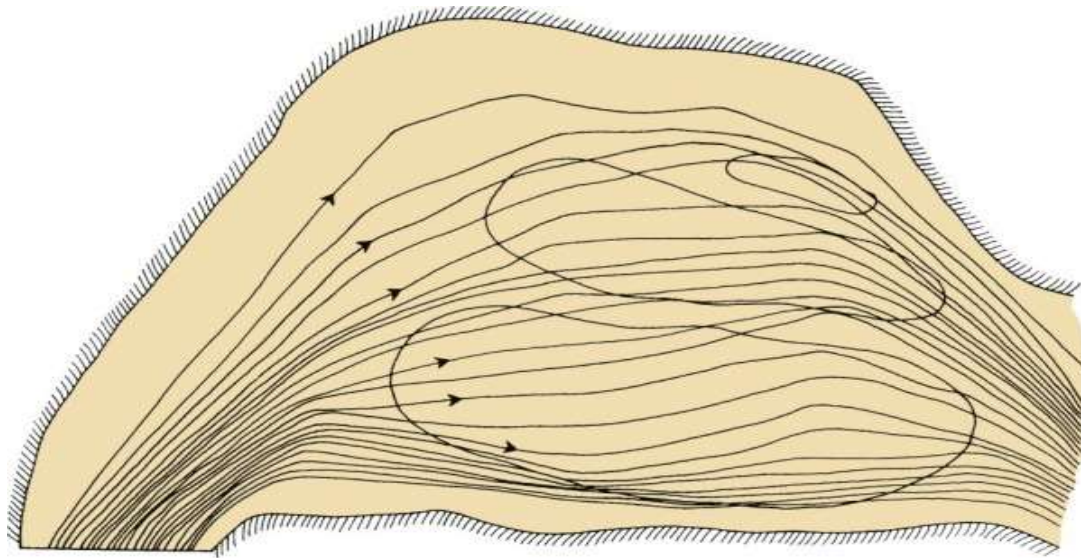


Olfactory Nerve Stimulation

- Requires odorant's molecules reaching the olfactory mucosa at the top of the nasal cavity
- Olfaction requires some type of nasal airflow
- Orthonasal flow: airflow toward the olfactory epithelium on inhalation
- Retronasal flow: during eating, stimulates olfactory receptors and contributes greatly to the flavor of food

Physiologic Airflow of the Nasal Passages

- 50% of the total airflow passes through the middle meatus
- 35 % of total airflow passes through the inferior meatus
- 15% of total airflow passes through the olfactory region



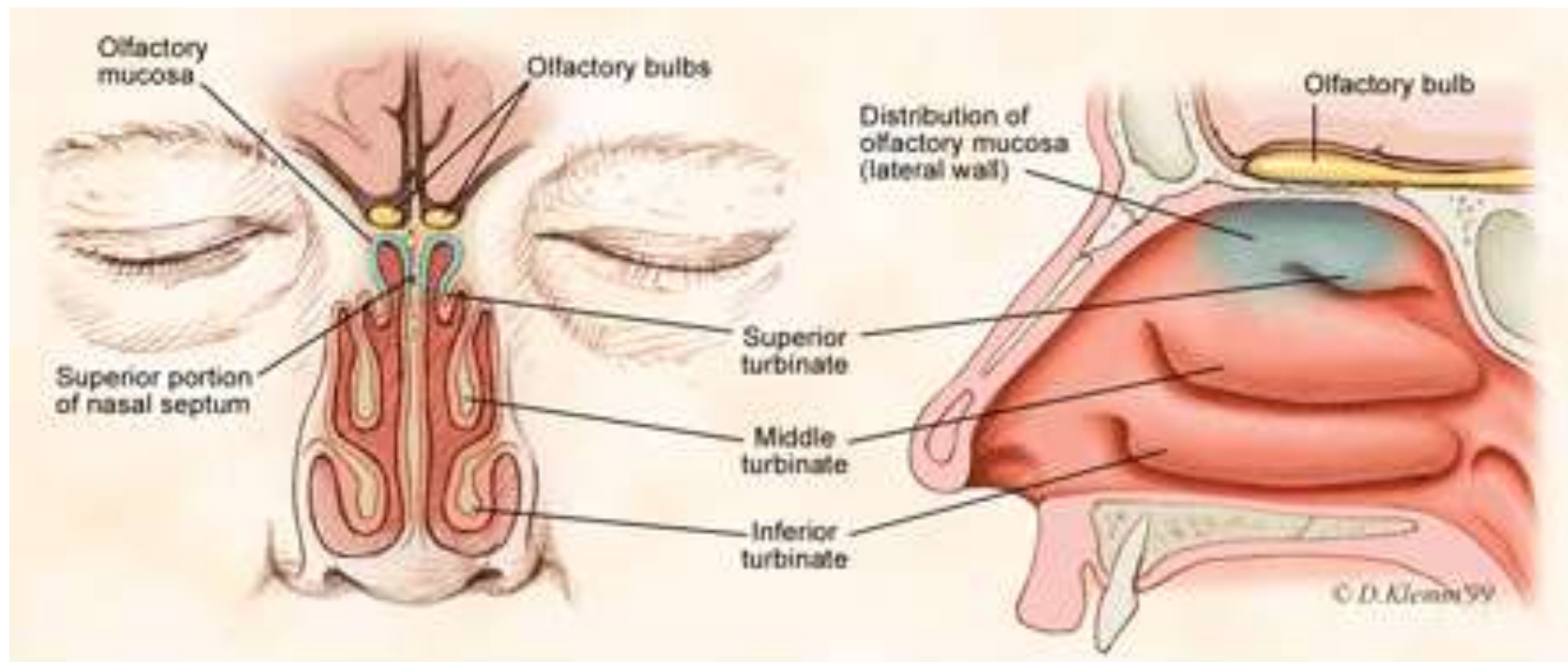
Why do we sniff?

- Effects of a rapid change in flow velocity on the in vivo airflow pattern remains unknown
- Scherer and colleagues found percentage and velocity of airflow to the olfactory region are similar for various steady-state airflow rates in the physiologic range
- Sniffing remains an almost universally performed maneuver when presented with an olfactory stimulus
- Sniff may allow trigeminal nerve to alert olfactory neurons that an odorant is coming
- Our natural sniff seems to be the optimal for our nasal anatomy

Olfactory Anatomy

- Olfactory molecules must pass through the tall but narrow nasal passageways
- Olfactory epithelium is wet, has variable thickness, and aerodynamically “rough”
 - Schneider and Wolf observed olfactory ability to be best when epithelium is moderately congested, wet, and red
- Olfactory ability seems to improve with narrowed nasal chambers
- Nasal cycle does not have any effect on olfactory ability

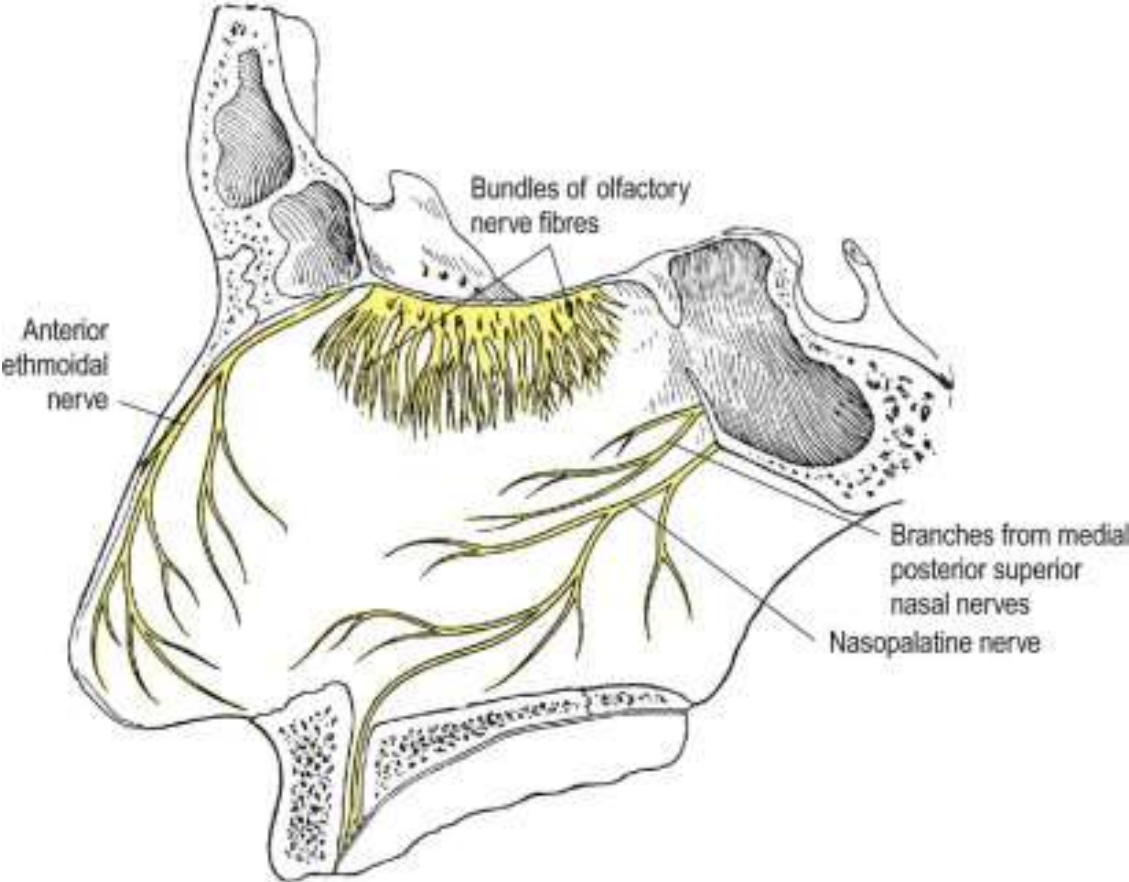
Olfactory Anatomy



Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

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Olfactory Anatomy



Absorption of Molecules

- Mucus-lined walls absorb molecules from the air stream and increase their travel time through the nasal passageways
- This may influence the spectrum of chemicals reaching the olfactory cleft
- Absorption of molecules may separate/sort odorants before reaching the olfactory mucosa
 - Highly absorbable chemicals may have minimal or no odor as they never reach the olfactory cleft

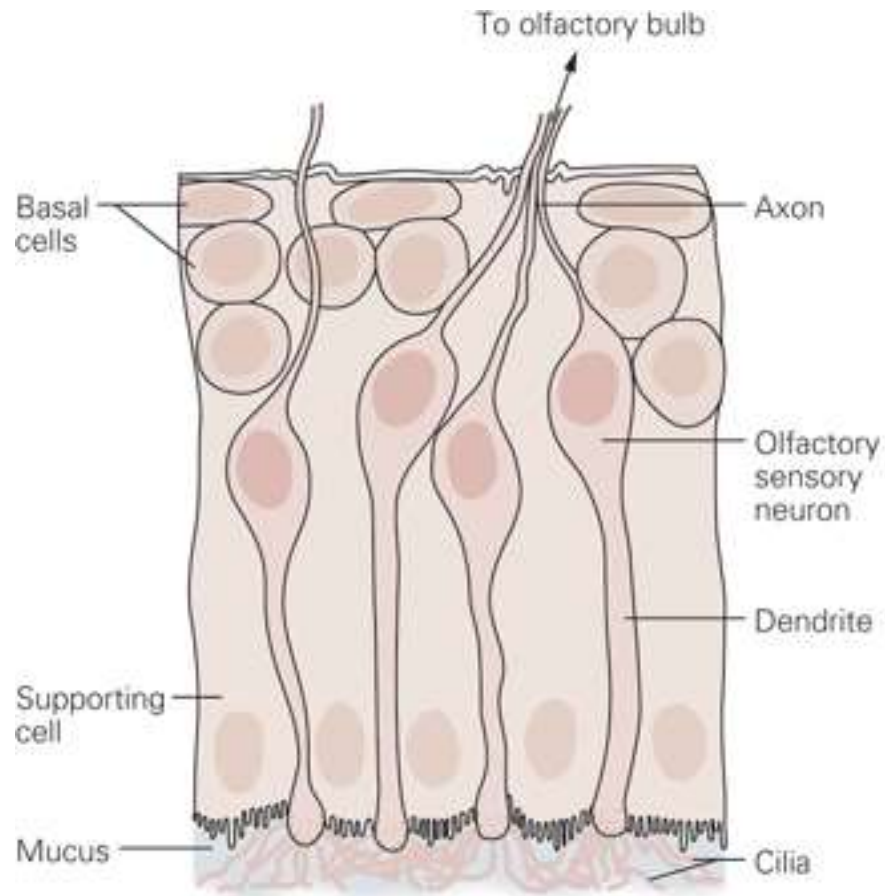
Olfactory Mucus

- When odorant molecules reach olfactory region, must interact with mucus overlying the receptor cells
- Produced by Bowman's glands and adjacent respiratory mucosa (goblet cells)
- Partitioning of odorant's molecules between air phase and mucus phase important in reaching olfactory epithelium
- Must be soluble in mucus but not too strongly captured to interact with the receptors
- Adrenergic, cholinergic, and peptidergic agents change the properties of mucus overlying the olfactory receptors

Olfactory Mucus

- In the olfactory mucus-epithelial system, clearing odorants is equally as important as absorption
- Olfactory mucus may exert a differential role in deactivating, removing, or desorbing odorants from the olfactory area

Olfactory Epithelium



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology*,
23rd Edition: <http://www.accessmedicine.com>

Olfactory Epithelium

- Olfactory sensory neurons protected in a 1-mm-wide crevice of the posterosuperior nose
- Covers roughly 1 cm² on each side
- Neuroepithelium is pseudostratified columnar epithelium
- Neurons exposed to the outside world through their dendrites and cilia
- Axons of these neurons synapse at the base of the brain in the olfactory bulb
- As least six morphologically and biochemically distinct cell types


Olfactory Neuroepithelium

- Bipolar receptor cell: projects from the nasal cavity into the brain without an intervening synapse
 - Major route of viral and xenobiotic invasion into the central nervous system
 - Cases of Naegleria infections caused by infiltration through the cribriform plate

Weather

Weather Alert: Avalanche Warning expires at 6:15 AM on 1/24, issued at 6:13 AM Alpine,

Deadly parasite kills two Neti Pot users

 Recommend 44

 Tweet 16

 Story Comments

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Updated: 12/16/2011 10:19 pm | Published: 12/16/2011 8:22 pm

Olfactory Receptor Cell

- Each receptor cell expresses a single odorant receptor gene
- > 1,000 different types of receptor cells present within the olfactory epithelium
- Olfactory receptor genes account for ~1% of all expressed genes of the human genome
 - Largest known vertebrate gene family
- Receptors not randomly distributed but confined to one of several nonoverlapping striplike zones
- Each cell is responsive to a wide, but circumscribed, range of stimuli
- Olfactory receptor proteins linked to stimulatory guanine nucleotide-binding protein G_{olf}

Olfactory Receptor Cell

- Derived from ectoderm
- First-order neurons, can regenerate after they are damaged
- Glial-type cells that ensheath olfactory neurons support axonal growth of both olfactory and nonolfactory neurons
 - Interest as potential agents for reversing spinal cord injuries and demyelinating disease

Olfactory Cilia

- Cilia differ from respiratory epithelium in being much longer, lacking dynein arms (lacking motility)
- Surface area of cilia exceeds 22 cm² in humans
 - Exceeds 700 cm² in German Shepherd dog

Olfactory Epithelium

- Supporting or sustentacular cell: contain microvilli and insulate the bipolar receptor cells and help to regulate composition of the mucus
 - Involved in deactivating odorants and assisting in protecting epithelium from foreign agents
- Microvillar cells: poorly understood cells located at the epithelial surface
- Fourth cell type lines the Bowman's glands and ducts
- Horizontal (dark) and Globose (light) basal cells: located near the basement membrane from which the other cell types arise

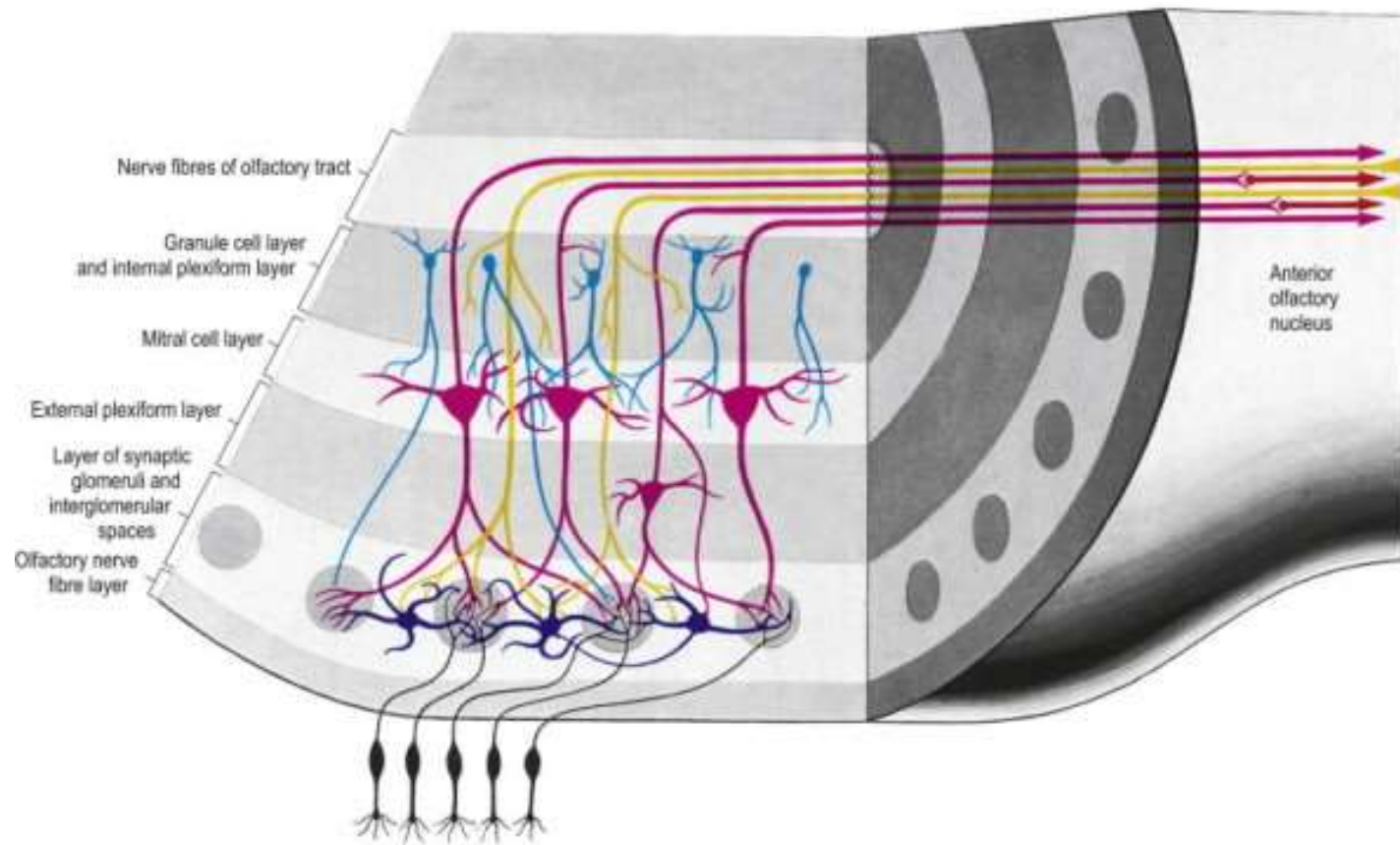
Vomeronasal Organ

- Identifiable pit or groove in anteroinferior part of the nasal septum
- Contains chemosensitive cells
 - In most animals, identifiable nerve connecting these cells to the CNS
 - No identifiable connection from Jacobson's organ in humans to CNS
 - Physiological studies have shown negative action potentials from this area without subjective response from individuals tested
- May function as a neuroendocrine system
- Presently, no evidence for symptom-related importance
 - However, this anatomic area should not be disturbed during surgery unless necessary

Olfactory Bulb

- Lies in base of frontal cortex in anterior fossa
- First relay station in olfactory pathway
- Synapses and their postsynaptic partners form dense aggregates of neuropil called glomeruli
- Given region of the bulb receives its most dense input from a particular region of the mucosa, inputs to a particular region of the bulb converge from many receptor cells distributed throughout a certain zone of the mucosa
- Excitatory and inhibitory influences narrow the neural stimulus
- Olfactory bulb specialized to narrow the spatial pattern of glomerular activation by an odorant or mixture of odorants

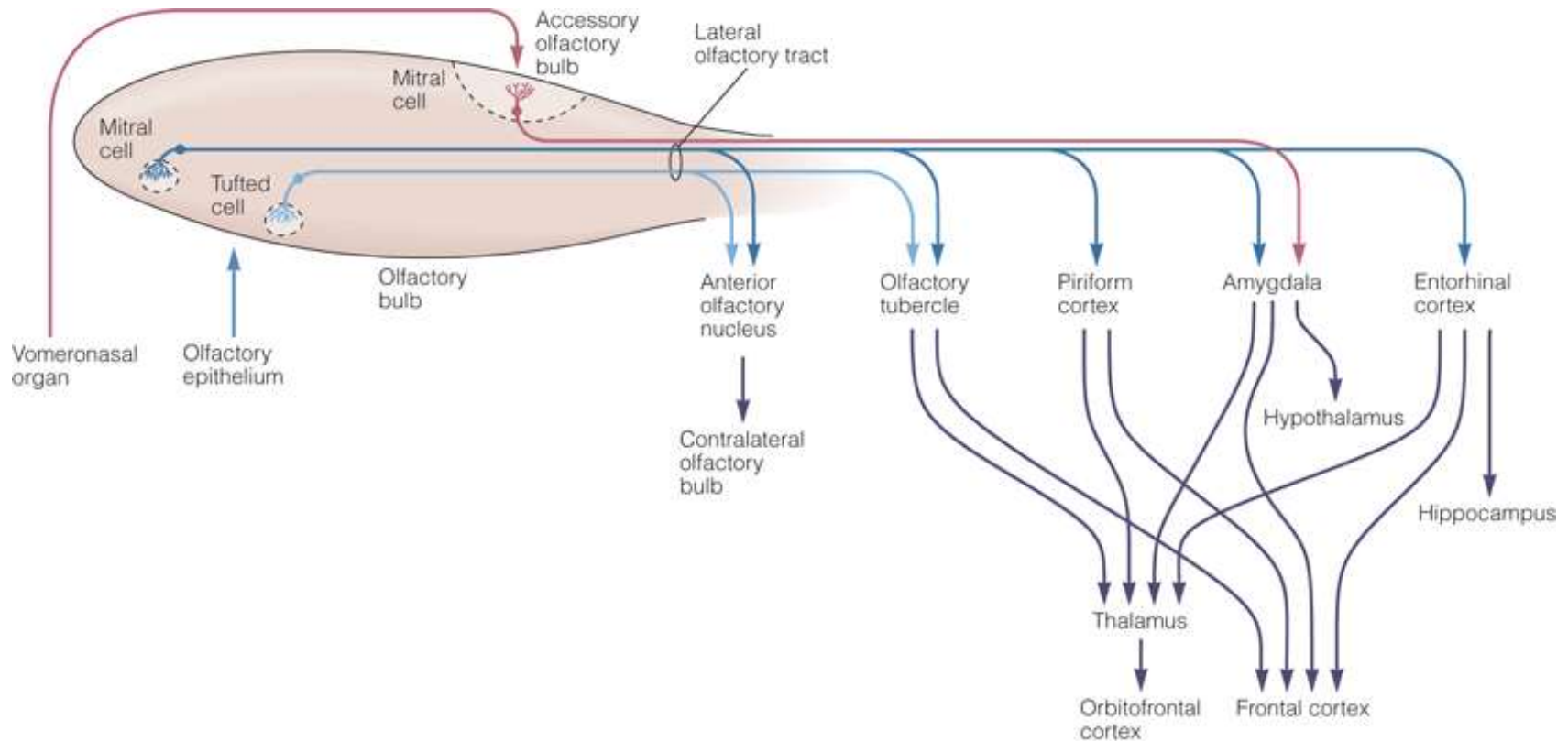
Olfactory Bulb



Olfactory bulb and aging

- Younger persons have thousands of these 50- to 200- μm glomeruli arranged in single or double layers
- Decrease in number with age
- Nearly absent in many persons older than age of 80 years

Olfactory connections to the Brain



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology*,
23rd Edition: <http://www.accessmedicine.com>

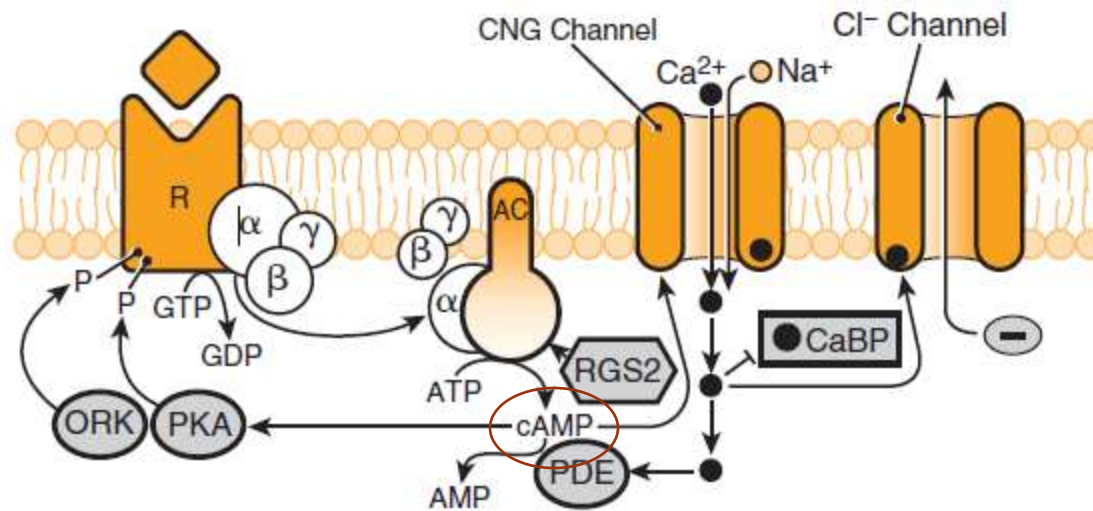
Olfactory Connections

- Central connections include:
 - Olfactory tubercle
 - Prepiriform cortex
 - Amygdaloid nuclei
 - Nucleus of the terminal stria
- These structures receive multiple inputs and serve other functions including: food intake, temperature regulation, sleeping cycles, vision, memory, hearing, and taste

Olfactory Transduction

- Olfactory Binding Proteins: bind and solubilize the hydrophobic odorant molecules into hydrophilic olfactory mucus
 - Increases concentration into the surrounding environment as much as 1,000 to 10,000 times more than their concentration in ambient air
 - May also act to remove odorant molecules from the region of the receptor cell

Olfactory Transduction



Olfactory Transduction

- cAMP and IP3 are primary signaling pathways mediating olfactory transduction
- G_{olf} : G protein exclusively localized to the olfactory epithelium
- cAMP binds to Na, Ca ion channel depolarizing the cell creating an action potential
- Type 1a Pseudohypoparathyroidism: deficiency in stimulatory G_{olf} , have olfactory loses

Olfactory Odor Map

- Mouse model shows their olfactory epithelium is roughly divided into four zones
- Group of different olfactory receptor subtypes confined within the designated zone
- Clinical evidence exists for receptor specificity of odorants
 - Loss of specific odor receptor genes creates an inability to perceive particular odorants

Olfactory Cognition

- We understand odors largely on experience; develop our own hedonic code within cultural restraints
- Studies show odor memory can last at least 1 year while visual memory lasts only a few months
 - Odor memory is facilitated by bilateral nasal stimulation, one study suggests patients with one-sided nasal obstruction may form poorer odor memories
- Macfarlane examined 30 newborns and 30 women
 - Women underwent washing of one breast and babies were placed in prone position between their breasts
 - 22 of the 30 newborns selected the unwashed (odorous) breast

Pheromones

- Chemicals released by one member of a species and received by another member resulting in a specific action or developmental process
- Anatomic and behavioral studies support the possibility of human communication through odorants
- Russell and associates placed underarm secretion and alcohol on 5 experimental subjects and alcohol on 6 control subjects
 - Over a period of 5 months, statistically significant (0.01) greater tendency for menstrual synchrony

Clinical Evaluation of Olfaction

- An evaluation of 750 patients with chemosensory dysfunction, demonstrated that most patients presented with both smell and taste loss, few (<5%) have identifiable whole-mouth gustatory deficits
 - Taste: true gustation
 - Flavor: olfactory-derived sensations from foods
- Whole-mouth taste function much more resistant to injury than olfactory function largely due to redundancy of innervation
- When CN I is damaged, leaves only sweet, sour, salty, bitter and umami (MSG-like) sensation

Clinical Evaluation

- Nature and onset of the chemosensory problem
- Associated events such as viral or bacterial infections, head trauma, exposure to toxic fumes, systemic disease, and signs of early dementia
- Important to distinguish between anosmia and hyposmia
- Localization to one or the other nasal chamber
- Dysfunction for all odorants or only a few
- Timetable of loss is important
 - Possibility of spontaneous recovery related to duration of the problem; spontaneous recovery is minimal after 6 months of damage
- Exploration of taste loss; Anosmia patient will be able to differentiate saltiness, sourness or sweetness in foods but unable to differentiate in those flavors

Past Medical and Surgical History

- Assessment of past medical and surgical histories
 - Endocrinologic state
 - Delayed puberty with anosmia: Kallmann syndrome
 - History of Radiation therapy
 - Medications
- Previous sinus and nasal surgeries
 - Although rare, olfactory deficit after nasal surgery can happen

Social History

- Explore smoking history
 - Olfactory ability decreased as a function of cumulative smoking dose
 - Cessation of smoking can result in improvement in olfactory function over time
- History of allergy along with past nasal or paranasal sinus infections

Physical Examination

- Complete otolaryngologic examination with anterior rhinoscopy and nasal endoscopy
 - Unfortunately, nasal endoscopy is not overly sensitive
 - During endoscopy, examine nasal mucosa for color, surface texture, swelling, inflammation, exudate, ulceration, epithelial metaplasia, erosion, and atrophy
 - Even minor polypoid disease at the olfactory cleft can account for olfactory dysfunction
- Cranial nerve examination
- Optic disc examination to determine presence of increased intracranial pressure

Foster Kennedy Syndrome

- Tumors of olfactory groove or sphenoidal ridge (meningiomas)
- Ipsilateral anosmia or hyposmia
- Ipsilateral optic atrophy
- Central papilledema

Olfactory Testing

- Essential for multiple factors:
 - Validate patient's complaint
 - Characterize specific nature of the problem
 - Monitor changes in function over time
 - Detect malingering
 - Establish compensation for permanent disability
- Many patients complaining of anosmia or hyposmia have normal function relative to age and gender
 - 90% of patients with idiopathic Parkinson's Disease have demonstrable smell loss, yet less than 15% are aware of their problem

Olfactory Testing

- Asking a patient to sniff odors is like testing vision by shining a light in each eye and asking whether the patient can see the light
- No current testing that can distinguish central and peripheral deficits
- Unilateral testing is often warranted
 - Sealing contralateral naris using Microfoam tape and having the patient sniff naturally and exhale through the mouth to prevent retronasal stimulation

Medical/Legal Considerations with Anosmia

- Common in head injury and often the only residual neurologic impairment
- Claims of accidental and iatrogenic smell disturbance often results in substantial financial awards
- Veterans Administration awards a 10% whole-body disability for total anosmia
- Occupation should be taken into account in disability issues

Olfactory Testing

- Psychophysical Testing
- Electrophysiologic Testing
- Neuropsychologic Testing

Psychophysical Testing

- UPSIT or Smell Identification Test
 - Can be administered in 10 to 15 minutes by most patients
 - 4 booklets of 10 odorants apiece
 - Stimuli embedded into 10- to 50- μ m diameter microencapsulated crystals
 - Multiple choice questions with four response alternatives
 - Test is forced-choice, required to choose an answer even if none seems appropriate
 - Chance performance is 10 out of 40 , lower scores can represent avoidance
 - Norms available based on administration to 4,000 people
 - Individuals are ranked relative to age and gender

UPSIT (continued)

- Test can classify individual's function into 6 categories:
 - Normosmia
 - Mild microsmia
 - Moderate microsmia
 - Severe microsmia
 - Anosmia
 - Probable malingering
- Very high reliability, test-retest Pearson $r = 0.94$

Medical/Legal Considerations with Anosmia

- UPSIT score sensitive to malingering
- Theoretical probability of true anosmic to score UPSIT 5 or less: 0.05%
- Theoretical probability of true anosmic scoring 0 on UPSIT: 0.00001

Electrophysiologic Testing

- 2 procedures are available but application largely experimental
- Odor event-related potentials (OERPs)
- Electro-olfactogram (EOG)

Odor Event-Related Potentials (OERPs)

- Discerning synchronized brain EEG activity recorded on the scalp from overall EEG activity following presentations of odorants
- Stimuli presented in precise manner using equipment that produces stimuli embedded in warm, humidified air stream
- Unable to perform necessary trials and test reliability is suspect
- No inference can be made regarding location of a lesion or deficit
- Can be usefully in detecting malingering

OERP



Electro-olfactogram (EOG)

- Measures electrode placed on the surface of the olfactory epithelium
- Few patients amenable to recordings
- Must place electrode under endoscopic guidance without local anesthesia
 - Can be quite unpleasant and sneezing/mucous discharge common
- Cannot reliably record in many subjects
- Presence of robust EOG does not always represent olfactory functioning
 - Anosmic patients with Kallmann syndrome and hyposmic patients with schizophrenia have large EOG responses

Neuropsychologic Testing

- Strong association between Alzheimer's, Parkinson's, and olfactory dysfunction
- Brief neuropsychologic testing warranted in some cases to determine presence of dementia
- Mini-Mental State Examination- brief screening tool for dementia and can be quickly administered in a few minutes for further referral as necessary

Neuroimaging

- Olfactory dysfunction of idiopathic etiology warrants CT imaging
 - High-resolution CT is most useful and cost-effective screening tool
- MRI: useful in evaluating olfactory bulbs, olfactory tract, and intracranial structures
 - MRI can detect decrements associated with anosmia and patients with schizophrenia

Olfactory Biopsy

- Small amount of superior septal tissue removed by experienced rhinologist
- Multiple biopsies needed to obtain true neuroepithelium

Disorders of Olfaction

- Approximately 2 million American adults with disorders of taste and smell
- More than 200 conditions associated with changes in chemosensory ability

Disorders of Olfaction

- Obstructive Nasal and Sinus Disease
- Upper Respiratory Infection
- Head Trauma
- Aging
- Congenital Dysfunction
- Toxic Exposure
- Neoplasms
- HIV
- Epilepsy and Psychiatric Disorders
- Medications
- Surgery
- Idiopathic Loss

Disorders of Olfaction

Table 41-1

Spectrum of Olfactory Loss as Reported at Four Chemosensory Centers

	Goodspeed and Colleagues (1987) ^{239*}	Davidson and Colleagues (1987) ^{226†}	Leopold and Colleagues (1987) ^{222‡}	Heywood and Costanzo (1986) ^{169§}
Total no. patients	441	63	198	133
Etiologic category (%):				
Obstructive nasal and sinus disease	30	33	29	20
Post-upper respiratory infection	19	32	15	17
Head trauma	9	10	19	32
Aging	0	0	8	6
Congenital	0	5	8	0
Toxins	1	11	3	0
Miscellaneous	14	10	8	16
Idiopathic	26	0	10	10

*Connecticut Chemosensory Clinical Research Center, Farmington, Connecticut.

†Chemosensory Perception Laboratory, University of California, San Diego.

‡Clinical Olfactory Research Center, SUNY Health Science University, Syracuse, New York.

§Smell and Taste Clinic, Medical College of Virginia, Richmond, Virginia.

Obstructive Nasal and Sinus Disease

- Nasal polyps, mucosal swelling and nostril occlusion produce anosmia which generally resolves when obstruction is released
- Opening toward olfactory cleft believed to be medial and anterior to lower part of middle turbinate
- 1- or 2-week course of steroids may diagnose obstructive cause of anosmia
- Rare that external nasal deformity can cause anosmia from obstruction
- Scarring from surgery between middle turbinate and nasal septum can effectively close off olfactory cleft to airflow

Obstructive Nasal and Sinus Diseases

- Chronic rhinosinusitis causes edema and polyps with obstruction of olfactory cleft
- Kern analyzed olfactory mucosa biopsies
 - Found inflammatory changes in olfactory epithelium
 - Inflammation-driven, primary neuron dysfunction may contribute to olfactory disability without obstruction
 - Evidence of active apoptosis of olfactory receptor neurons which may explain why anosmia unresponsive to oral steroids in patients with chronic sinus disease

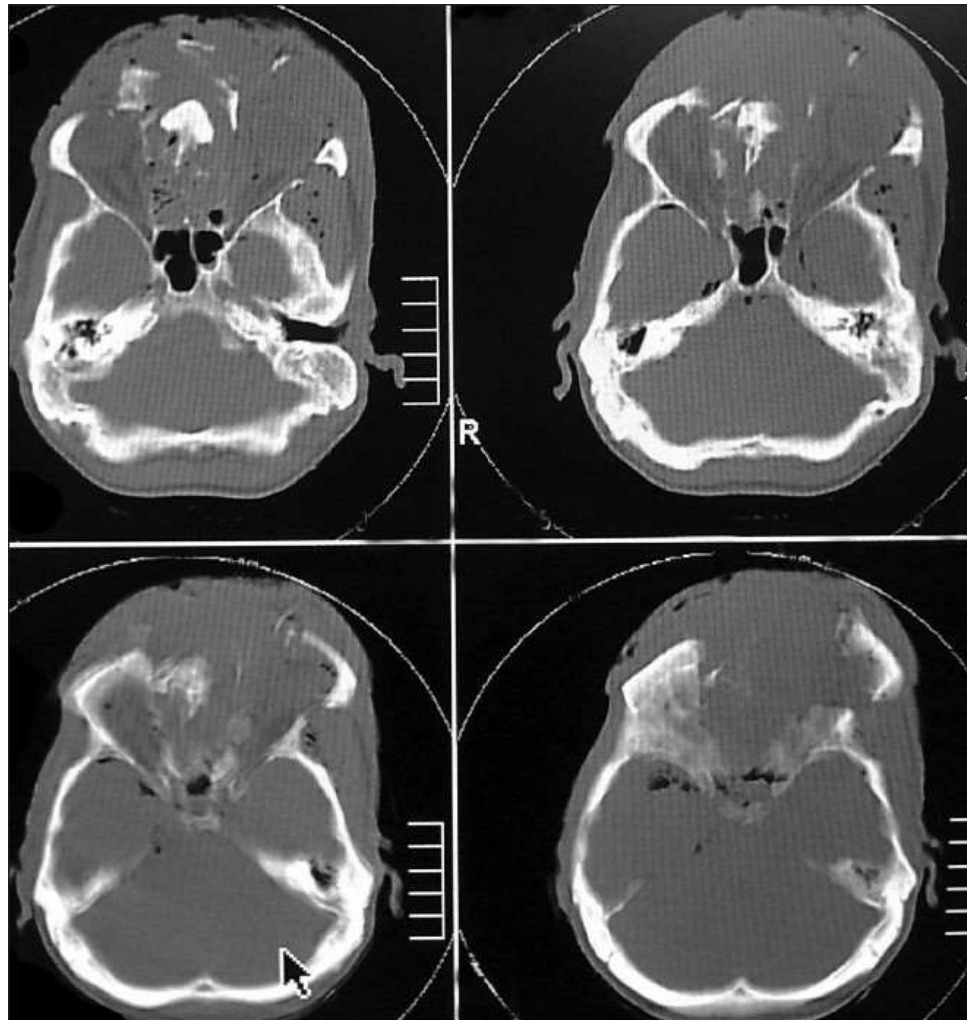
Upper Respiratory Infection

- Often, patients complain of olfactory loss secondary to URI
 - Likely secondary to obstruction and resolves in 1-3 days
- Small percentage of patients with total loss
 - Fourth, fifth, or Sixth decade of life
 - 70-80% women
- Biopsy specimens reveal decreased numbers of olfactory receptors
- Prognosis is generally poor

Head Trauma

- Incidence of olfactory loss in adult patients with head trauma: 5% and 10%
- Generally, severity of trauma associated with loss
- Frontal blows most frequently cause olfactory loss
- Occipital blow carries 5 times risk of total anosmia
- Onset generally immediate
- Rate of recovery less than 10% and quality of recovered ability generally poor
- Exact injury generally unknown but thought to be due to shearing of olfactory nerves or contusion to olfactory bulbs

Head Trauma



Aging

- Olfactory identification sharply decreases in sixth and seventh decades of life
- Decreased magnitude matching, changes in perception of pleasantness, decreased nutritional status, ability to discriminate flavor in everyday foods

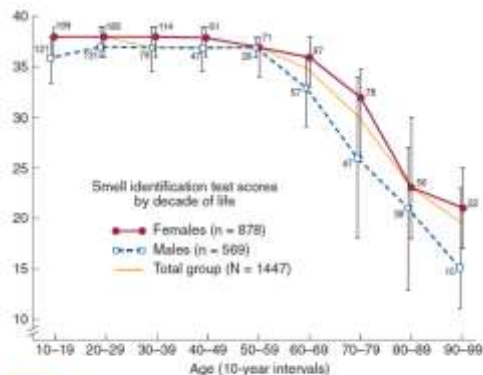


Figure 41.13. Relationship between the University of Pennsylvania Smell Identification Test scores, age, and gender in a large heterogeneous group of subjects. (From Octy RL, Shammah R, Damm M. Development of the University of Pennsylvania Smell Identification test: a standardized microencapsulated test of olfactory function. *Physiol Behav*. 1984;32:489.)

Dementia-related Diseases

- Alzheimer's disease and Parkinson's Disease
- Alzheimer's characterized by presence of neurofibrillary tangles and neuritis plaques in central olfactory pathways
 - Similar pathologic changes and testing abnormalities in Down syndrome suggesting possible genetic link toward olfactory losses
 - Pearson et al showed involvement of olfactory system contrasting with minimal abnormality in other areas of the brain
 - Possible environmental agent?

Parkinson's Disease

- Number of nonmotor defects including depression and cognitive loss
- Olfactory changes independent of cognitive and motor symptoms
- Neuronal losses identified in olfactory bulb with strong correlation to disease duration
- Patient diagnosed with Alzheimer's or Parkinson's Disease but testing does not reveal olfactory loss should be considered for different diagnosis

Congenital Dysfunction

- Most patients with total congenital loss unaware of loss until early adolescence
- Kallmann Syndrome
 - Hypogonadotropic hypogonadism
 - Defect in X chromosome KAL1 gene encoding anosmin-1
 - Agenesis of olfactory bulbs and stalks and incomplete development of the hypothalamus
 - Existence of syndrome may show strong association between sexual development and olfaction

Toxic Exposure

- Many toxins, mostly aerosol, exist
- Concentration and duration of exposure must be considered

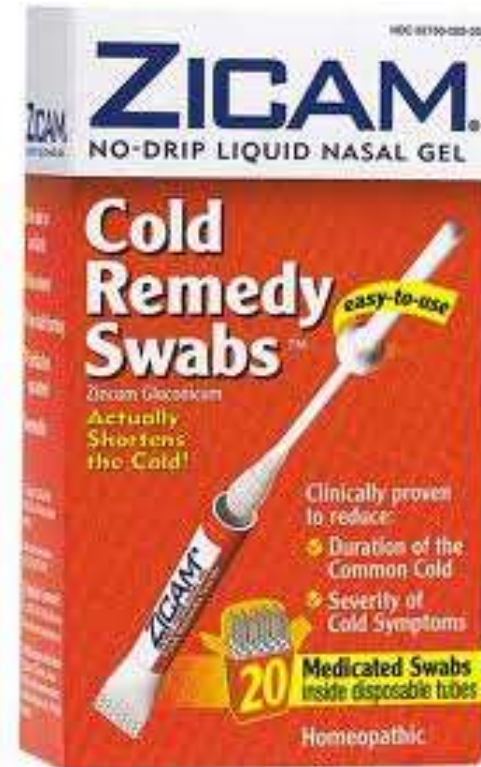
Zicam-Induced Damage to Mouse and Human Nasal Tissue

Jae H. Lim¹, Greg E. Davis¹, Zhenshan Wang², Vicky Li², Yuping Wu², Tessa C. Rue³, Daniel R. Storm^{2*}

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Zicam

- Homeopathic nasal spray marketed for cold and congestion relief
- Zinc gluconate



EOG response to Various Nasal Sprays

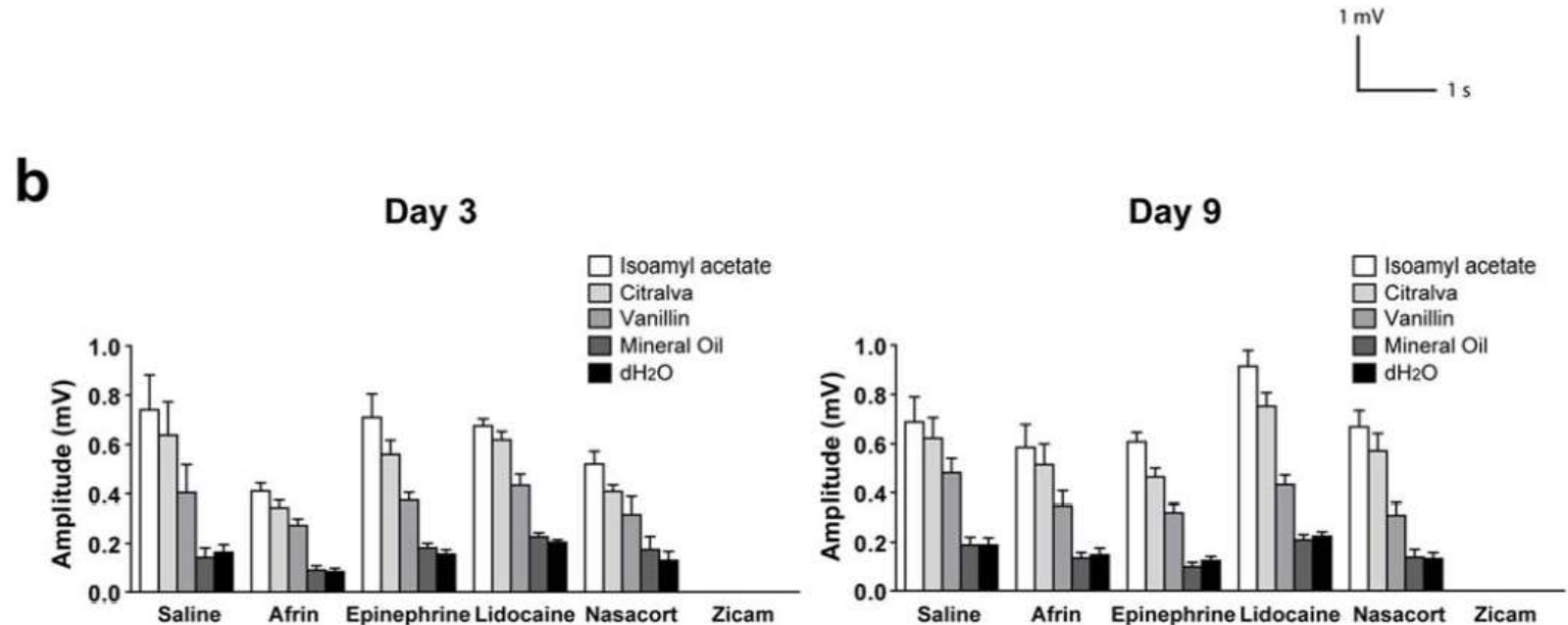
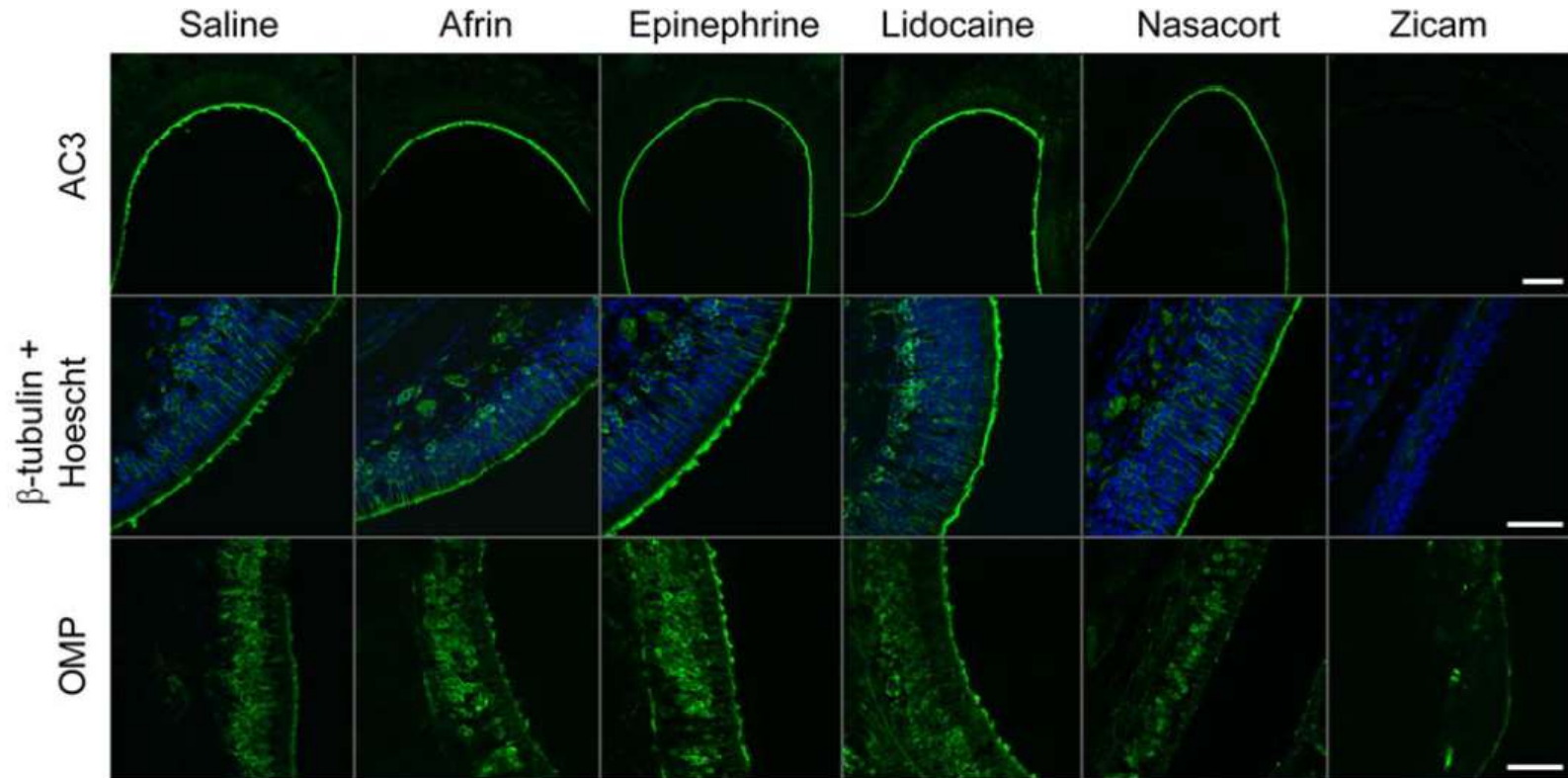


Figure 1. Odorant detection defects in the MOE of Zicam-treated mice. (a) Odorant-stimulated EOG responses from mice treated with either saline, Afrin, epinephrine, lidocaine, Nasacort or Zicam, 3 and 9 days following intranasal administration. Red arrowhead indicates the time at which the odorant was delivered to the MOE. (b) Summary of the mean EOG amplitudes in response to odorants on day 3 and 9 following intranasal agent administration. Only Zicam-treated MOE failed to elicit odorant-stimulated EOG response ($n = 5$ for all groups).
doi:10.1371/journal.pone.0007647.g001

Various Expressed Proteins in Olfactory Sensory Neurons



H & E microscopic Examination of Nasal Tissue in **a**

a

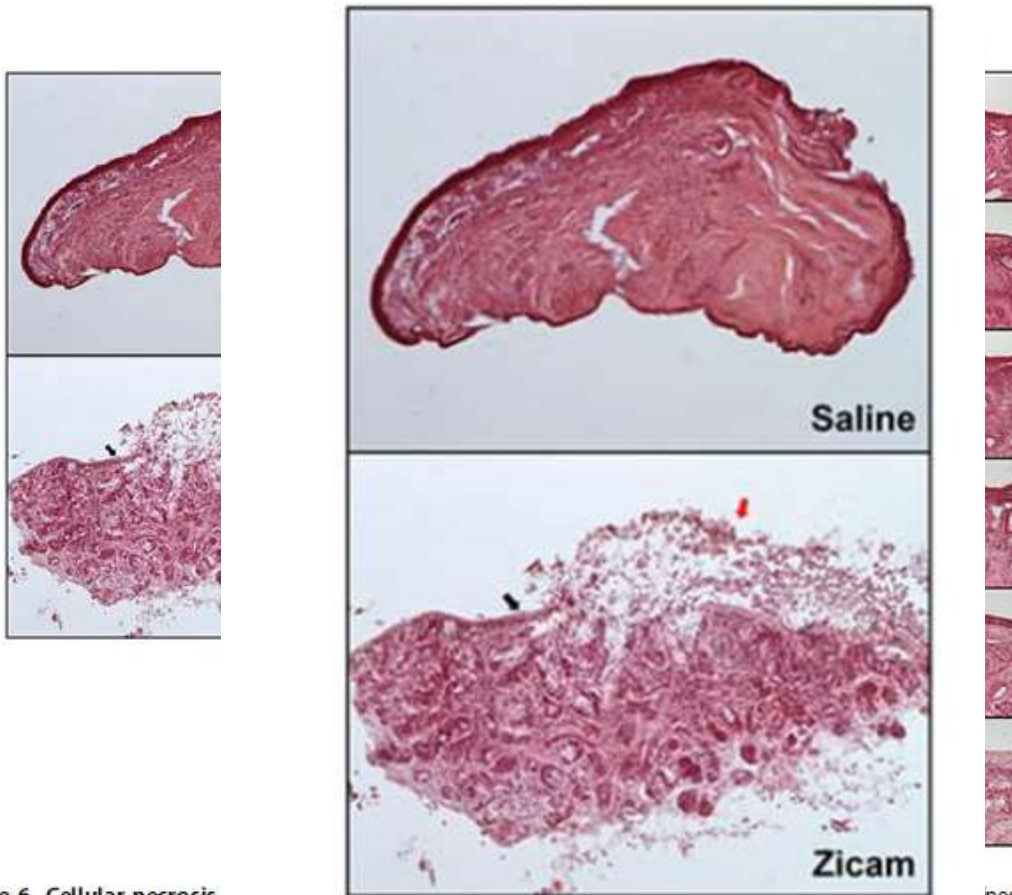


Figure 6. Cellular necrosis superior nasal septum following saline, lidocaine, Afrin, epinephrine, or Zicam. Black arrows depict basal surface of remaining epithelium. Note the infiltration of inflammatory cells and severe necrosis in Zicam treated-nasal explants. doi:10.1371/journal.pone.0007647.g006

ined human nasal explants from nasal regions treated with either

note basal surface of the remaining

Neoplasms

- Intranasal and intracranial tumors can affect smell
 - Intranasal tumors: inverted papillomas, adenomas, SCC, and esthesioneuroblastoma
 - Intracranial tumors: meningiomas, pituitary tumors, gliomas
 - Approximately 25% of temporal lobe tumors with olfactory disturbance

HIV

- Correlation among patients with HIV and olfactory disturbance
- Losses can be variable
- Does not correlate with CD4 counts, body weight, body composition, management or diet

Psychiatric Disease

- Olfactory complaints often in patients with depression, schizophrenia, and hallucinations
- Olfactory identification deficits only in schizophrenia
- Intrinsic olfactory hallucinations: patient believes smell emanates from own body
- Extrinsic olfactory hallucinations: patient believes odor comes from source other than patient's body
- Olfactory reference syndrome: obsessive concern over minor or absent odors; patients often bathe frequently and wear excessive perfume
- “Marcel Proust” syndrome: odors cause such drastic memories as to disrupt daily routine

Medications

- Amebicides and antihelmintics: Metronidazole; niridazole
- Local Anesthetics: Benzocaine; Procaine; Cocaine; Tetracaine
- Anticholesteremics: Clofibrate
- Anticoagulants: Phenindione
- Antihistamines: Chlorpheniramine
- Antiproliferatives: Doxorubicin; Methotrexate; Azathioprine; Carmustine; Vincristine
- Antirheumatic, analgesic-antipyretic, anti-inflammatory: Allopurinol; Colchicine; Gold; Levamisole; D-pencillamine; Phenylbutazone; 5-thiopyridoxine

Medications (continued)

- Antiseptics: Hexetidine
- Antithyroid agents: Carbimazole; Methimazole; Methylthiouracil; Propylthiouracil; Thiouracil
- Agents for dental hygiene: Sodium lauryl sulfate (toothpaste)
- Diuretics and antihypertensive agents: Captopril; Diazoxide; Ethacrynic acid
- Hypoglycemic agents: Glipizide; Phenformin
- Muscle relaxants and Parkinson treatment drugs: Baclofen; Chlormezanon; Levodopa
- Opiates: Codeine; Hydromorphone; Morphine

Medications (continued)

- Psychopharmacologics: Carbamazepine; Lithium; Phenytoin; Psilocybin; Trifluoperazine
- Sympathomimetic drugs: Amphetamines; Phenmetrazine; Fenbutrazate
- Vasodilators: Oxyfedrine; Bamifylline
- Others: Germin monoacetate; Idoxuridine; Iron sorbitex; Vitamin D

Surgery

- Losses of olfaction after rhinoplasty has been reported
 - Champion et al reviewed 100 consecutive rhinoplasty patients, 20% of patients complained of olfactory loss 6-18 months after surgery; 95% of losses were temporary
- Advances in endoscopic sinus surgery have allowed more accurate surgery and less olfactory damage
- Total Laryngectomy – decreased olfactory ability due to shunting of air away from nasal cavity; studies show olfactory receptors function after many years
- Cranial and Skull Base surgery may lead to total and permanent loss of olfactory ability

Treatment and Management

- Conductive Loss vs Receptive Loss
- Conductive loss of smell: major olfactory dysfunction responsive to treatment of nasal disease
- Opening air passageways:
 - Intranasal steroids
 - Antibiotics
 - Allergy therapy
 - Ethmoid Sinusitis
 - Intranasal tumors

Receptive Loss Treatment

- Vitamin A:
 - Necessary in repair of epithelium
 - White rats become anosmic on Vitamin A deficient diet
 - Mammalian olfactory epithelium with considerable amounts of Vitamin A
 - Duncan and Briggs studied Vitamin A supplementation and found successful restoration of at least partial olfactory ability in 50 of 56 pts
 - Other authors unable to reproduce benefit

Receptive Loss Treatment

- Zinc
 - Zinc-deficient adult mice probable anosmia
 - Severe deficiency rare and difficult to substantiate
 - Occasional reports of improvement in anosmia with zinc therapy
- Aminophylline
 - cAMP role in transduction

Managing Olfactory Loss

- If no known causes found: reassurance
- Discuss improving seasoning of diet for remaining sensory modalities
 - Emphasize taste, color, texture, viscosity and feel of foods
- Smoke and fire detectors are mandatory
- Patients should elicit confidential help for matters of odor
- Switch to electric appliances and non-explosive heating or cooling fuel from natural gas

Management of phantosmia

- Phantosmia: perception of odor in the absence of true odor, most often unpleasant
- Effective therapy is instilling four nasal saline drops in affected nostril with head positioned forward and down
- Topical cocaine hydrochloride administered to olfactory mucosa
 - Lack of good results with risk of total anosmia
- Neurosurgical resection of olfactory bulbs through craniotomy
- Removal of olfactory epithelium from underside of cribriform
 - Requires repair of CSF leak

Conclusions

- One of the most primitive of our senses
- Strong correlation with many of our other senses, our memories, and quality of life in general
- Often not addressed enough with patients
- Anosmia may be a marker for certain conditions and diseases
- Many different conditions can lead to anosmia
- Treatment options are often limited

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