Culinard 2004
Taste and smell in cancer.

Introduction:

With prolonging of life and the aging process,; cancer is and will continue to be a major health issue.

One in many, not the least important yet critical problem; is the ability of patients with cancer to support normal nutrition.

Basic assumptions are that cancer, a state of abnormal cellular behavior, imposes a catabolic state on the individual.

Documented further by recent technological development; PET scan is able to obtain images of cancer cell locations on the basis of the incorporation of radioactibly labeled glucose, as the result of their hyperactive metabolism.

If the individual is unable to keep up to the demand on the basis of incorporation or intake of nutrients; then malnutrition and weight loss is ensued.

Possible participation of endogenously released cytokines such as Interleukins, tumor necrosis factor.

Additionally, the cancer treatment modalities, are up today. Causes are substantial changes to taste, smell, and appetite. By either psychological trauma, neurochemical changes. Inflammatory cytolytic damage to the mouth, nose, gastrointestinal tract.

Infection, nausea, and vomiting further complicate cancer therapy.

Palliative modalities are pain control. Use of narcotic pain medications such as codeine, morphine and analogs, affect directly the central nervous system (limbic system). This affects the function of the gastrointestinal tract causing severe constipation and nausea and vomiting.

Most culinary literature available address the issues by attempting to minimize the smell of preparation, the impact of taste on intake and maximize appealing by garnishing and coloring.

Most nutritional literature available address the issues by the drastic use of involuntary nutrition such as total parenteral nutrition or TPN; tube feeding via gastrointestinal infusion through nasogastric or percutaneous endoscopicly placed gastric tube (PEG). All of these are unappealing and excessibly expensive interventions.

The use of high calorie oral supplements such as puddings, bars and boosters fail despite their easy availability due to the patient's intolerance. This mostly because of the high carbohydrate content which make the products excessibly sweet.

Appetite stimulants such as Marinol or Megace (registered trade names) have the disadvantage of causing mental status changes, sedation (THC). Exceedingly expensive; or in the case of Megace the unabilitity to use it in cases of hormone dependent cancers example (Prostate cancer/a very common cancer in adult males).

The management of cancer induced taste alteration should be aimed to maintaining optimal nutrition.(Brodie 1998) But above all quality of life.

I do not to the least think this is an easy project but will try the best possible.

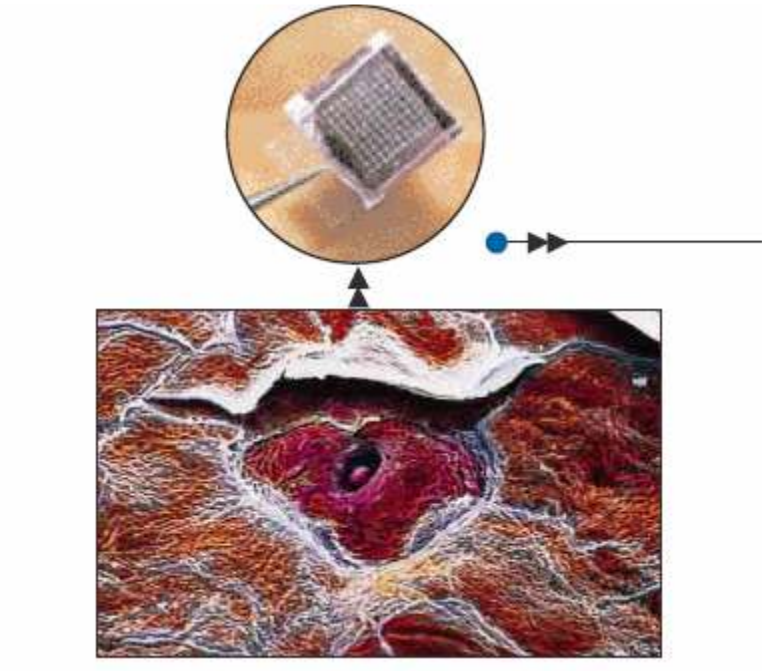
Taste;

Flavor is a complex mixture of sensory inputs (Smith 2001). Its components are gustation (taste), olfaction (smell) and tact (mechanics of chewing).

Described qualities of taste, traditionally, are sourness, sweetness, bitterness and saltiness. Some others may exist; notably *Umami*, most elicited by glutamate, enhancer of taste (commercially available as monosodium glutamate or MSG). The concept was developed by Chaudhari and Roper from University of Miami in 1998.loosely implying a "meaty" taste. Concept still not widely accepted.

Recent studies have described more specific receptors for tasting sensations and further research continues.

Electronic research has developed eSensors for taste in industry

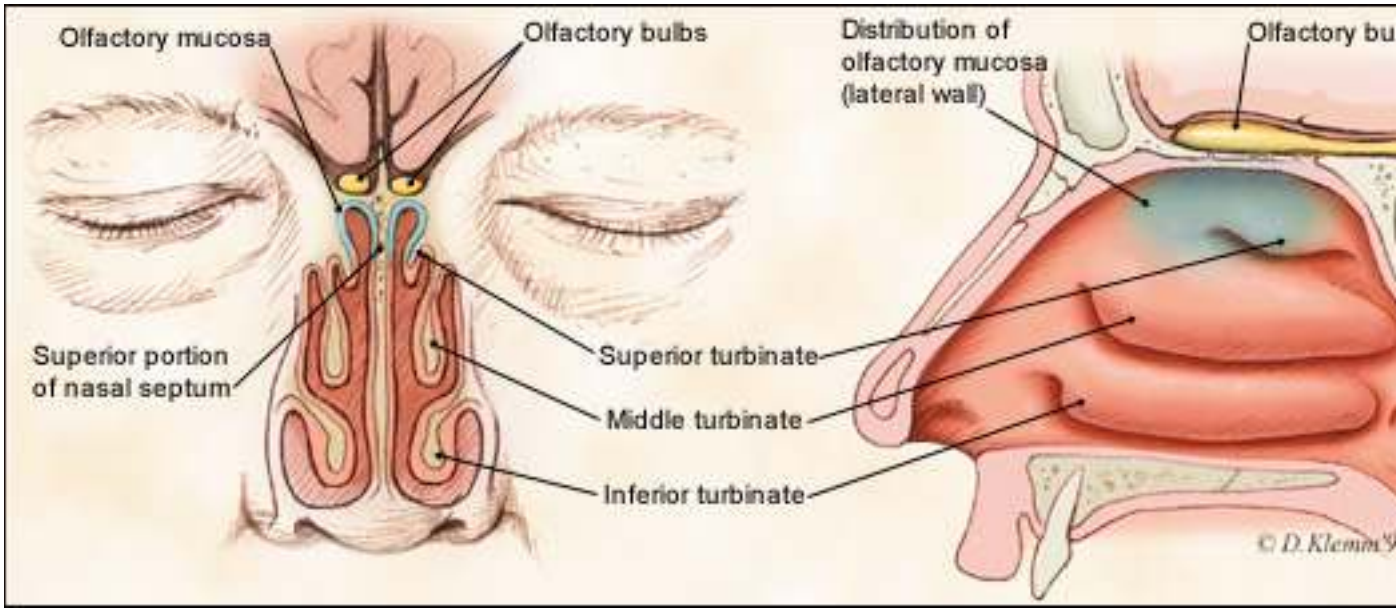


Smell:

Smell has played a very special role in the natural evolution of animals, specially the mammals, many of them nocturnal, had depend on olfactory guidance to detect food, avoid predators recognize territories, social groups and even sexual contact(McGee 1984).

Smell and taste cannot be separated. “Smell and taste form a single sense, of which the mouth is the laboratory and the nose is the chimney; or, to speak more exactly, of which one serves for the tasting of actual bodies and the other for the savoring of their gases” (Brillat-Savarin 1994)

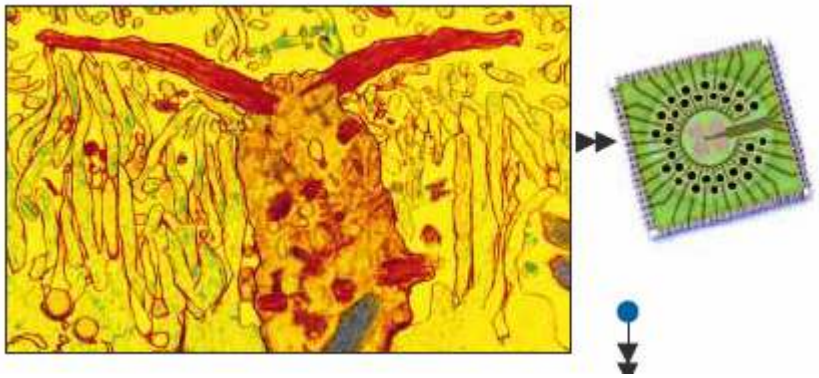
The human sense of smell depends on the functioning of cranial nerve I (Olfactory nerve) such as qualitative odor sensations (smell of roses, lemon or grass); portions (ophthalmic and maxillary divisions) of cranial nerve V (Trigeminal nerve) such as somatic sensory overtones of odorants (warmth, coolness, sharpness and irritation).



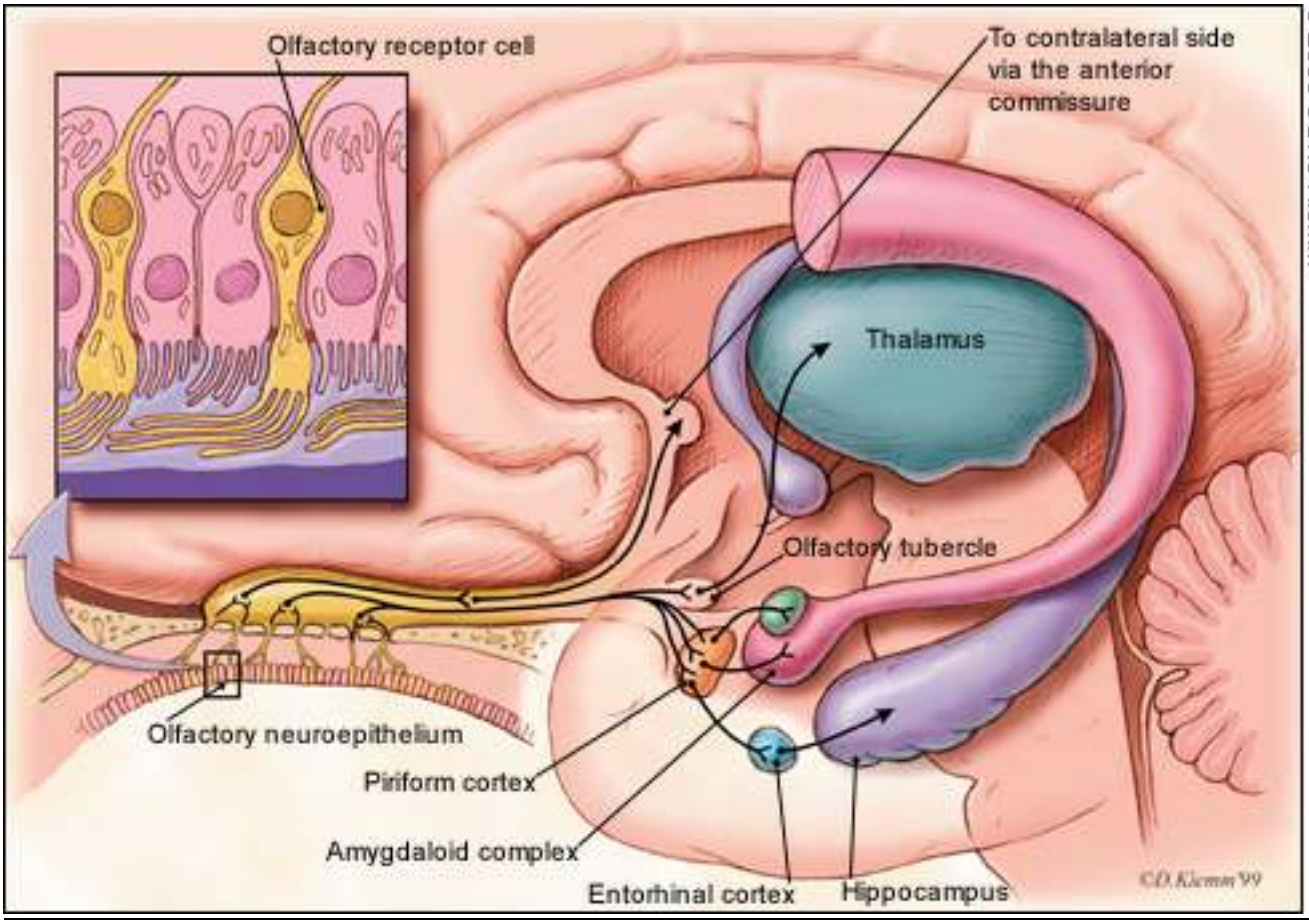
The olfactory neuroepithelium is located over the cribiform plate, the superior septum and segment of the superior turbinate and is rich on smell receptors.

As in the case of taste, odors attach to and dissolve within the covering mucus layer to obtain contact with the receptors.(Doty RL. Bromley SM 1997)

Prototype electronic sensors are been devised such as



Limbic system:



Thermal and mechanical receptors:

Tasting and smelling are not solely what makes it happen. Peppers are used in much cultures as a flavor enhancer, capsaicin, the active substance in peppers, increases the blood flow to the mouth and activate VRI receptor, a membrane channel protein, which exchanges calcium in and out of the cells, has 4 different subunits, which located in different sites of the mouth counts for the different effect in flavor by different kind of peppers. Been fat soluble and heat sensitive improves the taste for fatty food.

Chile Pepper

Peppers are if nothing else taste enhancers.

Their physiological function is based on three principles

Overwhelming inducer of blood supply to the mouth, please note yourself when exposed to minimal amount of peppers applied to your lips. That causes an increased production of saliva, vehicle to distribution of elements of flavor in the mouth. rapid hearth rate, and increase bronchial secretions and indices perspiration (cooling effect)

Depolarizers of the electrical charges to the taste and smell receptor.

Direct stimulant of the brain via pain sensory pathways. By reducing the availability of substance P and increasing levels of prostaglandins; both crucial elements of the inflammatory human response.

Both of them enhancing the brain capacity for taste, smelling; making the act of eating more pleasurable.

All these; well known to other cultures such as Latin America (Jalapeno, ancho), India (Sanaam, dundicut), china (tien tsin pepper). Where the use of peppers is intrinsically part of the culture.

Original of America; Maya, Inca and Aztec; was taken to the old world by Christopher Columbus as a substitute to the better known pepper. The medicinal effects where early recognized, pre-Columbian Mayan prepared *chillatolli* mixed maize flour with Chile, for all kind of respiratory ailments. Aztec would use the direct fruit for toothache pain control; Tukano Indians in Colombia used for the treatment of hangovers; Mayans and Aztecs as infection control for open wounds.

Less important is the assumption of peppers as anticancer chemical. Thought otherwise recognized well as pain controller and widely used in United States of America as anti arthritis, local medicine.

Peppers are not just “hot” they add flavors ex. Paprika

They are all graded in the intensity of the heat according to scale by Scoville heat unit system (Wilbur L. Scoville 1912); which is human rated, consequently subjective and liable to human error; in which by test and dilution pungency is established.

In essence attempt to document the many times dilution in neutral liquid to which the bite can not longer be detected by a normal human being.

The most scientific is high performance liquid chromatography which extracts and measure capsaicinoids chemicals.

SCOVILLE HEAT UNITS SCALE

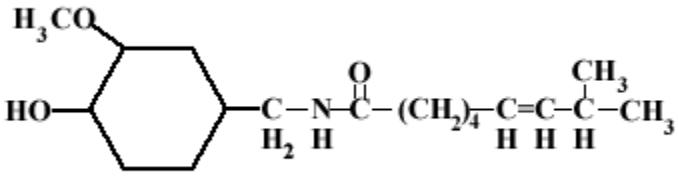
The following is a list of chiles, put into a scale to show the relative pungency levels and their Scoville Heat Units.*

Name	Pod Type	Species	Scoville Units
Orange Habanero	Habanero	C. chinense	210,000
Red Habanero	Habanero	C. chinense	150,000
Tabasco	Tabasco	C. frutescens	120,000
Tepin	Tepin	C annuum	75,000
Chiltepin	Tepin	C. annuum	70,000
Thai Hot	Asain	C. annuum	60,000
Jalapeno M	Jalapeno	C. annuum	25,000
Long Slim Cayenne	Cayenne	C. annuum	23,000
Mitla	Jalapeno	C annuum	22,000
Santa Fe Grande	Hungarian	C. annuum	21,000
Aji Escabeche	Aji	C. baccatum	17,000
Long Thick Cayenne	Cayenne	C. annuum	8,500
Cayenne	Cayenne	C. annuum	8,000
Pasilla	Pasilla	C. annuum	5,500
Primavera	Jalapeno	C. annuum	5,000
Sandia	New	C. annuum	5,000

	Mexican		
NuMex Joe E. Parker	New Mexican	C. annuum	4,500
Serrano	Serrano	C. annuum	4,000
Mulato	Ancho	C. annuum	1,000
Bell	Bell	C. annuum	0

Capsaicin

Chemical Structure of Capsaicin



capsaicin is the main recognized chemically active ingredient. Contrary to most understanding, not located in the seeds but in the placenta which are little sacs located in the fruit inner wall. Very fragile and easy to rupture when opening the fruit, splashing in to the seeds.

Capsaicin binds directly to the receptors (ex taste) and could be unbound by casein, protein obtained from milk, beans, nuts and chocolate (since used as moderators of pungency).

To date there are 14 different capsaicins, named capsaicinoids; each one with quite unique and characteristic properties on the nature of the bite; the location in the mouth that gets activated and the duration of its action.

Nordyhydrocapsaicin gives a mellow warming effect, rapidly on and off mostly at the front of the mouth and the palate.

By comparison dihydrocapsaicin, more potent and affecting the middle of the mouth and palate.

Homohydrocapsaicin is harsh, sharp and irritant, with slow onset, longer duration at the throat, back of the tongue.

Likewise heating of the tip of the tongue produces a sweetness taste, while cooling elicits a sour sensation

The process of mastication reduces the size of the particles to be swallowed, mixes the saliva to bind all together in a safe bolus. Likewise mixes the food for better exposure to digestive enzymes. Most people will chew about 20 cycles before swallowing.

Under normal circumstances the more likable the food the longer the mastication as a source of pleasure.

The slower and longer the mastication the more opportunity for Odorants, volatile molecules to travel up to the smell receptors via the back of the mouth. Case of chewing gums industry.

Neurobiology:

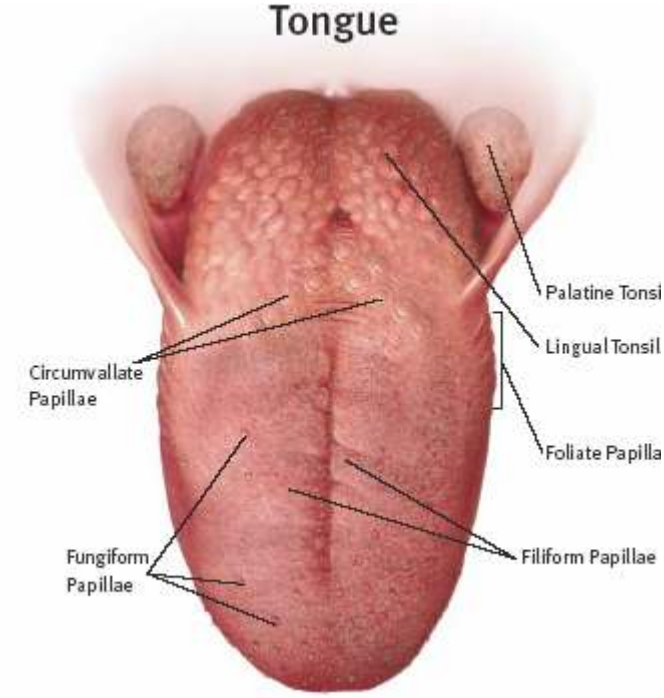
Taste primary sensations: sweet, sour, bitter and salty. Taste buds, receptors and conductors will respond to a sensation in particular but to all to certain degree. So the receptor for sweet will respond to mostly sweet taste but to bitter, sour and salty to a lesser degree.(Wickham 1999)

The locations of the receptors are the tongue, soft palate, glossopalatine arch and the posterior portion of the pharynx.

Most taste receptors are located to the tongue. They are located within the papillae, projection giving the tongue its velvety appearance.

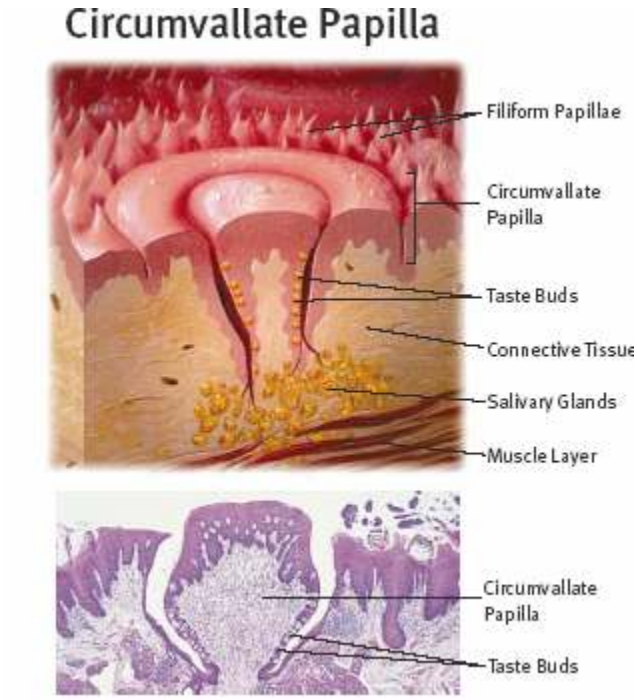
Several geographical areas on the tongue are identified. The tip, rich on taste buds (mushroom like); the back, distributed inverted V, are flat (circumvallates); lateral (folliate).

The filiform like at the from lack of tasting receptors yet provide tactile sensations.

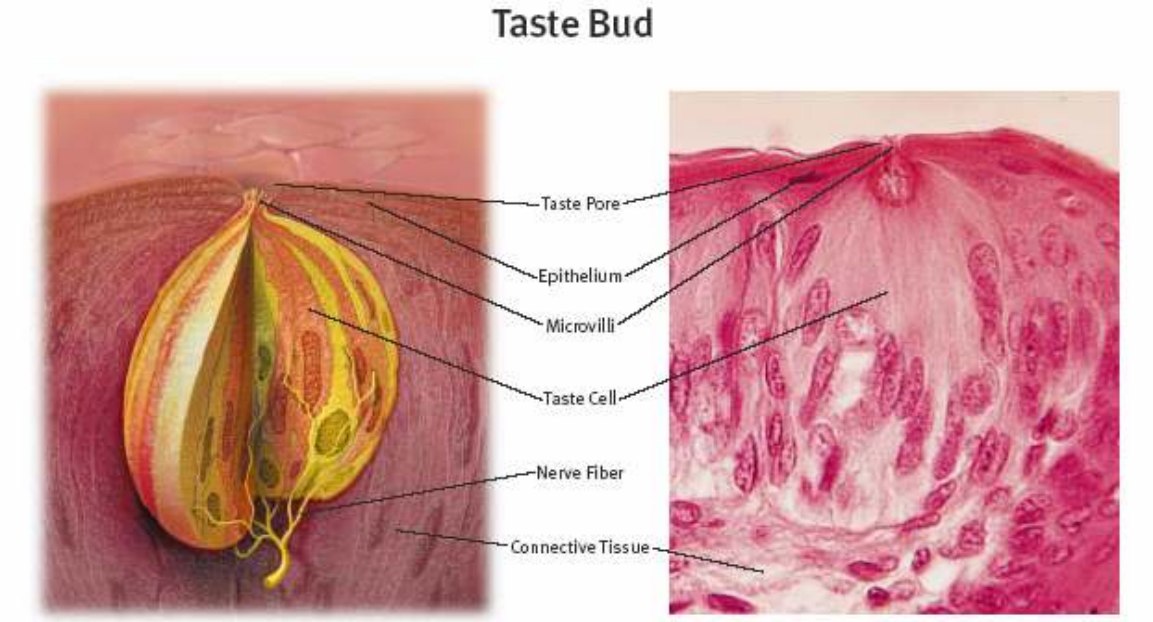


The concept of the geographic tongue is no longer sustainable. As each receptor is capable to react to more than one kind of stimuli at the time. They are not unique to a given taste nor are they geographically distributed as previously thought.

The taste buds contain about 50 to 100 taste cells. They are arrayed in a onion shaped fashion. With small microvilli poking through the opening at the top (taste pore)

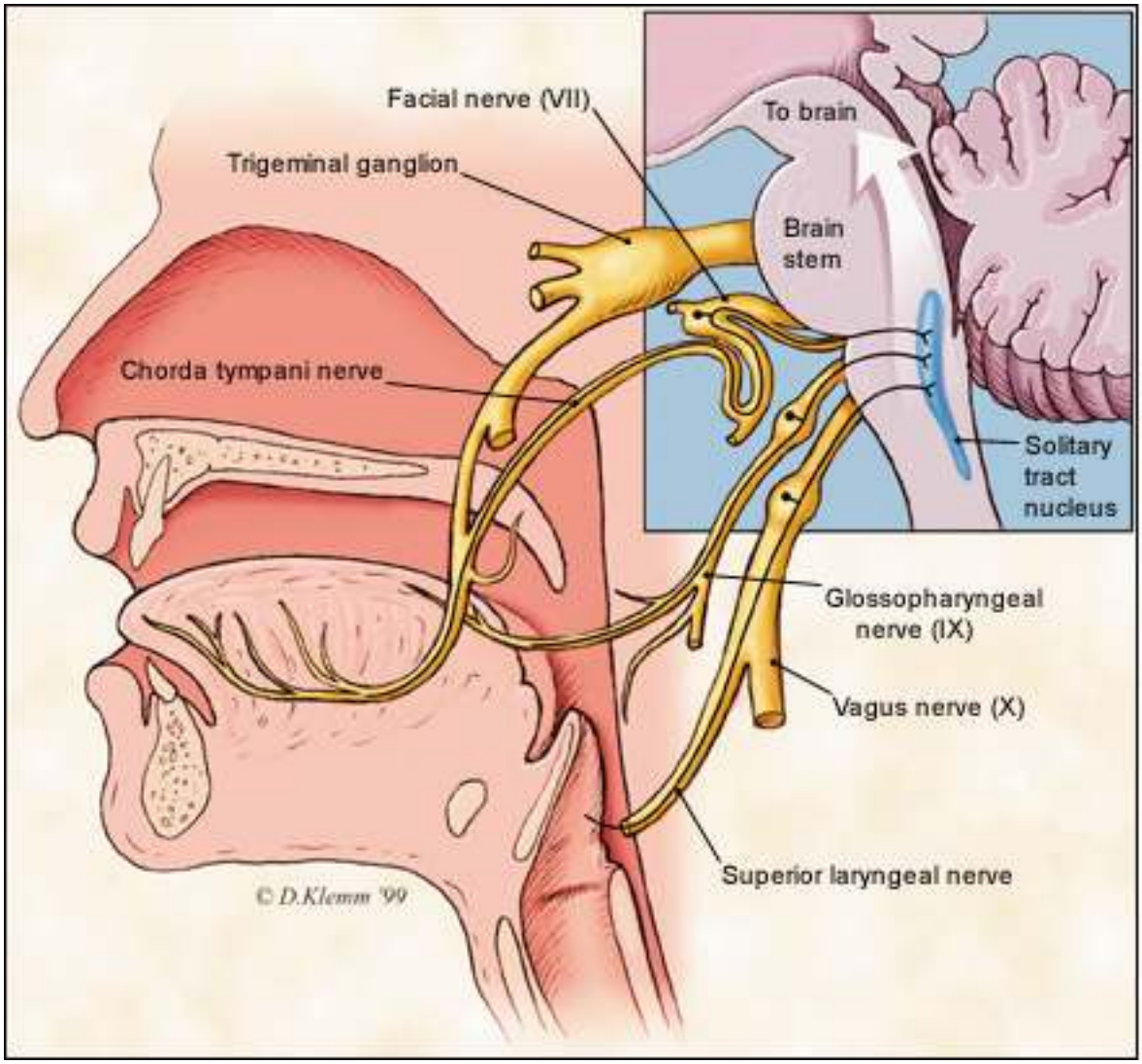


The vehicle for the taste is the saliva (Schiffman 1994). *Tastants* or food chemicals, dissolved in it, contact the receptors via the pore, activating the chemical, G-proteins (Gustducin and transducin) receptors (ion channels); which transform in to electrical impulses sent then to the brain.

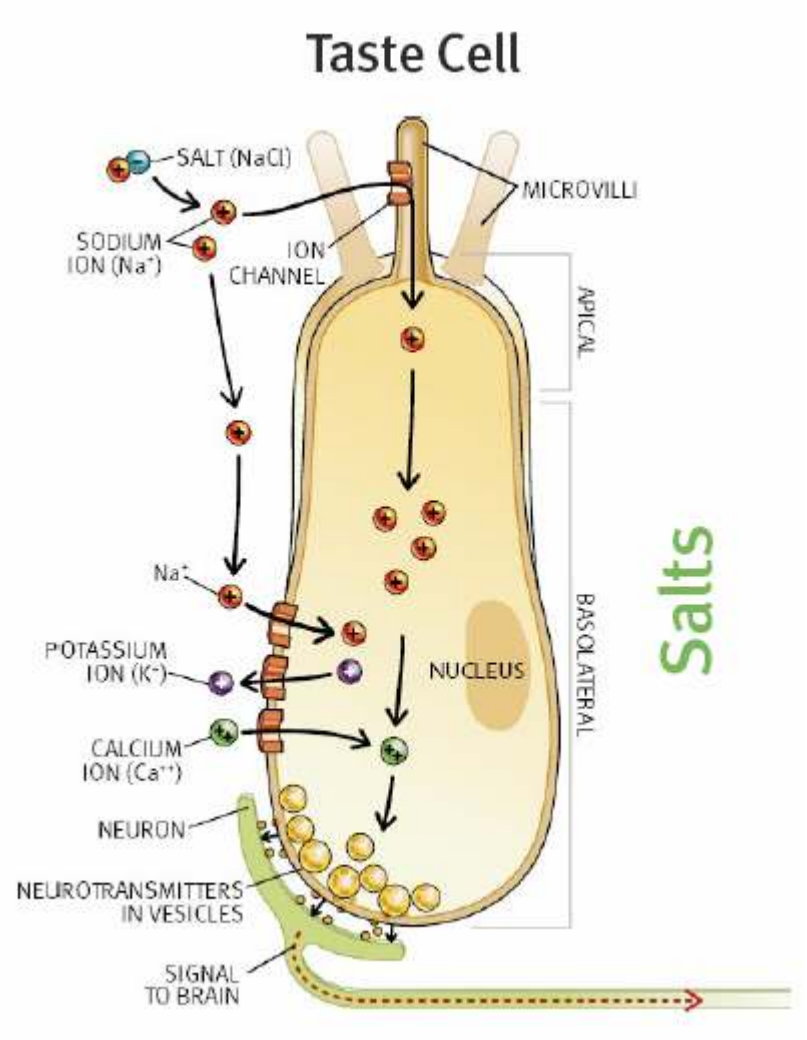


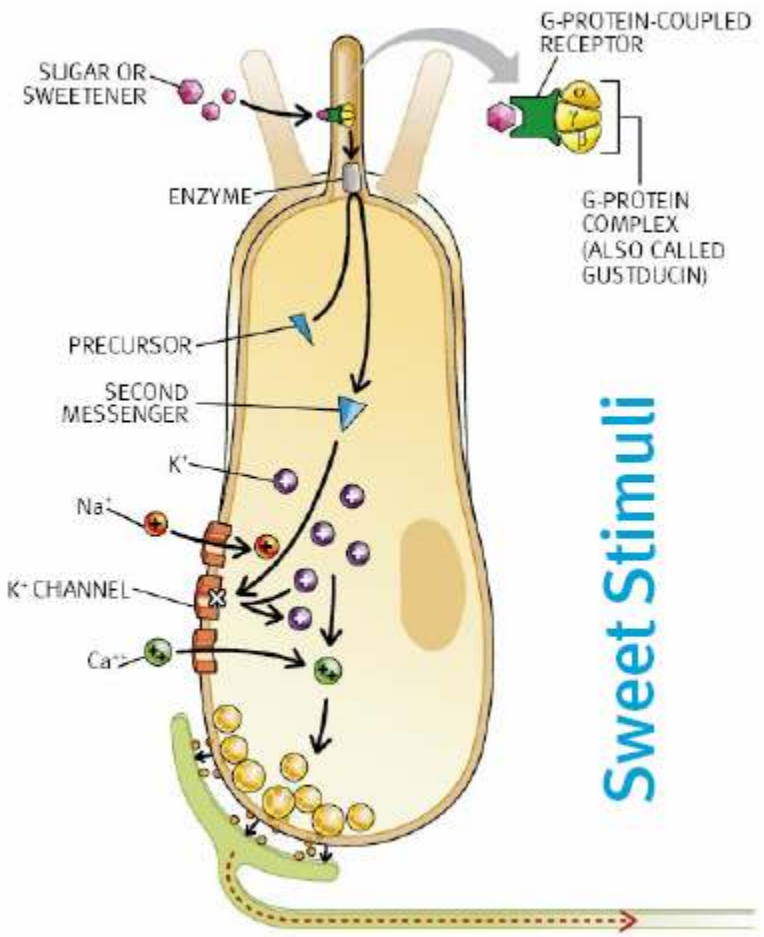
The receptors activated by the process of depolarization. The inside and outside of the cells are in constant electrical balance. In the case of taste receptors, they are charge negatively inside.

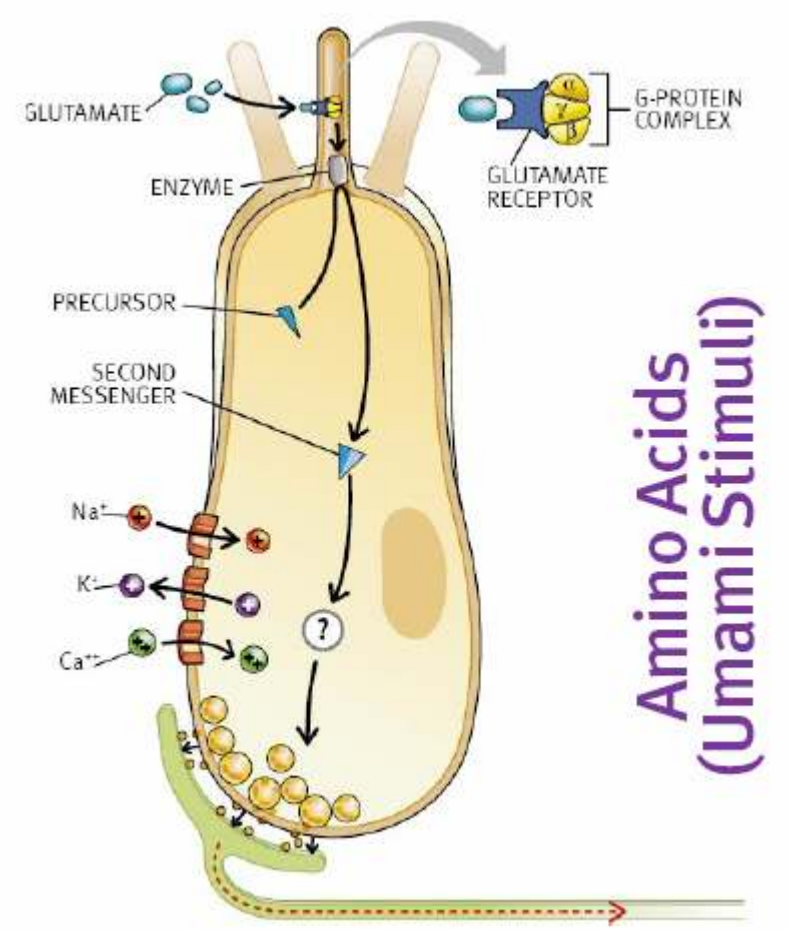
The contact with the stimulating agent tends to neutralize or turn the inside positively, creating a cascade of electrical current, which gets passed through the nerve line, at the end of which realizes a chemical neurotransmitter to communicate in rely to the next nerve cell until arrives to its destination in the brain. The final receptor, thought to be the parietal operculum, near the Rolando's fissure, now believed to be mostly located in the insula (This 2005).the likelihood is that there is not a single taste brain center but likely the electrical interaction of many areas allowing the brain to construct a global sensation.



The diagram bellow schematically represented for the plain Ionic, glutamine mediated and Umami mediated cellular activation:




G-PROTEIN-COUPLED
RECEPTOR
SUGAR OR
SWEETENER
ENZYME
G-PROTEIN
COMPLEX
(ALSO CALLED
GUSTDUCIN)
PRECURSOR
SECOND
MESSENGER
K+
Na+
K+ CHANNEL
Ca++
Sweet Stimuli



As the receptor, nerve line, rely points and end stations are electrically activated they become unable to respond to another stimuli (taste) until delivery of they become depolarized again. *Refractile or recovery phase*.

The impulses from the taste are then transmitted to the cerebrum via cranial nerves V, VII, IX, and X.(Bender 1999)

Chorda tympani (CT)is the primary inervation for the anterior tongue receptors in addition to provide the taste receptors structural and functional fitness(McCluskey 2002).

Surgical alteration of the tongue leads to loss of sweet and salty receptors. Surgery of the palate can alter sour and bitter receptors. (Grant 2000)

Taste and smell behavior:

Most flavor preferences and aversions are learned. There is an innate liking to sweetness (perhaps associated with common eating of fruits) and disliking to bitterness (most associated with poisonous and bitter alkaloids).

Social customs, opportunities and private associations with pleasant and painful moments. Imprint since early childhood.

Experimentally exemplified in well known studies such in the case of Pavlov and his experiences with dogs. Or repeated report of "craving" food, rich on given needed fundamental electrolytes or nutritional items. Ex. Water and salt in dehydration or water and carbohydrates in cases of Diabetes Mellitus. Pregnancy.

Preabsorptive Satiety refers to the point in time when sense of fulfillment of eating arises. Several mechanisms are believed associated with since the actual biochemical satisfactions of need cannot be corroborated. So pressure receptors in the wall of the stomach, chemical receptors in the wall of the intestine or downgraded affinity of the tasting receptors via blood glucose has been sited. (This could be nonetheless overridden by cultural pressures (obesity in USA)

Unclear why someone becomes full after a meal or why a given desired food intake becomes sickening in excess.

Pathophysiology

The life span of a taste cell is approximately 10 days. Because of this rapid proliferation they become highly susceptible to cellular destruction during chemotherapy (Strohl 1984)

In cancer patients in general there is a higher taste threshold as a result of a decrease in the number of taste buds.(Stubbs 1989)

Cytokines are proteins, manufactured by the body; they influence the cellular behavior by inducing specific cellular functions. Cancer up drive the production of them (Interleukins tumor necrosis factor). Known for lowering the threshold for bitter sensations. (Davidson 1998)

Radiation therapy to the head and neck area is known to cause alteration of taste: initial at 20Gy. 50% at 30Gy and permanent at 60Gy (Madeya 1996)

Radiation directly reduces the number of taste buds as well as damaging the microvilli of the cells. Initially impairing the bitter and salty sensations and later toi lesser degree the sweet taste.(Mossman K. 1978)

Chemotherapy on the other hand lowers the threshold for bitter tastes and increases it for the sweet taste (Madeya 1996), many patients complain about metallic taste. Main offending agents as Nitrogen Mustard, Cisplatin, Cyclophosphamide, Doxorubicin.

Repeated adverse reaction to chemotherapy has been known developed in to a behavioral adverse reaction by patient, by Pavlov's mechanism. (Bender 1999)

Does it make any difference?

Beyond the issue of pure quality of life and the enjoyment of eating, would nutrition make any difference? For most anyone, including medical or neophytes; the concept is yes. However the concept seen to be left to a second or third tier.

The fundamental are misunderstood in importance. The Positron Emitting Tomography (PET scan), the up-to-date technological tool in oncology; precisely depends on the cellular utilization of glucose by cancer cell.

Medicines:

Medication alter taste (Ackerman 1997)

Angiotensin-converting enzyme inhibitors (captopril) are among the medications most commonly associated with taste disturbances.(Ackerman 1997)

Stimulants:

In 1998 a double blind, random study, small sample, showed that administration of zinc sulfate three to four times per day restore not only the acuity of taste, slowed the worsening of taste alterations and taste bud anatomy. (Ripamonti 1998).

Monosodium Glutamate, commonly used in oriental food is becoming a good candidate as “flavor enhancer”; not only because its salty taste but stimulates Umami, the latest recognized taste, triggering release of glucagons and insulin. (This 2005)

Food chemistry

What normal people like

Taste of fat/concept of marveling
Taste of sugar/concept of caramelizing

Recommendations:

Because of the described metallic taste: use plastic utensils.(Stubbs 1989)

Patients should eat small and frequent meals through the day (Sherry 2002)

Chilled or frozen food more acceptable than warm food (brodie 1998)

Mouth care of crucial importance (Sherry 2002)

Provide rapid shifting tastes.
By enhancing receptors activities i.e. Pepper.
Cleansing of receptors
(Ginger/pickles)
Use of sauces of the nature of coulis (fruit based sauce with no fat)

I strongly advice the use of alcoholic beverages as a appetite stimulant

There will be a section on beverage added

The goals of this manuscript are to:

Review the most recent available literature with reference to

Physiology of taste

Smell

Hunger

Appetite

Pathology of the same

Brain storming into potential helpful hints to improve them

Cooking hints.

Disclaimer:

This paper is to the least pretend to be a scientific presentation; in as much a compilation of information and ideas; in the attempt to improve quality and perhaps quantity of the lives of patients afflicted by cancer.

Hope to provide a simple, superlative, and high quality to patients afflicted with cancer and the treatment consequences.

Acknowledgement:

To God and to those patients to whom this manuscript is dedicated and intended.

Recommendations:

- Drink a glass of alcohol before main meal. Red wine recommended.
- Food presentation should be simple, small and colorful
- Portions should be small

Bibliography

Ackerman, B., &Kasbekar, N., (1997). "Disturbances of taste and smell induced by drugs." Pharmacotherapy **17**: 482-496.

Bender, C. (1999). Taste Alteration. Nursingmanagement of symptoms associated with chemotherapy. J. Yasko. Bala Cynwyd, PA, Meniscus Healthg Care Communicatios.**:** 55-63.

Brillat-Savarin, J.-A. (1994). The Physiology of Taste. Harmondsworth, Middlesex, England, Penguin Books.

brodie, K. (1998). Taste alterations. Clinical guidelines for symptom management in oncology. F. P. R. Cunningham. New York, Clinical insights Press**:** 73-77.

Davidson, H., Pattison, R., & Richardson, R. (1998). "Clinical undermutrition sates and their influence on taste." Prosceeding of the nutrition Society **57**: 20-30.

Doty RL. Bromley SM, M. P., Hummel T. (1997). Laterality in human nasal chemoreception. Cerebral asymetries in sensory and perceptual processing. C. S. New York, Elsevier**:** 497-542.

Grant, M., & Kravits, K., (2000). "Symptoms and their impact on nutrition." Seminars in Oncology Nursing **16**: 113-121.

Madeya, M. (1996). "Oral complications from cancer therap." Oncology Nursing Forum **23**(part 1): 801-807.

McCluskey, L. H., David (2002). Sensitive periods for the effect of dietary sodium restrictiion on intact and denervated taste receptor cells, American Physiological Society. **2004**.

McGee, H. (1984). On Food and Cooking The Science and Lore of the Kitchen. New York, SCRIBNER.

Mossman K., H., R. (1978). "Radiation-induced changes in the taste acuity in cancer patients." International Journal of RadiationOncology **4**: 66-670.

Ripamonti, C., Zecca, E., Brunelli, C., Fulfaro. F., Villa, S., Balzarini, A., et al. (1998). "A randomized, controlled clinical trial to evaluate the effects of Zinc sulfate on cancer patients with taste alterations cause by head and neck irradiation." Cancer **82**: 1938-1945.

Schiffman, S. (1994). "Changes in taste and smell:drug interactions and food preferences." Nutritiion Reviews **52 (8, Pt.2)**: s11-s14.

Sherry, V. W. (2002). Taste Alteration Among Patients With Cancer.

Smith, D. a. M., R. (2001). "Making Sense of Taste." Scientific American: 32-39.

Strohl, R. (1984). "Understanding taste changes." Oncology Nursing forum **85**(3): 81-84.

Stubbs, L. (1989). "Taste changes in cancer patients." Nursing Times **83**(3): 49-50.

Stubbs, L. (1989). "Taste changes in cancer patients." Nursing Times **85**(3): 49-50.

This Herve' (2005) "Molecular Gastronomy" Columbia University Press.

Wickham, R. S. R., M., Kefer, C., Shott, S., Abbas, K., Glynn-Tucker, E., et al. (1999). "Taste changes experienced by patients receiving chemotherapy." Oncology Nursing forum **26**: 697-705.

Bibliography on pepper:

Christopher, John R. *Capsicum*, Springville, Utah: Powder River Press, 1980.

Graham, D., et al. "Spicy Food and the Stomach: Evaluation by Videoendoscopy." Digestive Disease Section. Veterans Administration Medical Center and the Baylor College of Medicine, Houston. *Journal of the American Medical Association*. 1988; 260:3473-3475.

Kawada et al. "Effects of Capsaicin on Lipid Metabolism in Rats Fed High Fat Diet," *American Institute of Nutrition*, 1986; 1272-1278.

Lacroix, J.S., et al. "Improvement of Symptoms of Non-Allergic Chronic Rhinitis by Local Treatment with Capsaicin." Clinic of Otorhinolaryngology, University Cantonal Hospital, Geneva, Switzerland. *Clin. Exp. Allergy*. September 1991, 21(5); 595- 600.

Mahindru, S.N. *Spices in Indian Life*, New Delhi: Sultan Chand & Sons, 1982.

Matucci-Cerinic, M., et al. "Effects of Capsaicin on the Metabolism of Rheumatoid Arthritis Synoviocytes in Vitro." Comment in: *Ann. Rheum. Dis.* 49(8):653, August, 1990. Institute for Clinical Medicine IV, University of Florence, Italy.

Mowrey, Daniel B. *Proven Herbal Blends*. New Canaan, CT: Keats Publishing, Inc, 1986.

Sicuteri, F., et al. "Substance P Theory: A Unique Focus on the Painful and Painless Phenomena of Cluster Headache," *Headache,* Jan. 1990; 30(2):69-79.

Takeuchi, K., et al. "Gastric Motility Changes in Capsaicin- induced Cytoprotection in the Rat." Kyoto Pharmaceutical University, *Jpn. J. Pharmacol.* 1991; 55:147-155.

Visudhiphan, S. et al. "The Relationship Between High Fibrinolytic Activity and Daily Capsicum Ingestion in Thais." Hematology Division. Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 7, Thailand. *The American Journal of Clinical Nutrition 35*,: June 1982, 1452-1458.

Herbal Research Foundation, Boulder, Colo., 1-800-748-2617.

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