Taste and Smell Dysfunction in Alzheimers Disease and Related Disorders.

Diagnosis, Treatment, Morbidity

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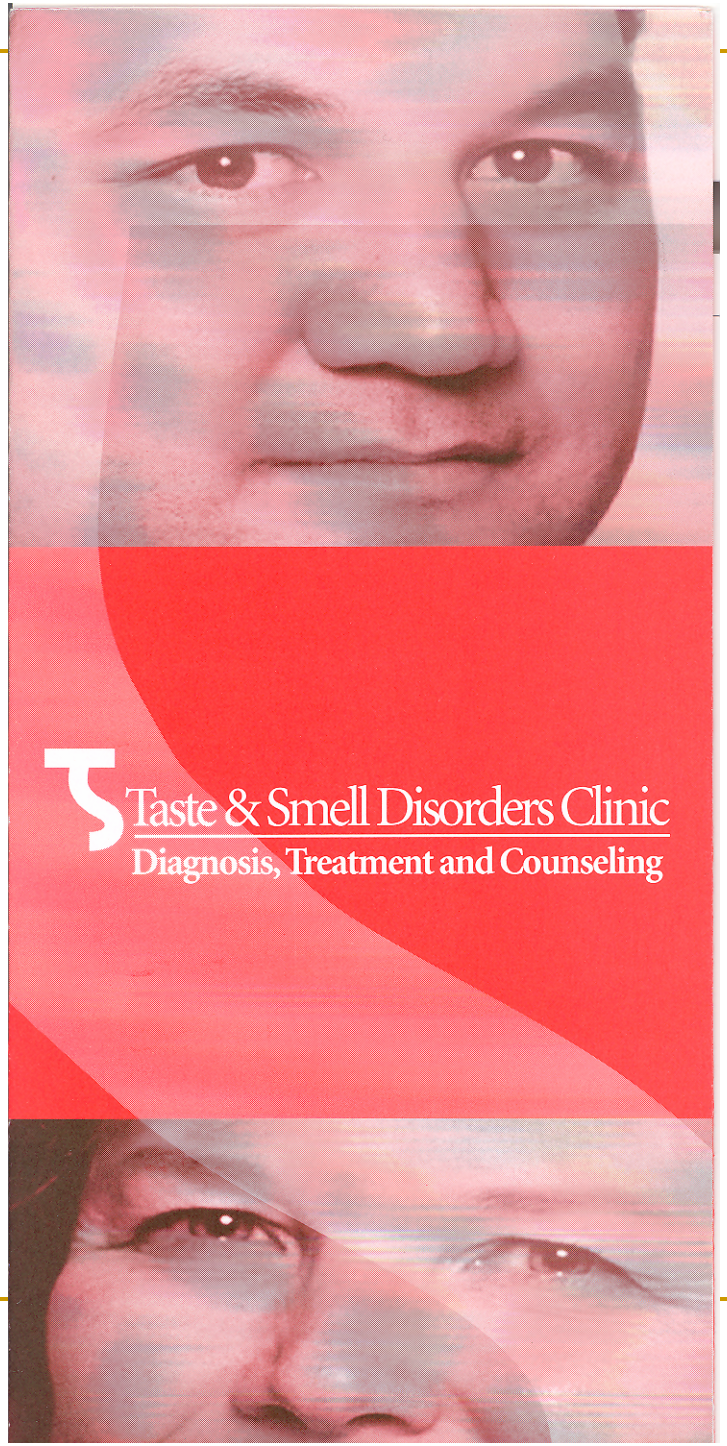
Taste & Smell Disorders Clinic
Diagnosis, Treatment and Counseling

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- TASTE AND SMELL IMPAIRMENT IN ALZHEIMERS DISEASE AND RELATED DISORDERS HAS BEEN RECOGNIZED SINCE THE 1980`S.

- Related Disorders are: Frontal Dementia,Vascular Dementia,Parkinsons Disease & Dementia,Lewy Body Dementia

- NO CURRENT CLINICAL OR RESEARCH EVIDENCE REPORTED, THAT VASCULAR OR FRONTAL DEMENTIA HAVE A SPECIFIC TASTE AND SMELL DISORDER.

CASE STUDY

- M.T. is a 74 year old female in my clinic with a three year history of mild to moderate Alzheimers Disease. She lives with her daughter and has a sitter who stays with her all day till her daughter comes home from work. She is in excellent medical health and is taking only Razadyne ER 16mg/day, Namenda 20mg/day and a baby aspirin.She is a non smoker.

- Over a three month period,her daughter noted that she had less interest in eating,picking at her food,and lost 12 pounds. Her family physician saw her for weight loss and ordered a panel of blood tests,urinalysis, chest and abdominal xrays and stool analysis for blood. All these tests were normal. He was concerned that her Alzheimer drug Razadyne could be causing her reduced appetite and weight loss.He suggested she discontinue Razadyne and be referred to a gastroenterologist.

- In the meantime,she had come back to see me for followup exam. In addition to my regular followup exam for her dementia,I listened to the story of weight loss and decreased appetite.I asked the patient if she had noticed a change in the taste of her food,or wether her smell had changed. The patient told me that many of her favorite foods didn’t taste the same.

- Her daughter remembered her mother saying that on occasion.
- I was concerned about 2 issues that could be causing her change in appetite and weight loss. 1. She was likely experiencing a smell impairment that is common and usually unrecognized in Alzheimers disease,which in turn interferes with taste. 2.She has been staying daily with a sitter who has not played a very active stimulating role in her care.

- I did not believe Razadyne played any role in her weight loss,since she had been taking it for over 2 years without any problems.Alzheimers medications rarely cause this problem,and if it does,it occurs very early on. I also did not feel that a gastrointestinal consult was needed right at this time until a different treatment approach was attempted.

CASE STUDY (continued)

- How did I treat M.T.,the 74 year old mild to moderate Alzheimers patient with 3 month history of weight loss and decreased appetite
- First , with the help of our questionaire I asked the daughter to sit down with M.T. and compile a list of all her favorite foods,spices and what she normally has been eating prior to her weight loss and decreased appetite.

- I gave M.T. a few samples of the smell test,knowing,because of her dementia, she may have problems choosing the correct smell from a list of choices. I gave her samples of very common and easy smells like gasoline and coffee,which she could not identify. I felt confident from this simple smell test and the knowledge from research studies that she most probably had moderate smell loss with secondary taste change.

- This meant that her basic tastes appreciation (sweet,sour bitter,salt and umami) were normal. Her Trigeminal system(appreciation for food texture,hot and cold and spices)was intact. However her ability to recognize and appreciate Flavors was seriously impaired.
- With the help of our clinic food consultant we put together some recipes and modified her regular previous enjoyable foods with emphasis on flavor enhancement(adding flavors,small amounts of MSG and spices)

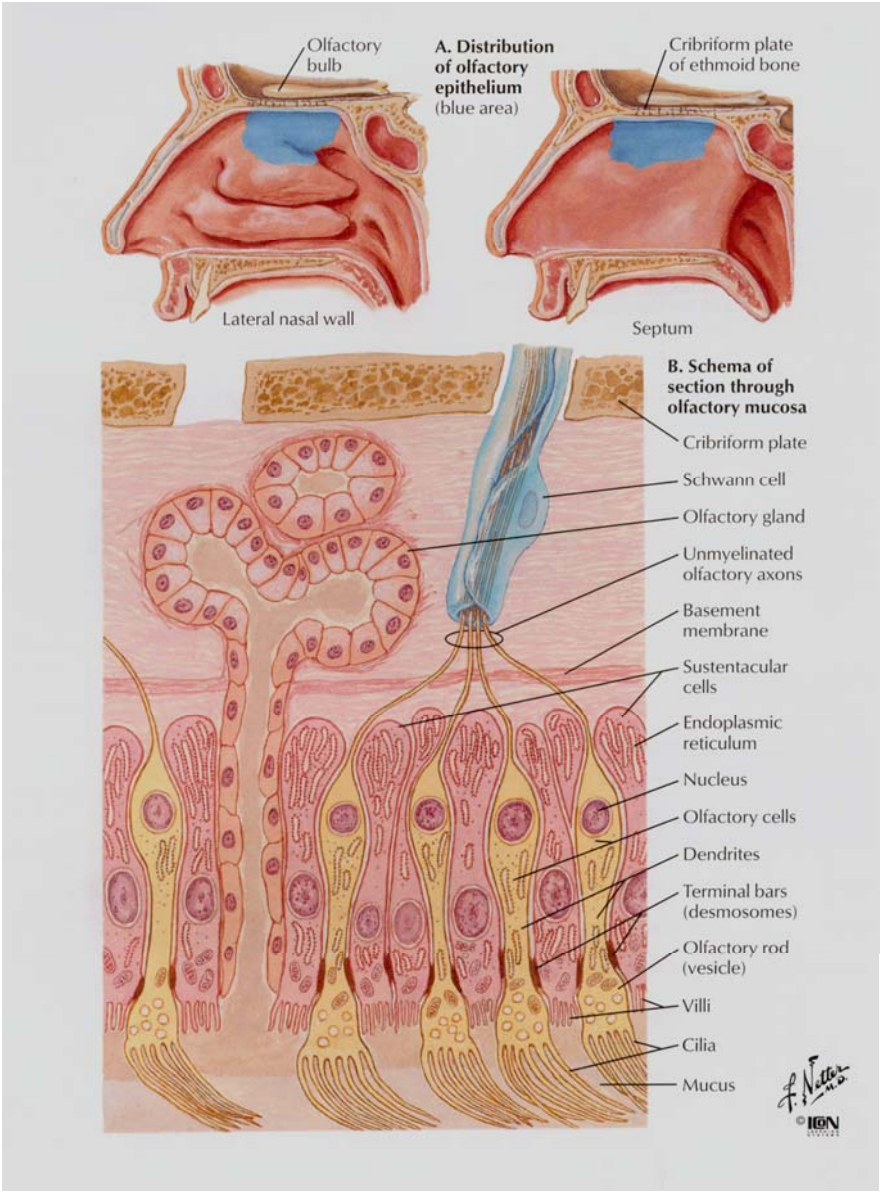
- We also told the daughter that her working all day from early morning till evening and having a sitter to oversee her mother is producing social isolation. This has been shown to produce loss of appetite,weight loss and disinterest in eating. Humans are very social,and interest and pleasure from eating also depends on social contact.Going out to eat with family can also improve food intake.
- I suggested she make breakfast and dinner, for herself and her mother and socialize awhile. The sitter should do the same at lunch,not just tell her to eat.

- With these suggestions,M.T. gradually increased her food intake and gained 3 pounds in 2 weeks. We continued to moniter her weight and appetite and 3 months later she gained most of her wight she had previously lost.

BASIC ANATOMY AND FUNCTION OF SMELL AND TASTE

- OLFACTORY ORGAN,VERY SMALL,LOCATED IN APEX OF NOSE.
- DETECTS ODORS
- DETECTS FLAVORS(chocolate,vanilla) Main reason why olfactory disorders present most often as taste complaints
- TASTE RECEPTORS ARE WIDESPREAD.

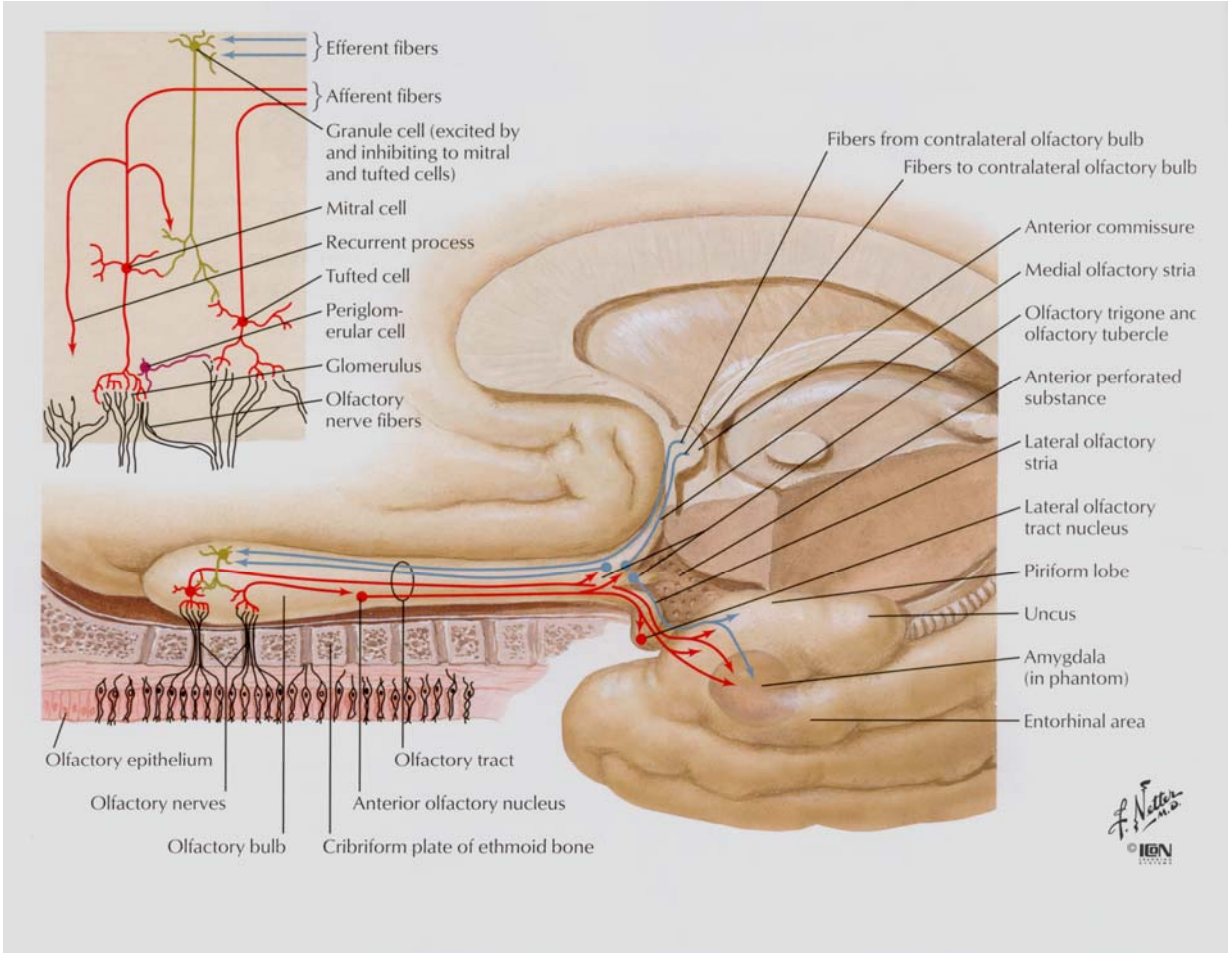
  (tongue,palate,upper pharynx)


Olfactory bulb
A. Distribution of olfactory epithelium (blue area)
Cribriform plate of ethmoid bone
Lateral nasal wall
Septum
B. Schema of section through olfactory mucosa
Cribriform plate
Schwann cell
Olfactory gland
Unmyelinated olfactory axons
Basement membrane
Sustentacular cells
Endoplasmic reticulum
Nucleus
Olfactory cells
Dendrites
Terminal bars (desmosomes)
Olfactory rod (vesicle)
Villi
Cilia
Mucus

OLFACTORY ANATOMY

- SEPTAL AREA VIA CINGULATE TO HIPPOCAMPAL FORMATION
- AMYGDALA TO PARAHIPPOCAMPAL GYRUS ,THALAMUS AND SEPTAL AREA
- PRIMARY OLFACTORY CORTEX (uncus and prepyriform cortex)
- ORBITAL FRONTAL CORTEX(association)

CENTRAL OLFACTORY ANATOMY

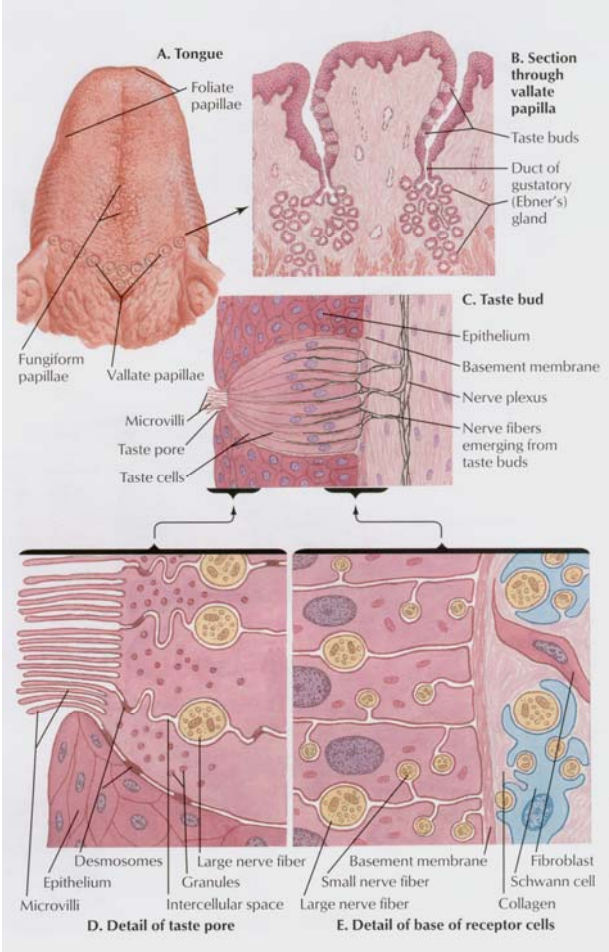


0LFACTORY PHYSIOLOGY

- ALL OLFACTORY CELLS(10 million) RESPOND IN VARYING DEGREE TO MOST ODORANTS/FLAVORS REGARDLESS OF STRUCTURE
- OLFACTORY NEURONES VARY DISCHARGE RATE ACCORDING TO ODOR CONCENTRATION
- PLEASANT AROMAS PROCESSED IN LEFT BRAIN,UNPLEASANT IN RIGHT

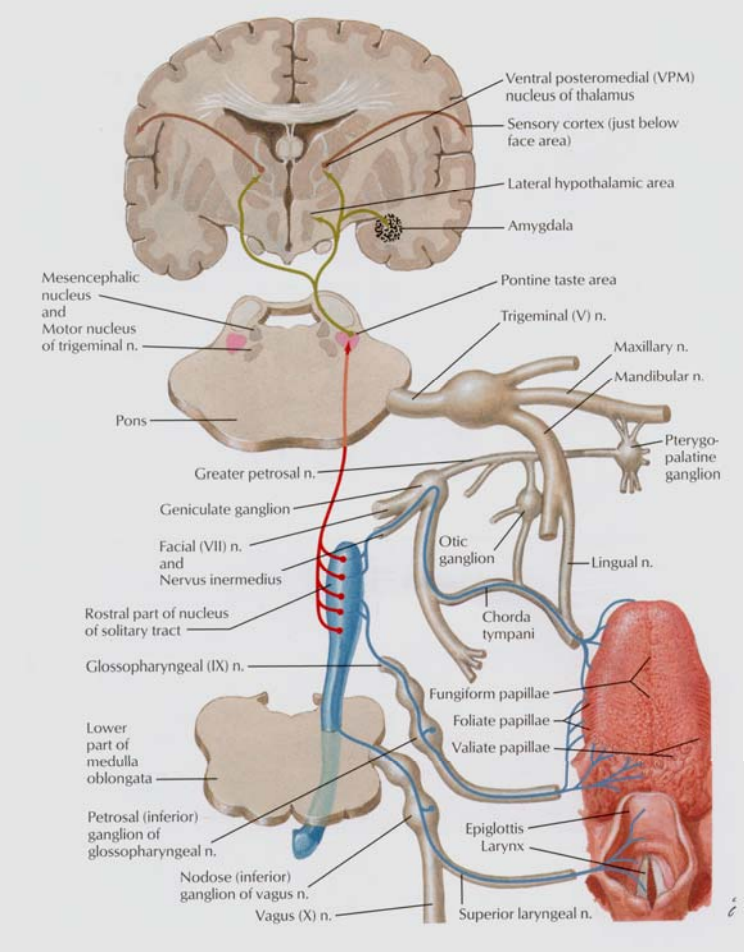
- ANATOMY
- Taste organ made up 10,000 taste buds present on tongue,soft palate,posterior mouth and upper esophagus
- Each taste bud has 50-150 receptor cells
- Taste receptors regenerate every 10-20 days
- Collection of taste buds form papillae on the tongue

TASTE BUD ANATOMY



- ANATOMY (cntd)
- Nerve fibres from cranial nerves 7,9 & 10 travel to Solitary nucleus in medulla,ipsilateral to central tegmental tract to posteromedial ventral nucleus of thalamus,to: 1.Frontal opercular and insular cortex 2.amygdala and hippocampus
- Some gustatory fibres cross in lower midbrain

NEUROANATOMY OF TASTE



- THERE ARE 5 TASTE SENSATIONS: Sweet,Sour,Bitter,Salt & Umami(savory,msg)
- TRIGEMINAL NERVE RESPONSIBLE FOR:

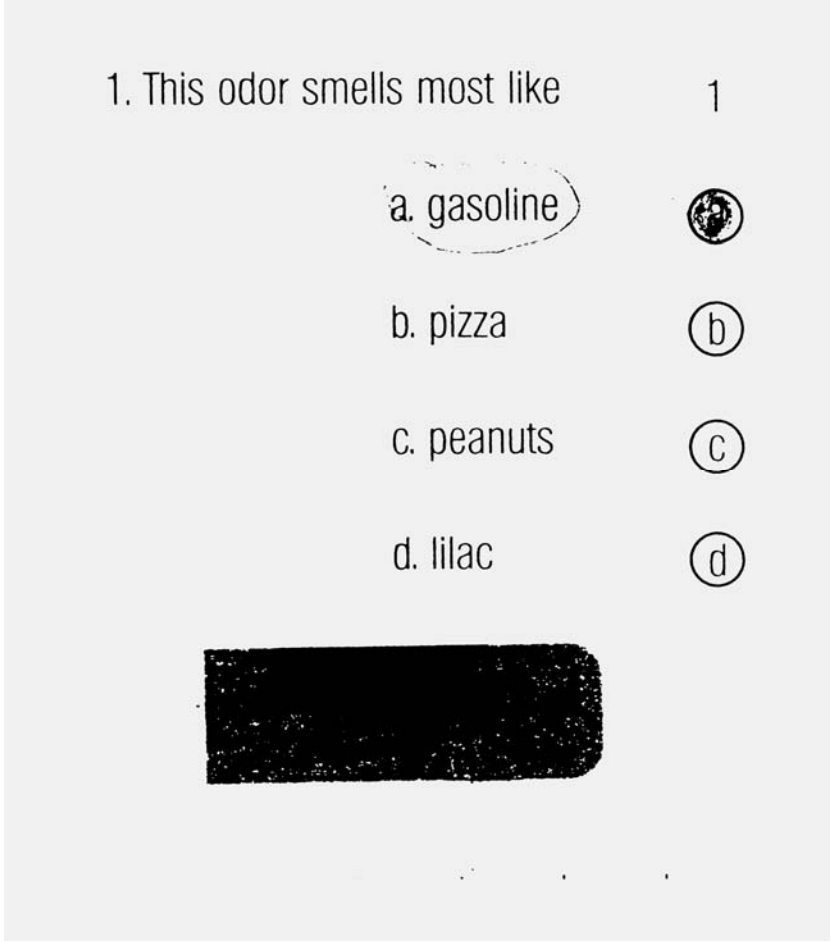
  Texture,temperature & taste of Spicy food

Over 90% of patients with taste complaints usually have an OLFACTORY disorder on testing. Primary taste disorders less frequent.

CLINICAL EVALUATION OF OLFACTORY DISORDERS

- SMELL TESTING
  University of Pennsylvania Smell Identification Test (UPSIT)
  a. 40 item scratch and sniff test,forced choice
  b. normal values studied in 4000 normals across age and gender ,very easy to perform
  c. valuable in peripheral and central disorders
  d. high test and retest reliability
  e.BEST STANDARDIZED TEST AVAILABLE
  f. THIS TEST used in majority of studies

UNIVERSITY OF PENNSYLVANIA SMELL IDENTIFICATION TEST



1. This odor smells most like 1

a. gasoline

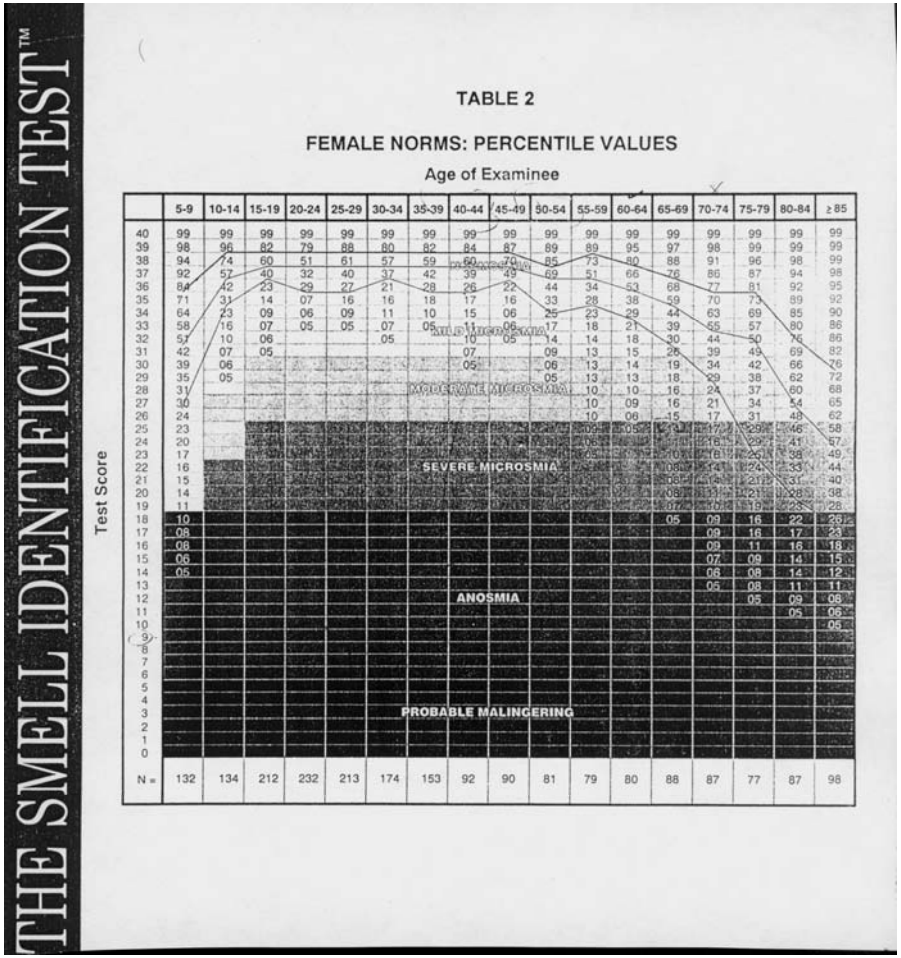
b. pizza (b)

c. peanuts (c)

d. lilac (d)

[redacted]

UPSIT


THE SMELL IDENTIFICATION TEST™
TABLE 2
FEMALE NORMS: PERCENTILE VALUES
Age of Examinee
Test Score
5-9 10-14 15-19 20-24 25-29 30-34 35-39 40-44 45-49 50-54 55-59 60-64 65-69 70-74 75-79 80-84 ≥ 85
MILD MICROSMIA
MODERATE MICROSMIA
SEVERE MICROSMIA
ANOSMIA
PROBABLE MALINGERING
N = 132 134 212 232 213 174 153 92 90 81 79 80 88 87 77 87 98

- TASTE EXAMINATION
  No standardized test,like UPSIT for smell, is available.
- Whole Mouth Taste Test is frequently used.

PRIMARY TASTE DISORDERS: CLINICAL ASSESSMENT

- WHOLE MOUTH TASTE SOLUTIONS : Sweet(1 M sucrose) Salt(1 M Nacl), Bitter(.001M caffeine), Sour(.032M citrate) , Umami(1 M msg) USE DISTILLED WATER
- Patient asked to swish 5ml of water ,rinse, then 5ml of a solution. They are asked to identify which sample had a taste and, the name of the taste. All solutions are used.

CLINICAL EVALUATION OF OLFACTORY DISORDERS

- IMAGING
- High resolution Cat Scan is best source to evaluate sinus and nasal tract disease
- CT scan with 5mm cuts can show bony structures in Ethmoid,Cribiform plate,Olfactory cleft & temporal bone near Cranial nerve 7 and Chorda Tympani

CAT SCAN OF NASAL AND SINUS REGIONS

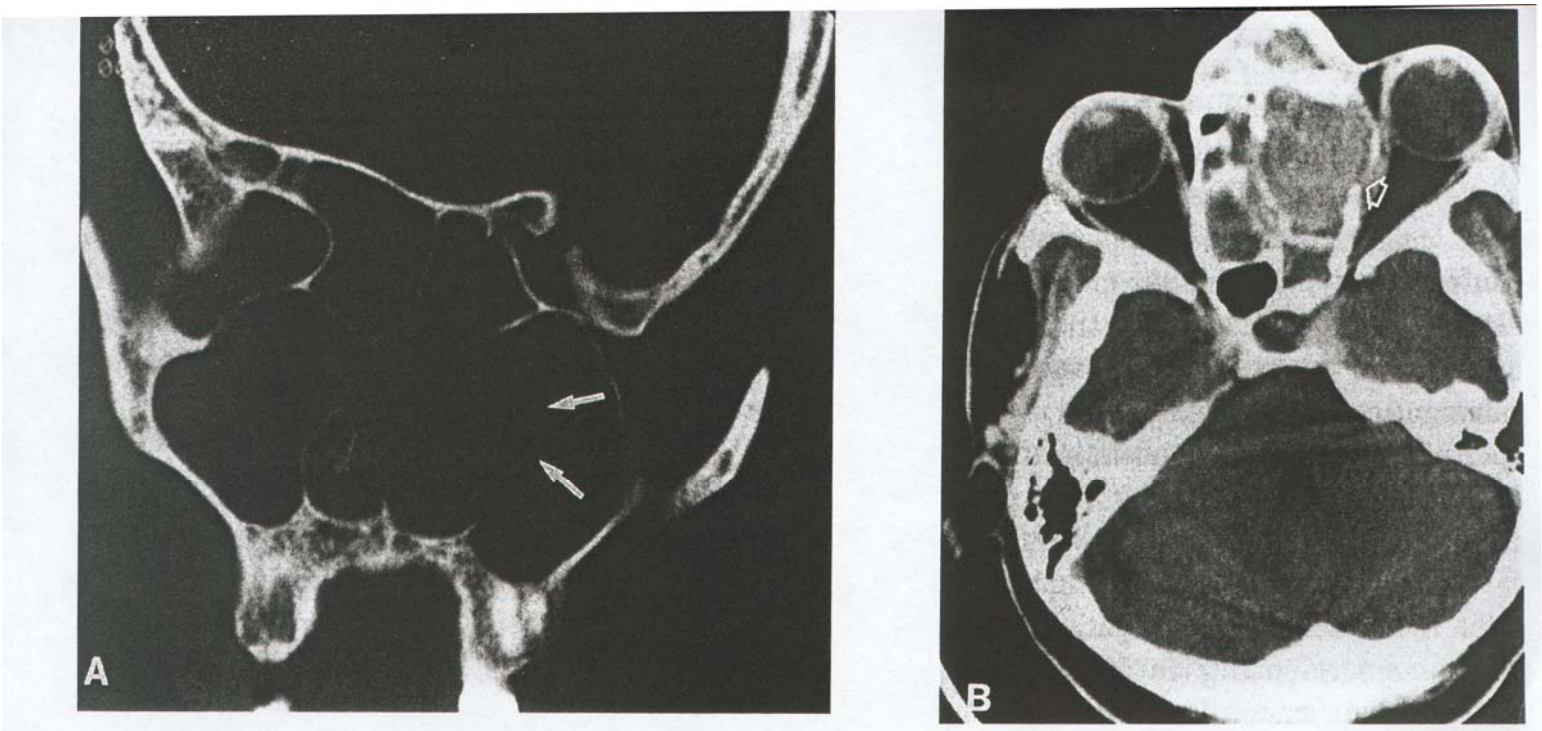


Figure 1 A 40-year-old woman with 3-month history of decreasing smell sensation and left nasal obstruction. (A) nal CT shows an expanded opacified left nasal cavity with bowing of the lateral nasal wall (arrows) and opacificati lary and both sphenoid sinuses. (B) Axial contrast-enhanced CT scan shows erosion through the left lamina pap displacement of the medial rectus and globe laterally. The differentation between tumor and obstructed secretions is with CT. Histological diagnosis: nasal cavity carcinoma arising within a dysplastic inverted papilloma.

CLINICAL EVALUATION OF OLFACTORY DISORDERS

- IMAGING (CNTD)
- MRI with contrast,superior ,evaluating soft tissue like olfactory bulb,tracts,facial nerve,inferior frontal and medial temporal lobes,skull base invasion of sinonasal tumors or dural leptomeningeal involvement.
- Conventional nuclear medicine scans only used in CSF leaks

NORMAL MRI OF OLFACTORY SYSTEM (CORONAL VIEW)

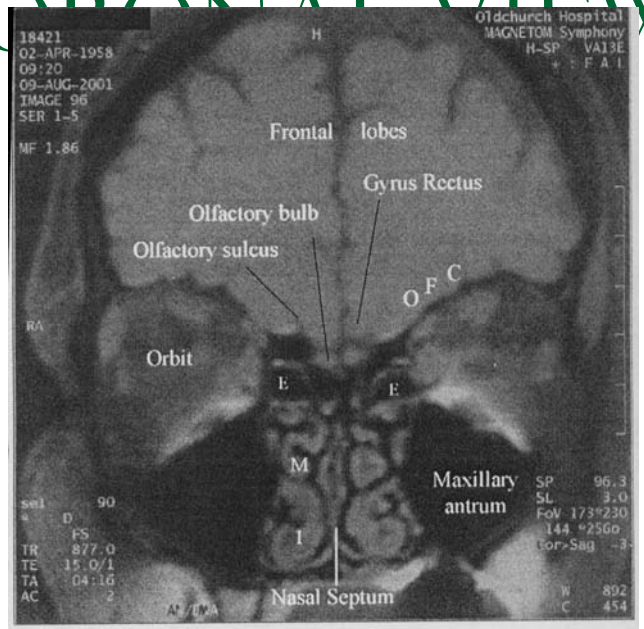


Figure 1-2. MRI scan (coronal T1 weighted) in healthy 45-year-old woman showing frontal lobes, orbits, olfactory bulbs, olfactory sulcus, and gyrus rectus. OFC is the orbitofrontal cortex. Letter "E" indicates part of the ethmoid sinuses that are frequently honeycomb structures. Letter "I" is the right inferior turbinate; "M" is the right middle turbinate. The superior turbinate and infundibulum are not clearly shown due to the posterior coronal section.

CLINICAL EVALUATION OF OLFACTORY DISORDERS

- NASAL ENDOSCOPY
  Main reliable way to evaluate nasal structures and olfactory organ.
  Safe office procedure done by ENT physician
  Should be routinely done in undiagnosed patients and in postviral and nasal trauma induced smell loss to assess damage and prognosis(scarring,polyps etc)

FUNDAMENTAL CLINICAL PEARLS

- Prevalence of smell loss in aging population is 25% age 55 and older. This increases to 75% by age 80. NOTE:Majority, no symptoms, Picked up by smell testing NOTE: smells like chocolate,licorice,rose [2]

Strawberry,watermelon,coconut and grass(no change)

Prevalence more common in men: odorants induce more brain activation in women

- Neurological aging disorders like Alzheimers, Parkinsons etc add further insult

PRIMARY TASTE DISORDERS

- Primary taste disorders much less common than secondary disorders
- Taste acuity decreases with age,but much less than smell
- With age the threshold for salt and sweet increases in foods,not when given pure. 3
- 5 taste sensations: sweet,salt,bitter,sour, & umami(savory,msg)

TASTE DISORDERS

- GENERAL COMMENTS
- Pure loss of taste is very uncommon due to widespread taste receptors and multiple cranial nerve innervation
- Taste sense overall declines with age
- PERIPHERAL DISORDERS INCLUDE: Heavy smoking,poor mouth and dental hygiene,saliva deficiency,dry mouth especially in the elderly,medications,dietary deficiency(B6,calcium and zinc)

CLINICAL FEATURES

- 90% of Alzheimers,parkinsons disease,with /without Dementia & Lewy Body Disease[1,6,7] have moderate /severe smell loss by testing.
- Majority unaware of this. If questioned may say, “food has no taste,I eat because I have to” [6]
- Many develop. WEIGHT LOSS,DECREASE APPETITE & INCREASING DEPRESSION.

- Usually attributed to MEDICATIONS,GI DISORDERS,CANCER AND OTHER DISEASES.
- Smell loss in Alzheimers worsens as disease progresses.(upsit score usually < 30/40, Bsit <7/12. [9]
- Parkinsons w/wo Dementia and Lewy Body Dementia develop maximum smell loss early. Upsit score <25/40. [10]

- 10 odors specifically found to be impaired in Alzheimers: menthol,clove,leather,strawberry,lilac,smoke, pineapple,soap,natural gas,& lemon. [5]
- 5 odors specifically impaired in the Parkinson Disease group : gasoline,banana,pineapple, smoke & cinammon. [11]
- Smell loss in all disorders,unrelated to disability,medication or gender. [12]

- Smell abnormalities in the related disorders predate motor symptoms by 2 yrs.
- Impaired Sniffing occurs in the related disorders which contributes further to smell impairment.
- Smell testing can help separate the related disorders from other parkinson like conditions (progressive supranuclear palsy,cortical basal degeneration,vascular parkinsons etc)

TASTE AND SMELL LOSS:IMPACT ON QUALITY OF LIFE

- Less interest in eating and socializing [8]
- Decrease appetite w/wo weight loss [8,15]
- More likely to eat spoiled food and accept Food with unpleasant odors
- Weight loss common [8,15]
- Weight gain much less common(8%) due to attempt to find the right tasty foods [8,16.]
- Impaired smoke detection,burnt food and gas leaks
- Likely to use much more salt and sugar increasing risk or worsening of Diabetes and High blood pressure.

WHY SMELL AND TASTE LOSS IN ALZHEIMERS & RELATED DISEASE

- In Alzheimers,amyloid plaques and neurofib tangles,the hallmark of this disorder are found in: smell organ in nose,olfactory bulb,and medial temporal lobe of the brain.
- In Parkinsons w/wo Dementia and Lewy body disease, Alpha synuclein,amyloid and Lewy bodies,the hall mark of these disorders are also found in the entire olfactory system as in Alzheimers. 6,7,23

TREATMENT OF SMELL AND TASTE LOSS IN THESE DISORDERS

- EDUCATION ,HEALTH AND SAFETY.

- Inform the patient and caregiver about smell and taste changes in these disorders and that weight changes,decreased appetite and depression can often occur. (use a model or pictures of the smell and taste system to show where the abnormalities occur.)

TREATMENT (CNTD)

- Place of residence should have a working smoke alarm and gas leak moniter.
- All perishable foods should be properly stored in the fridge and opened foods labeled and dated.(many patients with mild dementia can still read and understand these labels.It also informs outside help about these foods)
- Carefully observe the amount of ingredients add to recipes.

- Encourage and moniter the use of appropriate amounts of perfume and deoderant.

SMELL AND TASTE DISORDERS: WORK UP

- Detail Hx(meds,trauma,smoking,cognitive change) & exam(tongue,gums,CN1 5,7,9,10 ,cognition)
- Smell testing (General or Alzheimer BSIT,UPSIT)
- Whole mouth taste testing(sweet,sour,salt.
- Cbc,sed rate,B12,folate,fasting glucose,TSH metabolic profile(hepatic,renal ,ANA,antibody screen(sjogrens etc), Zinc level.
- MRI Brain,olfactory regions & petrous temporal bone,ENT evaluation (nasal endoscopy)

TREATMENT (CNTD)

- COMPENSATION STRATEGIES: FOOD PREPARATION
- Remember that palatability of food depends on: SMELL,TASTE,TEXTURE,TEMPERATURE, FLAVORS,AND VISION.
- Alzheimers and related disorders often have: IMPAIRED SMELL AND FLAVOR DETECTION, NORMAL BASIC TASTE(sweet,sour,salt,bitter,umami) NORMAL DETECTION OF TEMPERATURE,TEXTURE AND SPICYNESS & USUALLY REASONABLE VISION.

FOOD PREPARATION: GENERAL PRINCIPLES

- The patient and/or caregiver should compile a list of foods and spices that have always been enjoyed.
- Choose and prepare foods that have a good appearance and texture. Foods that are bulky.sticky,thick and creamy stay in the mouth longer and stimulate all the taste and sensory receptors for a longer time.(be sure no swallowing issues)

- Prepare some foods and beverages with oranges and lemons to give a tart like taste which stimulate the mouth sensory nerves & sour and sweet receptors on the tongue and inside mouth.
- Hot and steamy foods are often more appreciated because they permeate all nasal and mouth sensory receptors
- Fish,Chicken or Beef can be marinated in sweet or tart fruit juices,wine,sweet and sour sauce or salad dressing.

- Add any of the enjoyed spices to baked potato,steak,chicken or beef(eg. SALSA, MUSTARD,TOBASCO SAUCE,etc)
- Monosodium Glutamate(MSG),is responsible for the appreciation of the savory taste of beef and chicken,and best emphasized in chicken broth and chinese food.This UMAMI taste is spared in the smell impaired and elderly.

- Adding a pinch of MSG,to many different foods,or eating foods with high MSG concentrations can enhance palatability and flavor. MSG has one tenth the amount or sodium than regular table salt and can be helpful to lower blood pressure .
- NOTE: 19% of the normal population can not taste MSG due to genetic reasons,and a tiny percent of the population may get some congestion or headache.(much overplayed in our society)

Table 2. Free glutamate in foods (mg/100g)	
Meat and poultry	
Beef	10
Pork	9
Chicken	22
Seafood	
Scallop	140
Snow crab	19
Blue crab	43
Alaska king crab	72
White shrimp	20
Seaweed	
Dried lever	1378
Konbu (Dried seaweed)	1608
Wakame (*Undaria pinnetifida*)	9
Vegetable	
Cabbage	50
Spinach	48
Tomato	246
Green asparagus	49
Corn	106
Green peas	106
Onion	51
Potato	10
Shampignon	42
Shiitake mushroom (fresh)	71

Fruits	
Avogado	18
Apple	4
Grape (*V.labrusca*)	5
Kiwi	5
Cheese	
Emmental	308
Parmigiano reggiano	1680
Cheddar cheese	182
Milk	
Cow	1
Goat	4
Human breast milk	19
Concentrated extract s (Paste)	
Vetemite	1431
Marmite	1960
Bovril	498
Oyster sauce	900

TREATMENT OF OLFACTORY AND SECONDARY TASTE PROBLEMS

- COMPENSATION STRATEGIES: FOOD PREPARATION
- Little information in literature in regard to specifics of food preparation
- Different needs in food prep for other family members creates difficulty.
- Devere and Food professionals(04): Pilot study of blinded 7 anosmics and 3 normals, 15 recipes with various concentrations of spices and tastants

Treatment: Compensation strategies Food Preparation

- Study found some recipes that were easy to make and satisfied the taste of normal and smell impaired subjects.

ASIAN CHICKEN SALAD

This recipe was modified for taste and smell disorder patients by enhancing standard tastants (sweet, sour, bitter, etc) in the vinaigrette recipe in order to trigger trigeminal stimulation. Otherwise, the ingredients remain constant.

VINAIGRETTE

½ cup say sauce
3 tablespoons seasoned rice vinegar
3 tablespoons vegetable oil
2 tablespoons Asian sesame oil
2 tablespoons Dijon mustard
2 tablespoons finely grated, peeled, fresh ginger
2 teaspoons dried hot red pepper flakes

Variations

B – 1 1/5 tablespoons vinegar

C - 1 tablespoon tarragon

D – 1 ½ teaspoons salt

SALAD

4 cups coarsely shredded cooked chicken (about 1 pound)
½ pound Napa cabbage, cut into 1 inch pieces (3 ½ cups)
¼ pound snow peas, cut diagonally into 1 inch pieces
1 seedless cucumber, quartered lengthwise and cut into 1/2 inch pieces
3 scallions, finely chopped
½ cup chopped, fresh cilantro

Whisk together all vinaigrette ingredients.
Toss salad ingredients with vinaigrette in a large bowl until well combined

TANDOORI SALMON

4 Salmon Fillets, 6 oz each
2 teaspoons cayenne pepper
1 teaspoon salt and ½ teaspoon of freshly ground black pepper
2 teaspoon coriander seeds
2 teaspoons cumin seeds
2 teaspoons black or yellow mustard seeds
½ cup plain yogurt
2 tablespoons chopped, fresh ginger
2 cloves chopped garlic

Variations

B – ½ seeded of 1 jalapeno (seeded), 1/8 teaspoon cayenne

C – 1 tablespoon ginger

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½ cup plain yogurt
2 tablespoons chopped, fresh ginger
2 cloves chopped garlic
2 chopped, seeded jalapeno peppers

Variations

B – ½ seeded of 1 jalapeno (seeded), 1/8 teaspoon cayenne

C – 1 tablespoon ginger

Place salmon fillet in a shallow dish. Combine cayenne, salt and black pepper. Sprinkle over fish and let sta 30 minutes. Combine coriander, cumin and mustard seeds in small skillet over medium high heat. Toast, shaking pan often until seeds pop and start to color. Transfer to blender. Add yogurt, ginger, garlic and jalapeno and grind until smooth. Spread over fish, cover and refrigerate 4 hours. Heat oven to 450 degrees. Brush most of marinade off of the salmon leaving a thick glaze. Transfer to foil lined baking sheet. Roast about 10 –12 minutes. Top should be crusty, if not, place under broiler quickly.

Simple food preparation suggestions by our smell and taste impaired patients they have found helpful in improving taste and palatability.

Steaks: salty seasonings

Hamburger: Charred on grill (almost burnt)

Fish: Salmon with chopped onions on top, grilled

Pork: Grilled, just as hamburger, almost burnt

Chicken: BBQ Sauce during cooking, and after cooking

Beef: Salty seasoning, grill seasoning, and Grilled

Suggested recipes by our Smell and Taste impaired patients they found helpful in improving taste and palatability.

BBQ Ground Beef

1 lb. ground beef
2 tbsp. mustard
1 cup green pepper chopped
1 cup diced onion
1 tsp. salt
1 cup of ketchup
1 tbsp. vinegar
1 tsp. cloves
2 Tbsp. liquid smoke (Figaro Brand)

Saute meat and mix other ingredients as listed. Cook on low heat for 30 minutes
Serve on hamburger buns.

MEATLOAF

1 ½ lbs. ground beef
1 cup fresh bread crumbs
1 finely chopped onion
1 egg
1 ½ tsp. salt
¼ tsp. pepper

(Sauce)

1 can tomato sauce
1 can tomato paste
½ cup water
3 tbsp. vinegar
3 tbsp. brown sugar
2 tbsp. prepared mustard
2 tsp. Worcestershire

Mix together meat, bread crumbs, onion, beaten egg, salt, pepper, and ½ of the can of tomato sauce from the sauce recipe. Form into a loaf and place in and 7x 10 inch pan.

Combine all the ingredients together for the sauce and mix well. Pour over the loaf. Bake 350 Degrees for 1 hour and 15 minutes

Smell Loss as it relates to : Cognitive changes,MCI,pathological and clinical AD

- Studies suggest that normal elderly with no smell or taste complaints,moderate impaired smell testing and followed for 4 yrs develop more short term verbal memory problems and faster rate of cognitive decline compared to elderly with normal or mild smell loss.[17,18]
- One study showed that 15% of normal elderly,with no smell complaints but moderate smell loss on testing,were found to have moderate Alzheimers changess in the medial temporal lobe at autopsy.[19]

- Recent study of 589 cognitively normal elderly who had smell testing,had greater than 50% risk of developing amnestic MCI if their Bsit score was 8/12 or less,compared to Bsit score of 10 or more/12.[20]
- 60% of People with amnestic MCI have been shown to be actually in the very early stages of Alzheimers.40% of the remainder could improve or remain the same.[22]

- Smell testing using Bsit score less than 8/12 or Upsit score less than 34/40 and being sure no other cause is present for smell loss, can be helpful in predicting the development of AD.(100% sensitive,50% specific)in MCI patients.
- This testing can be helpful in AD prediction.
- studies combining smell testing and other possible predictive tests like Pet Scans,ApoE4 testing,Spinal fluid for Tau and Beta amyloid etc should be done.
- Further studies are needed. However smell testing is the least expensive and very easy to perform.

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