# Taste Disturbance Because Of Drug Therapy Or Systemic Diseases

A Al-Shehri

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#### **Abstract**

Disturbance of taste does not often appear in dayly practice [9] and mostly is an transient disorder within cold diseases. Permanent loss or disturbance of taste, however, is followed by a fatal impairment of quality of life, as eating and drinking practice changes thoroughly. The patient is no longer able to realize aromatics and cannot recognize inedible or spoiled food. Besides of local processes and disturbances of cerebral nerves specific symptoms of taste disorders can be guiding to a systemic disease or to side effects of drug therapy in the treatment of systemic diseases.

#### INTRODUCTION

In the diagnostic of dysgeusia we have to distinguish between

- quantitative dysgeusia: ageusia (total loss of taste) of hypogeusia (attenuation of taste) for some or all aromatics or taste qualities
- qualitative dysgeusia als false interpretation of the applied aromatics (parageusia).

Within diagnostic measures the patient's history often leads to correct diagnosis. The posed questions concerne diseases of the nose and the nasal sinus, recent virus infections, allergies, contaminant load within the area of the place of employment (e.g. vapor), intake of drugs etc (s. Tab. 1).

#### Figure 1

Table 1: Differential diagnosis of taste disturbances

#### Actual complaints:

- Which taste qualities do you no longer realize?
- Is there any taste, that you always realize?
- Are there any kinds of smell that cause a special sense of taste?
- Do you have an disturbance of smelling? What can you smell?
- Do you prefer some food, and is there any food that is very unpleasant?

## History:

- Rhinitis, sinusitis, cold, diseases of the lung and the lower airways
- Allergy
- Surgery of the nose, the nasal sinus, the head, larynx, pharynx
- Injury of the head
- Smoking and abuse of alcohol
- Treatment of the teeth
- Diseases of the stomach, water brash, diabetes and other metabolic diseases, climacterium, neurologic diseases
- Contaminant load within the employment area, e.g. vapor, gas, adhesives, mould fungus etc.
   drug intake, esp. antihypertonics, drugs that cause increased blood flow, digretics, antihipotics
- therapeutical solutions for local application on the oral mucosa, antidiabetics, antidepressives
- Radiation therapy, chemotherapy

Many people cannot distinguish between disturbances of taste or smelling, they actually realize, that they cannot taste anymore [3]. So the physician should give the patient an example, how to distinguish the two senses: e.g. in coffee the bitters can be tasted, but the aromatics can be smelled, and both of them lead to the specific stimulant. With questions for the realization of intensive odours as e.g. garlic, perfumed soap and cooking odours the physician can find out, whether the patient cannot smell anything of if smelling only is reduced.

Standardised measures to proove the sense of smell and taste are still not available. There are several test-sets, which still are very expensive and take a large expenditure of time  $[_{10}]$ . (The basic equipment of Cobal costs about 180 DM with a durability of one year.)

Gustometry is done by application of supraliminal solutions of salt, sugar, citric acid and chinin sulfate via spray, drops, paper sheets of capsula, being applied globally or on one side each. The application form of gustometry, however, is not yet standardized [10]. Electrogustometry is done in cases of expert appraisement.

#### **SYMPTOMS**

Xerostomia alone can lead to taste disturbances. First of all xerostomia is an effect of aging with anatomical changes of the skin and mucosa and the additional effect of changes of drinking habitation (dehydratation). But there are a lot of drugs (antipsychotic drugs, atropine, acid blocking agents, antihistaminic drugs, codeine, false dosage of diuretics) or systemic diseases, such as diabetes or kidney insufficiency, that often appear in the elderly and cause xerostomia as well. In some cases there is a deficiency of estrogene (climacterium), anemia, rheumatic diseases, radiation sialadenosis or sicca syndrome.

Putride taste as a subjective form of paresthesia is caused by putride infections of the nose, the nasal sinus, teeth, phayrynx or larynx as well as by putride bronchitis, pneumonia or pulmonary gangrene.

A bitter or biliary taste occurs in cases of affection of the liver or the gallbladder. Locally there is a yellow smear on the surface of the tongue. Foetor hepaticus guides to a liver cirrhosis. A bitter taste is also a side effect of treatment with nitroimidazolen, e.g. Clont®.

Glossodynia often is a symptom besides of taste disturbances and a typical side effect of the treatment with beta blocker.

In many cases fur of the tongue is not realized by the patient itself. In some cases, however, the fur causes glossodynia as well as taste disturbance. Mostly they lead to a systemic disease (s. Tab. 2). Smokers have a brown fur, and after they withdrew smoking they are aware of a better and more specific sense of taste. Well known are the symptoms of oral candidiasis, that in small children may lead to disturbances of drinking and eating, or that occur as a side effect of antibiotic or cytostatic therapy.

#### Figure 2

Table 2: Fur of the tongue that lead to a systemic disease

thick white fur	<ul> <li>disease of the digestive canal</li> </ul>
	<ul> <li>anemia</li> </ul>
yellow fur	<ul> <li>disease of the gallbladder</li> </ul>
	<ul> <li>disease of the pancreas</li> </ul>
grey smear fur of the tongue, the adenoids and	agranulocytosis
the palate	<ul> <li>Angina Plaut-Vincent</li> </ul>
white fur	· cold, infection of the upper and lowe.
	airways

#### LOCAL SYMPTOMS OF THE HEAD

As smell is involved in all sensations of taste, diseases of the mouth as well as diseases that cause disturbance of smelling can lead to taste differences. In most cases there are viral and bacterial infections with rhinitis, sinusitis, pharyngitis, stomatitis.

In case of loss of a single taste quality the identification of the injured cerebral nerve is possible because of the topography of the single taste bud and its nerval supply .Other symptoms of the oral cavity lead to systemic diseases, that may cause an affection of the cerebral nerve.

Central and peripheral disturbances of the n. trigeminus (n. mandibularis) after cerebral injury, esp. of the skull base of the ethmoidal labyrinth, of the n. olfactius or bulbus, as well as tumors of the anterior calvaria (e.g. olfactorius menigeoma), peripheral facial lesions within the pars mastoidea can also cause taste disturbances.

Paroxysmal abnormal sensations of taste or smell after head injury can be a symptom of temporal lobe epilepsia.

Taste disturbances can be found in case of many cerebral processes as e.g. meningitis, encephalitis, injury of the medulla oblongata of the thalamus as well as lesions of the cerebral cortex.

# SYSTEMIC DISEASES CAUSING TASTE DISTURBANCES

Diabetes mellitus: In cases of diabetes mellitus there often occurs an idiopathic paresis of the facialis nerve with disturbance of taste in the ventral two thirds of the tongue. A peripheral lesion of the n. mandibularis (V3) occurs in case of diabetic polyneuropathy. Other symptoms of the oral cavity may be glossodynia, xerostomia. There was an electrogustometric proof of an increased taste threshold in juvenile diabetics [7].

Hypertension: Although hypertension itself is not associated with taste disturbances, there are many drugs in the treatment of hypertension that induce this side effect, esp.

ACE-inhibitors. Many diuretics cause xerostomia.

Gastroesophageal refluxe: The reflux disease can cause an affection of the pharynx, larynx and posterior tongue even without symptoms of water brash. Halitosis and a white fur can lead to the correct diagnosis as in case of a 46 year old patient that complained of a broad loss of taste lasting for more than three months and told of recession of the symptoms after treatment with a proton pump inhibitor for about four weeks.

Kidney diseases: Patients with hemolysis in the end stage of renal failure showed changes of the oral cavity with xerostomia, fur and taste disturbance [4].

Multiple sclerosis is accompanied by peripheral and central affections of the n. mandibularis and n. intermedius, that lead to taste disturbance  $\lceil^2\rceil$ .

Zoster oticus: In this case an affection of the ganglion geniculi of the n. intermedius can be found. If the facialis nerve is involved, facial paresis, hyperacusis and taste disturbances are pussible, as the n. intermedius approaches with secretomotoric fibers für the sublingual and submandibular glands as well as with taste fibers for the ventral two thirds of the tongue, before he leaves the brain stem [²].

Sick Building Syndrom: The SBS describes a sum of unspecific irritative symptoms people suffer from in the internal part of buildings. Most of these symptoms vanish when they leave the building. Following the NIOSH-Study [8] the most causative agents are: false function of the airconditioning, smoking, detergents, adhesives, building materials furniture, bacteria, fungus, outdoor air conditions as well as false building ventilation without efficient vaporaization of adhesives and other solutions fungal invasion of the building. Even psychological components such as bad working conditions may lead to SBS. Symptoms are tiredness, weakness of concentration, affection of the skin and mucosa as wel as unspecific allergic reactions with rhinitis, irritation of the eye, asthmatic complaints without diagnosis of asthma and disturbance of taste and smell.

#### Figure 3

Table 3: Causative agents of taste disturbances

Causative agents of the head	systemic causative agents
diseases of the  o nose o nasal sinus o oral cavity diseases of the o n. trigeminus o n. ofactorius o bulbus olfactorius tumors of the anterior cranial cavity peripheral facial lesions within the pars mastoidea injury of the o skull base o ethmoidal labyrinth meningitis encephalitis injury of the medulla oblongata injury of the thalamus lesions of the cerebral cortex temporal lobe epilepsia after head injury	diabetes mellitus hypertension (drug side effect) gastroesophageal reflux disease multiple sclerosis deficiency of vitamin-B or zinc zoster oticus neuroborreliosis [2] Sick-Building-Syndrom hypothyreosis adrenocortical insufficiency Sjögren syndrome [6] Morbus Boeck [4] collagen diseases [4] inflammatory diseases mit affection of the central nerve system, e.g. lues, syringobulbia, amyloidosis, sarkoidosis (Heerfordt syndrome) polyneuritis cranialis pseudohyp oparathyreoidism, Ulrich-Turner syndrome, familiar dysautonomia [7] Melkersson-Rosenthal syndrome [2]

Drug induced taste disturbance: There are many drugs that can induce a mainly reversible disturbance of taste (s. Tab. 4a, 4b).

#### Figure 4

Table 4a: Drugs that can cause a change of taste (after: [2] and own researches]

Antibiotics	<ul> <li>tetrazycline (systemic use, very seldom so- called black hairy tongue)</li> </ul>
	<ul> <li>chloramphenicol</li> </ul>
	<ul> <li>trimethoprim (abnormal taste, gingivitis, glossitis)</li> </ul>
Antidiabetics	biguanide
Antidiarrheals	loperamid (seldom)
Antiepileptic drugs	carbamazepine
	<ul> <li>phenytoin (xerostomia, gingiva hyperplasia)</li> </ul>
Antihypertensive drugs	ACE-inhibitors, e.g.
	<ul> <li>captopril (glossitis, xerostomia)</li> </ul>
	<ul> <li>enalapril</li> </ul>
	<ul> <li>nifedipin</li> </ul>
Antiphlogistics	acetylsalicyl acid
	<ul> <li>phenylbutazone</li> </ul>
Antirheumatics	gold (stomatitis)
	<ul> <li>NSAIS, e.g. phenylbutazone (stomatitis,</li> </ul>
	siala denitis - seldom)
	<ul> <li>penicillamin (lesions of the mucosa)</li> </ul>
Chemotherapeutic agents	<ul> <li>nitroimidazole, e.g. metronidazol (Clont®- bitter taste)</li> </ul>
	<ul> <li>pyrimethamin (Daraprim® - treatment of toxonlasmoss: stomatitis)</li> </ul>

#### Figure 5

Dermatic agents	retinoids, e.g. Roaccutan® (cheilitis, xerostomia)
Agents against gout	allopurinol (intoxication)
Immunotherapeutic agents	literferone (stomatitis)
Antilipemic agents	dextrothyroxin
Mukolytic agents	acetylcystein (stomatitis, seldom)
Agents for local treatment of the mouth	e.g. chlorhexidin
Nootropics	pyritinol
Psychoanaleptic agents	e.g. AN1®, Captagon®, Ritalin® (unpleasant taste, stomatitis, xerostomia)
Psychopharmaceuticals	L-dopa     lithium
Sympathomimetics	e.g. • ephedrin • epinephrin (chronic nasal obstruction)
Thyreostatics	thiamazol, Carbimazol, Thiouracil (dysgeusia, ageusie – very seldom)
Tuberkulostatics	Protionamid (ektebin® - metallic taste)
Cystostatic agents	e.g.  • Methothrexat/ Vincristin/ Cyclophos- phamid/ Vinblastin (stomatitis)  • Cisplatin (stomatitis, neurotoxic agent)

**Figure 6**Table 4b: Drugs that cause xerostomia

Alpha-Sympathomimetics	Methyldopa
Analgetics, central	e.g. Codein, Dihydrocodein, Hydrocodon, Morphin, Pethidin, Fentanyl, Pentazozin, Levomethadon, Tramadol, Tilidin, Naloxon
Antiarrhythmics	Mexiletin, Ipratropiumbromid, Dilsopyramid
Antibiotics	Penicilline
Anticholinergic agents	Atropine (side effect even in local application), N-butylscopolamin, Scopolamin, Pirenzepin
Antiepileptic agents	Phenytoin
Antihistaminic drugs	e.g. Astemizol
Antihypertensive agents	Beta blocker, ACE-inhibitors (e.g. Captopril), Guanethidin, Clonidin, Alpha-1-blocker, Re- serpin
Antitussive agents	Hydrocodon
Diuretics	loop diuretics, Thiazid derivates, Triamteren, Xipamid
Acidity blockers	<u> </u>
Muscle relaxant	Baclofen
Psychopharmaceuticals	Benzodiazepine, Imipramin, Lithium salt, neuroleptics (derivates of Phenothiazin, Thioxanthen, Azaphenothiazin, Butyrophenon), Doxepin, tri- and tetracyclic antidepressive drugs
Vasodilatators	Cinnarizin

Intoxications: Intoxication with trichlorethylen, stilbamidin, allopurinol can cause a peripheral leasion of the n. mandibularis (V3). Carbon monoxide poisoning can be followed by central dysgeusia [<sup>3</sup>].

#### **CONCLUSIONS**

Physiological changes of taste caused by hormonal changes and aging appear very often. Even isolated ageusia concerning one single substance, e.g. in bakers, cooks and perfume producers, are quite common [<sup>3</sup>].

In about 70 % [², ³] pathologic disturbances of taste are caused by diseases of the smelling system. Therefore differential diagnosis should always include the olfactorial parameters to delimit a pure taste disturbance from nasal diseases. These patients must be instructed about the causality of their supposed taste disturbance, as they often do not understand the causal relationship.

As the taste disturbance is not a monocausal disease, there is no causal therapy. First of all causal agents have to be eliminated resp. treated. These measures include the reduction of drug side effects, the improvement of antidiabetic treatment and elimination of noxious agents. Some authors demand for substition of high dosages of vitamine B and A or zinc [³] if deficiency is proved, wereas the prove of these substances is not part of the routine diagnostics. In the treatment of diseases, which are associated with these deficiencies, as e.g. chronic liver diseases or alcohol abuse, the authors require a substition of vitamine B and zinc even without the expensive diagnostic of trace materials.

In the treatment of ageusia substituion of zinc is successful even in those cases, in which deficiency of zinc was not proved. Some authors think the concentration of zinc in the reserve proteins having direct influence on the sensitivity of the taste buds, as in patients with hypogeusia a deficiency of zinc in the reserve proteins could be proved. Latent intracellular zinc deficiency in the oral mucosa may be compensated by high dosages of zinc [1, 2, 3].

In most cases there is a passagere manifestation of taste disturbance, that disappear with the healing of the systemic disease or that in cases of central disturbances of the nerval system can be compensated (by learning effects?)

However, a permanent manifestation of taste disturbance is a fatal disorder, as it has a severe influence on eating and drinking conditions, changing the quality and amount of food intake as well. There are only few possibilities to compensate this loss. Especially in elderly or lonesome patients, who are not able to look after themselves sufficiently, the combination of inappetence and loss of taste may lead to severe nutrition disorder. In these cases the exact differential diagnosis of the remaining and disturbed taste is essential, as to offer the patient a diet that may compensate nutrition deficiencies in consideration of the remaining taste qualities. For these patients, an individual nutrition plan must be developped with the help of a qualified diatician, including the patient's preferred food and the remaining taste qualities as well, securing a balanced alimentation.

### **CORRESPONDENCE TO**

Dr. A. Wegener, Buschweg 39a, D-53229 Bonn, Germany e-mail: angelica.wegener@gmx.net

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# **Author Information**

Ali Maeed Al-Shehri, PhD.

Consultant Doctor of E.N.T. Department, College of Medicine and Medical Science, King Khalid University